

# **The effect of noise exposure on vestibular function**

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## Abstract

Damage to the auditory mechanism in the inner ear due to noise is well established. However, exactly how noise affects the human vestibular system is still unclear. Therefore, this thesis examines the effect of noise exposure on the human vestibular system, particularly saccular function. This was achieved by proposing several hypotheses, tested via a series of studies and described in separate chapters. The literature suggests that the saccule is the potential site of noise damage in the vestibular system. To date, the only available clinical tool to evaluate the saccule is cervical vestibular evoked myogenic potential (cVEMP). Although cVEMP data have been widely published, cVEMP methodology is still being explored. First of all, cVEMP optimal methodology using head rotation-sitting (HR-S) as a sternocleidomastoid (SCM) muscle activation procedure was established before going on to investigate the effect of noise exposure on vestibular function.

The optimal cVEMP protocol (HR-S as a muscle activation procedure, blood pressure manometer as a biofeedback method and amplitude normalization as a data analysis technique), pure tone audiometry and distortion product otoacoustic emissions (DPOAE) were used to investigate the effects of noise exposure on the audio-saccular function of adults working in potentially noisy environments. The lifetime cumulative noise exposure levels for participants were estimated based on their self-reported noise exposure data. Overall thesis findings support the existence of cochlear and saccular dysfunction in noise-exposed workers with and without hearing loss. Results indicate that noise exposure may alter saccular function and result in symptoms before noise-induced cochlear damage is detected by routine clinical testing. Findings suggest that combining cVEMP findings with self-reported data along with findings obtained from other noise sensitive diagnostic procedures like DPOAE may help to identify people at risk of developing noise-induced saccular dysfunction.

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## **Chapter 1**

### **General introduction and overall review of literature**

## 1.1 Introduction

Damage to the auditory mechanism in the inner ear due to noise is well established and extensively investigated. The most important auditory effect of noise exposure is noise-induced hearing loss (NIHL). NIHL has been investigated by numerous studies in the literature (Sliwinska-Kowalska and Davis, 2012; Hong et al., 2013). However, vestibular damage and vestibular symptoms associated with noise exposure have received less attention. Likewise, data on the nature and characteristics of self-reported vestibular symptoms from noise-exposed individuals are limited. Although the literature suggests that the saccule is the potential site of damage in the vestibular system as a result of noise exposure, only a few studies have investigated the effect of noise on saccular function. Hence, the current thesis aims to investigate the effect of noise exposure on the human vestibular system, mainly saccular function, using a physiologic response: cervical vestibular evoked myogenic potential (cVEMP).

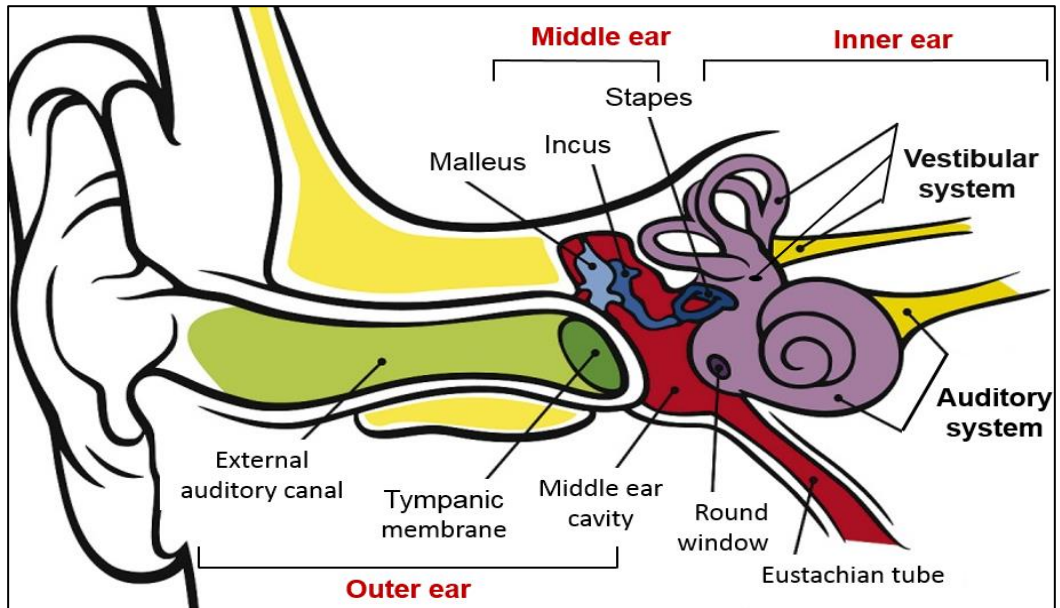
The second chapter determines the optimal methodology to control muscle contraction variability during cVEMPs recording among normal adults. In Chapters 3 and 4, the possibility of saccular damage measured by cVEMP and associated vestibular symptoms are investigated among noise exposed workers with and without hearing loss. The present chapter reviews the current evidence of the effect of noise exposure on the inner ear with a focus on the peripheral vestibular system. This chapter also reviews the VEMP, as it is the main diagnostic tool applied throughout the thesis. The present chapter concludes by identifying the research question of this thesis and the hypotheses designed to address this question. The hypotheses are addressed via a series of three experimental works described in separate chapters. Prior to describing the effects of noise exposure on inner ear function, it is first necessary to briefly review the anatomy and physiology of the peripheral audio-vestibular system.

## 1.2 Anatomy and physiology of the peripheral audio-vestibular system

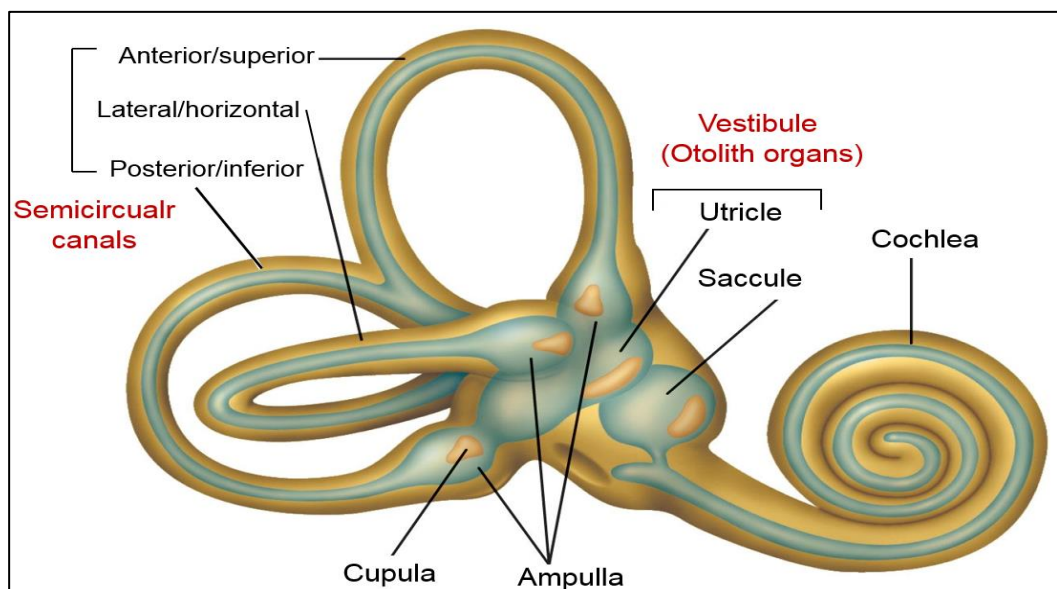
The inner ear is located within the temporal bone of the skull and forms the peripheral audio-vestibular system (Figure 1.1). It is made up of a series of tubes or channels filled with fluid. The channels are formed by bones and known as the *bony labyrinth* and filled with a fluid called the *perilymph*. The bony labyrinth consists of three parts a) the *cochlea* which forms the auditory part of the inner ear responsible for hearing b) three *semicircular canals* (horizontal/lateral, anterior/superior and posterior/inferior) and c) the *vestibule* which connects the cochlea with the semicircular canals. The three semicircular canals and the vestibule form the vestibular part of the inner ear. The bony labyrinth itself contains a set of cell membrane lined channels known as the *membranous labyrinth* filled with a fluid called the *endolymph*.

The membranous labyrinth contains the cochlear or auditory hair cells and the vestibular hair cells, which are the sensory receptors in the inner ear. Neurons of the vestibulocochlear nerve (VIII cranial nerve) innervate both cochlear and vestibular hair cells. Cochlear hair cells are tuned to respond to acoustic inputs between 20 and 20,000 Hz and have the greatest sensitivity to frequencies between 2000 to 5000 Hz (Gelfand, 2011). However, vestibular hair cells are tuned to respond to acoustic inputs at lower frequencies (< 3000 Hz) and have the greatest sensitivity to frequencies between 400 to 800 Hz (McCue and Guinan, 1997; Todd et al., 2000; Todd et al., 2009). Each semicircular canal is enlarged at one end to form the *ampulla*. Within each ampulla, there is a gelatinous structure called the *cupula*, which separates the canals from the vestibule. Positioned beneath the cupula is the *crista* that contains the sensory hair cells and the vestibular afferents. The vestibule comprises the *utricle* and the *sacculle*, collectively known as the *otolith organs*. Both the sacculle and the utricle are filled with endolymph and each has a sensory organ called the *macula*. It should be noted that the closest vestibular structure to the cochlea is the vestibule, particularly the sacculle (Figure 1.2).





**Figure 1.1.** A picture of the human ear (right ear) showing basic ear sections (outer ear, middle ear and inner ear). The inner ear is the end organ of the ear comprised of the peripheral auditory system and the peripheral vestibular system. This picture was modified and taken from Wikimedia Commons (<https://commons.wikimedia.org>).



**Figure 1.2.** A picture of the inner ear (right ear) showing the components of the vestibular system. The vestibular system contains three semicircular canals and the vestibule or the otolith organs (utricle and saccule). Note the close proximity of the saccule to the cochlea. This picture was modified and taken from Pearson Education Ltd.

### 1.3 Vestibular function and balance maintenance

Balance is defined as the ability to maintain the body's centre of gravity over the base of support. Human balance is a complex brain function established by receiving information from three linked peripheral sensory systems (the vestibular system, the visual system and the somatosensory system). Although the vestibular organs in the inner ear (the semicircular canals, utricle and saccule) contribute to balance control, the visual and the somatosensory systems play an important role. While the visual system provides information from the eyes about head orientation in relation to the surrounding environment/objects, the somatosensory system collects information from the skin, muscles and joints regarding the orientation of body parts relative to one another and to the support surface. The vestibular organs measure gravitational, linear and angular accelerations of the head in relation to the neck and space. In order to do so, they sense head motion and respond with compensatory reflexive eye movements that stabilizes images on the eyes during motion. To maintain clear vision and prevent us from falling, the vestibular organs use all these pieces of information to perform a number of vestibular reflexes. The vestibulo-ocular reflex (VOR) performs rapid compensatory eye movement that stabilizes images on the fovea of the retina during head movement. The vestibulo-spinal (lower and upper limb muscles) and vestibulo-colic (neck muscles) reflexes provide postural stability during standing, walking and running. All these reflexes along with the information combined from the somatosensory and visual systems interact to detect centre of gravity and maintain balance and body stability (Shchubert and Shepard, 2016).

Each vestibular organ responds to a particular head movement. Each semicircular canal detects angular/rotary motions in one plane. The otolith organs detect linear acceleration and decelerations. While the utricle detects linear horizontal motions, the saccule detects linear vertical (up/down) motions. When the right and the left vestibular systems in each inner ear are functioning properly, they send synchronized signals to the brain. The brain receives nerve impulses from both left and right peripheral vestibular systems, then it communicates with the visual system to enable clear vision during movement. The brain communicates as well with body muscles to coordinate

movement so balance is maintained during positions and movement changes. However, if the transmitted sensory signals are interrupted anywhere along the vestibular pathway by a disease, disorder or injury, vestibular dysfunction results and the patient is likely to experience balance disturbances.

#### **1.4 Vestibular pathology and symptoms**

Damage to the peripheral vestibular system can lead to abnormalities in both sensory and motor mechanisms leading to a variety of symptoms. Unlike the other sensory organs (i.e. auditory, visual), most individuals are not aware of the vestibular system during everyday activities. Not until the vestibular system starts to function abnormally, does the person recognize its importance. Loss of vestibular function from one or both vestibular organs can lead to a variety of symptoms ranging from a mild imbalance or unsteadiness to severe balance dysfunction leading to falling and causing serious injuries. Damage to the vestibular end organs is usually caused by loss or damage to the vestibular hair cells or the nerve fibres innervating them. In the case of a vestibular pathology, one or more of the vestibular reflexes are affected; vestibule-ocular, vestibule-spinal or vestibule-collic (Khan and Chang, 2013). Examples of common peripheral vestibular disorders are benign paroxysmal positional vertigo, vestibular neuritis, vestibular schwannoma, vestibular migraine, Meniere's disease and semicircular canal dehiscence (SCD). More information about these disorders can be found in Furman et al. (2010). Other causes which might also impair vestibular function, via an effect on vestibular hair cells and result in balance disturbances, are exposure to ototoxic agents (Black and Pesznecker, 1993; Tsuji et al., 2000) and high noise levels (Golz et al., 2001; Wang et al., 2006; Wang and Young, 2007; Wu and Young, 2009; Kumar et al., 2010; Akin et al., 2012; Tseng and Young, 2013). The effect of noise exposure on the vestibular system is discussed in detail later in this chapter (section 1.7.2).

Generally, the type and severity of vestibular symptoms vary considerably among patients. The most common vestibular symptom reported by patients affected by peripheral vestibular dysfunction is vertigo. Vertigo has been defined as a false sensation

of movement of the patient or the environment. Patients often describe vertigo as a spinning, whirling or rotary sensation. Vertigo often occurs in the absence of head movement. The most common source of damage associated with vertigo is unilateral semicircular canal damage. Such damage may cause a debilitating vertigo with other associated autonomic symptoms like nausea, vomiting, and tilting of the head or body to one side. Another sign occurring occasionally with vertigo is nystagmus which is an involuntary abnormal eye movement resulting from an imbalance in neural activity within either the peripheral vestibular system or central vestibular pathway. Some patients feel their nystagmus and report it as a feeling of their eyes flickering. More information about vestibular symptoms can be found in [Roland et al. \(2016\)](#).

Vestibular symptoms result from the information being mismatched between the three input sensory systems responsible for balance. Vestibular symptoms could also result from unilateral or asymmetrical lesion present anywhere along the vestibular system. Most otologic disorders typically affect only one labyrinth at a time. A common example of these disorders is acute unilateral horizontal semicircular canal lesions. Patients affected by unilateral vestibular lesions often report debilitating symptoms (e.g. vertigo) due to asymmetric signals being received by the brain simulating actual movement. However, many patients with such lesions report reduced or no symptoms overtime, which is likely due to functional recovery and vestibular compensation ([Barin, 2016](#)). Vestibular compensation happens as a result of the high degree of plasticity within the central vestibular pathways ([Curthoys and Halmagyi, 1995](#)). On the other hand, patients with bilateral or symmetrical vestibular lesions commonly seen secondary to ototoxicity (i.e. aminoglycoside toxicity) or excessive noise exposure, often do not experience troublesome symptoms due to the incoming signals being symmetrical ([Jen, 2009](#); [Kim et al., 2011](#)). Consequently, patients with bilateral or symmetrical vestibular lesions often report unsteadiness, imbalance, loss of visual acuity, blurred vision, disorientation in complex sensory environment and oscillopsia; a sensation of stationary objects moving, particularly during quick head movements (i.e. dynamic symptoms). Most of what has been reported so far about peripheral vestibular pathologies and their symptoms has been derived from studies conducted on semicircular canals lesions. Because of the great similarity in vestibular hair cell ultrastructure between the

semicircular canals and otolith organs, otolith lesions probably perform similarly to canal lesions in this respect. However, up to this date, this is an assumption and no systematic evidence has been shown yet on how otolith lesions might express themselves behaviourally.

There is a general consensus in the literature that the type of symptoms reported depends on which aspect of the vestibular system is affected. For example, semicircular canals are sensitive to angular acceleration explaining why patients with canal lesions often describe their symptoms as rotary or spinning “vertigo”. Otolith structures respond to linear and gravitational accelerations or decelerations. Hence, patients with otolith dysfunction often report symptoms which are predominantly linear in nature, such as feeling a sensation of rocking back and forth, tilting, walking on pillows, being pushed or pulled (Brandt, 2001; Basta et al., 2005c). However, there is a lack of data on the exact nature and characteristics of symptoms resulting from otolith dysfunction in general and the same is true for vestibular symptoms caused by noise-induced lesions. While it is important to understand the symptoms and the pathophysiological basis of vestibular pathologies, a thorough clinical examination is needed to provide accurate diagnosis. There is a wide range of available diagnostic tools to evaluate the integrity of the vestibular system. The following section briefly reviews how the vestibular system is evaluated in most clinical settings.

## **1.5 Vestibular assessment**

Different types of vestibular symptoms correlate with different sites of lesions. Thus, before vestibular testing commences, a thorough case history should be obtained from all patients. Generally, vestibular disturbances are commonly expressed by patients as *dizziness*. However, the word “*dizzy*” is vague and could mean anything from a slight feeling of imbalance to a severe unsteadiness that might cause falling. In order to select the appropriate assessment procedure for vestibular disorders, the health care provider should always work with patients to narrow down the subjective assessment process by encouraging patients to provide more specific descriptions of their vestibular disturbances. This should help to approach the gap between subjective and objective

vestibular findings often encountered in clinical settings. The case history for patients with vestibular pathologies should include a detailed neurologic history, past history of physical trauma or illness prior to symptoms, history of medications and an association of hearing loss or other auditory symptoms, such as aural fullness and tinnitus along with the onset of vestibular symptoms. It is also important to ask the patient to characterize symptoms by providing information about the duration, frequency and the trigger factors (e.g. specific head movements) of their dizziness episodes. Further details on the use of clinical case history to evaluate vestibular disorders can be found in [Baloh and Halmgyi \(1996\)](#). Objective vestibular evaluation can be divided into three main categories 1) tests of peripheral and central vestibulo-ocular pathway (ocular motor tests, caloric testing and rotational chair testing) 2) postural control assessment and 3) otolith function tests (utricle and saccule function tests). Ocular-motor tests and rotational chair testing uses videonystagmography to record patients' eye movements during different visual and vestibular stimulations. In ocular-motor testing, the visual and VOR pathway is evaluated. Depending on the type and direction of nystagmus observed, a lesion in the peripheral vestibular system or central pathway is inferred.

In caloric testing, the VOR is measured by a non-physiologic stimulation to one of the lateral/horizontal semicircular canals. Caloric testing is the only available test to evaluate horizontal semicircular canals one side at a time. However, it only provides information about the horizontal semicircular canals. In rotational chair testing, the patient is sitting in a chair that rotates sinusoidally at different velocities and eye movements are recorded. Although rotational chair testing evaluates the horizontal semicircular canal in a similar way to caloric testing, because both ears are stimulated simultaneously during the test, rotational chair testing cannot identify unilateral peripheral vestibular lesions ([Lang and McConn Walsh, 2010](#); [Phillips et al., 2011](#)). The second category of vestibular assessment evaluates postural control. A common example of these tests is computerized dynamic posturography ([Duarte and Freitas, 2010](#)). This test evaluates patients' sensory and motor adaptive mechanisms, which contribute to balance control. Since posturography evaluates the integration of vestibular, visual and somatosensory systems, it aids in differentiating impairments in

those systems. It helps also to isolate postural control abnormalities caused by peripheral sensory lesions from central nervous system lesions. [Hale et al. \(2015\)](#) provided a detailed description on how to perform and interpret the above mentioned vestibular test procedures.

Although there seems to be a wide range of tools to evaluate the vestibular system, it is obvious that each test provides information about only one particular functional aspect and there is no single test that evaluates the whole vestibular system. Thus, a test battery is often required to gain a complete picture of vestibular function. Due to practical and technical difficulties in evaluating the vertical semicircular canals and the otolith organs, those two structures have received less attention in terms of assessment. Some tests of otolith function are available, like the subjective visual vertical and the subjective visual horizontal tests. In these tests, the patient is sitting and the head is fixed in an upright position and then the patient is asked to look at a light bar in complete darkness and to either adjust his/her body position or to adjust the light bar by turning it clockwise or counterclockwise with a push button to their own perceived vertical or horizontal line. The tests are administered at different testing conditions and the head and body tilt angles to the right and left are measured ([Clarke et al., 2003](#)).

The usefulness of the subjective visual vertical and horizontal tests has been demonstrated in evaluating otolith dysfunction in some pathologies like Meniere's disease ([Kumagami et al., 2009](#)) and unilateral vestibular neuritis ([Min et al., 2007](#)). Although these tests were introduced very early in literature ([Fischer, 1927](#)) and procedures were renewed and updated recently by a number of investigators ([Andreas and Mast, 1999](#); [H. Clarke, 2001](#); [Akin et al., 2011a](#)), because of the complexity of the equipment setup required to perform these tests, their use is still restricted to research laboratories. On the other hand, the use of vestibular evoked myogenic potential (VEMP), which is also a measure of otolith function, has found a more widespread use in the clinical and research settings because of the simplicity of the procedure and the availability of its recording system. The following section provides more details about VEMPs.

## 1.6 Vestibular evoked myogenic potentials (VEMPs)

The early observations of [Dr. Pietro Tullio \(1929\)](#), who documented eye movements and postural changes in animals following surgical fenestrations of the vestibular bony labyrinth, form the basis of VEMP testing. VEMPs are short-latency inhibitory muscular potentials generated by stimulating the vestibular system with high-level acoustic signals and recorded using surface electrodes placed over muscles. [Von Békésy \(1935\)](#) documented eye movements in response to sound in normal human subjects which were proven to be independent of cochlear function. Nowadays, the term *Tullio Phenomenon*, is sometimes used to describe symptoms of vestibular stimulation by sounds reported by patients. Tullio Phenomenon is a sound-induced vestibular symptom and is mainly a physiologic response of the vestibular system in response to high sound intensity levels ( $\geq 70$  dB normal hearing level 'nHL'). Tullio Phenomenon becomes pathological if it is provoked by normal sound intensity levels ( $< 70$  dB nHL) ([Deggouj, 2008](#)).

After the works of Tullio and Békésy, another group of investigators recorded short latency evoked potentials in normal subjects from the inion, which is the lowest point of the skull from the back of the head, and showed that these responses were generated by electromyogenic (EMG) activities of neck muscles in response to high level clicks, and called them the *inion responses* or the *inion potentials* ([Bickford et al., 1964](#)). The inion response was confirmed to be of myogenic origin because it was eliminated when neck muscles were relaxed. The study also indicated that this myogenic response was present in two patients with bilateral profound hearing loss and normal vestibular function and absent in one patient with similar hearing loss but with vestibular dysfunction, which suggests that this response is mediated by the vestibular system. Subsequent studies using patients with specific audio-vestibular disorders suggested that the origin of this myogenic response is the otolith organs, primarily the saccule ([Cody et al., 1964](#); [Cody and Bickford, 1969](#); [Townsend and Cody, 1971](#)). Additional histologic and electrophysiological studies performed on guinea pigs indicated the presence of this myogenic response following significant destruction of the ampulla, utricle and cochlea with preservation of the saccule ([Cazals et al., 1980](#); [Cazals et al., 1982](#); [Cazals et al.,](#)



1983). Then for almost three decades, this response was neglected because the inion responses were inconsistent and thus, no further work was done to establish its clinical application.

In 1992, this response was reinvestigated again in human subjects by recording EMG activities from surface electrodes placed over the belly of contracted sternocleidomastoid (SCM) muscle (Colebatch and Halrnagyi, 1992). In this study, three patients presenting with sensorineural hearing loss as a result of Meniere's disease underwent selective vestibular nerve section. The patients had intact horizontal semicircular canals indicated by normal caloric responses. Because this myogenic response was abolished post-surgery, the authors suggest a vestibular origin of this response, distinct from the horizontal semicircular canal. Similar findings were established by Colebatch et al. (1994a). The study found that this myogenic response was absent in patients who underwent selective vestibular nerve section and present in patients with severe sensorineural hearing loss with no apparent vestibular dysfunction. A subsequent study found that this response was abolished in patients who undergone a vestibular nerve section, particularly, inferior vestibular nerve, and had normal auditory function (Brantberg and Mathiesen, 2004). Hence, these myogenic responses are not mediated by the cochlea and appear to be independent of the degree of sensorineural hearing loss. Instead, these responses are believed to arise from vestibular afferents, specifically innervating the saccule, in response to sufficiently loud sounds which can be recorded from the EMG of neck muscles (Colebatch and Rothwell, 1993; Colebatch et al., 1994b; Bronstein et al., 1995). After Colebatch and colleagues' studies published in 1992 and 1994, the term "vestibular evoked myogenic potential" was introduced and the VEMP procedure became available for clinical use. Thus, the fact that the otolith organs were responsive to high levels of sound in addition to their sensitivity to linear acceleration, forms the basis for VEMP procedure. Over the last decade, the VEMP procedure has gradually evolved and is currently being used as an objective measure to evaluate the integrity of the otolith organs. Although both VEMP and Tullio Phenomenon share a similar mechanism and we could say that VEMP is a reflection of a physiologic Tullio Phenomenon because both involve the induction of

sound pressure waves in the otolith organs' fluid, they are distinct in terms of their clinical application.

### 1.6.1 Anatomic pathway of VEMP

Morphologic and physiologic studies performed in experimental animals have confirmed that VEMPs originate from the otolith organs (Murofushi et al., 1996a; McCue and Guinan, 1997; Murofushi and Curthoys, 1997; Kushiro et al., 1999). The evidence that the VEMP response is dependent on activation of vestibular afferents was also documented in humans, as the response was abolished in patients following selective vestibular nerve section (Colebatch and Halrnagy, 1992; Colebatch et al., 1994a). Further evidence supporting otolith origin of VEMP has come from the findings of intact VEMPs in patients with cochlear and semicircular canal pathologies but intact otolith structures (Yokota, 2000; Sheykhholeslami and Kaga, 2002). When connections were made between the otolith organs and the SCM muscle by selective electrical stimulation of saccular nerves in cats, results showed that although both saccular and utricular nerve stimulation evoked predominantly inhibitory postsynaptic potentials in the ipsilateral SCM motor neurons, saccular nerve stimulation resulted in little or no activation of contralateral SCM muscle (Kushiro et al., 1999). Subsequent reports reconfirmed that the SCM muscle was the source of VEMP response and supported the laterality and peripheral origin of VEMP in humans (Colebatch and Rothwell, 2004; Basta et al., 2005a). Hence, the evidence suggests that VEMP response recorded from SCM muscle is mediated by an ipsilateral anatomic pathway, which includes the saccular sensory cells, afferent inferior vestibular nerve (cranial nerve VIII), brainstem vestibular nuclei, lateral vestibular nucleus, descending medial vestibulo-spinal tract ending at the motor neurons of the SCM muscle. This pathway is commonly known as the sacculo-collic reflex. Thus, the presence of VEMP indicates the integrity of this pathway (McCaslin and Jacobson, 2016).

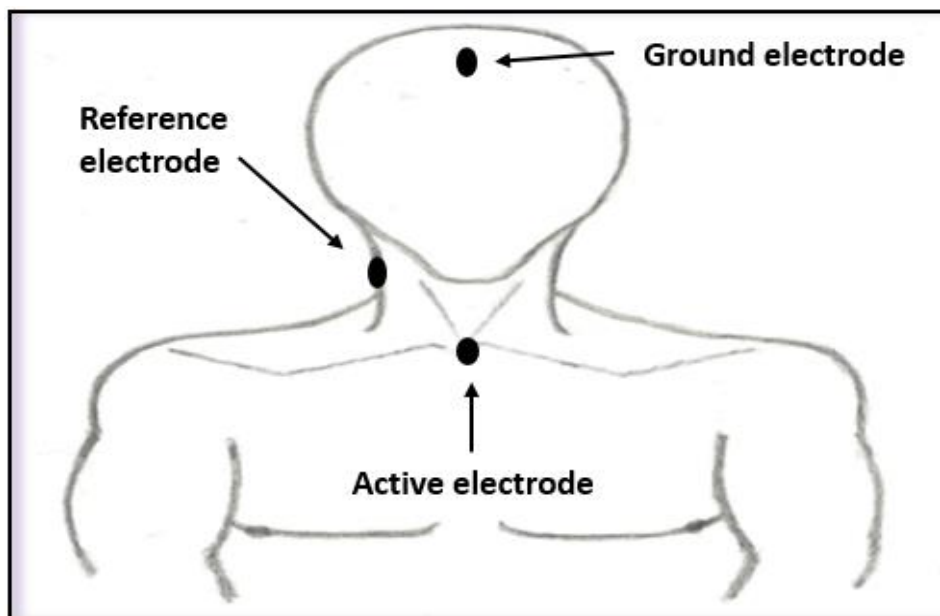
The conventional method for recording VEMP involves measuring brief inhibitions of EMG activity from tonically contracted SCM muscle, which is now referred to as the cervical VEMP (cVEMP). Similar sound evoked myogenic responses could be elicited also

from other muscle groups, such as the trapezius, triceps and gastrocnemius muscles (Ferber-Viart et al., 1997; Watson and Colebatch, 1998; Rudisill and Hain, 2008; Cherchi et al., 2009; Brooke et al., 2014). More recently, there have been other developed forms of VEMP responses, such as the ocular VEMP (oVEMP). oVEMPs are myogenic responses recorded from the extra-ocular muscles of the eyes and represent EMG activities associated with VOR (Rosengren and Kingma, 2013). However, cVEMP is the most investigated and thus, the most commonly applied clinical procedure (Rosengren et al., 2010; Papathanasiou et al., 2014). While compelling physiologic evidence derived from animal studies indicates that the saccule and the inferior vestibular nerve are the primary generators of cVEMP (Curthoys, 2010), the ipsilateral utricular macula and superior vestibular nerve were found to be the predominant source of air conducted oVEMP (Iwasaki et al., 2008; Iwasaki et al., 2009; Nguyen et al., 2010). Thus, cVEMP is an inhibitory reflex measured from the ipsilateral SCM neck muscles (Kushiro et al., 1999; Wit and Kingma, 2006) whereas oVEMP is a crossed excitatory reflex measured from the inferior oblique eye muscle (Weber et al., 2012). Although this section reviews VEMP in general, the remaining sub-sections provide detailed information only about cVEMPs evoked by air conduction since it is the most commonly applied clinical procedure and the one used in the work described in this thesis.

### **1.6.2 Stimulus and recording parameters of cVEMPs**

cVEMP responses can be recorded using different stimulus and recording parameters. The cVEMP electrode configuration illustrated in Figure 1.3 has been shown to produce the largest cVEMP amplitudes (Sheykholeslami et al., 2001; Papathanasiou et al., 2014). During recording, the subject should be in a supine or sitting position and the surface electrodes are placed over the muscles while intense air-conducted sound (usually 95 dB above normal hearing level (nHL) which is roughly equivalent to 125 dB SPL and a stimulus duration of less than 1 second) is delivered to the subject's ears through headphones or insert phones. Although the stimulus intensity level used in cVEMP testing is relatively high, the short testing time and the transient nature of the stimulus negate this and the procedure is well tolerated (Ochi et al., 2001; Akin et al., 2003).

cVEMP responses can be obtained using either clicks or short tone burst stimuli. Several studies demonstrated that low frequency tone bursts between 500 and 1000 Hz generate higher cVEMP amplitudes compared to those obtained by clicks and higher frequency short-tone bursts (Murofushi et al., 1999; Akin et al., 2003; Lin et al., 2006). Hence, there is a general consensus in the literature that the optimal auditory stimulus to obtain cVEMP is a 500 Hz short tone burst. Either monaural or binaural stimulation/recording can be used (McCaslin and Jacobson, 2016). However, since cVEMP is an ipsilateral response, the monaural paradigm is more commonly used. Very recently, a cVEMP guideline was produced by a panel of international experts (Papathanasiou et al., 2014). The report provides a recommendation for the minimum requirements to obtain a reliable and reproducible air conducted evoked cVEMP response (Table 1.1).



**Figure 1.3 cVEMP typical electrode configuration.** The active electrode (non-inverting) is attached to the sternum. The reference (inverting) is attached to the tested neck muscles; midpoint of sternocleidomastoid (SCM) muscle. The common/ground electrode is attached to the forehead. In this picture, the right SCM muscle is the tested side.

**Table 1.1 Summary of recommended stimulus and recording parameters for cervical vestibular evoked myogenic potential (cVEMP) evoked by air conduction** (Papathanasiou et al., 2014).

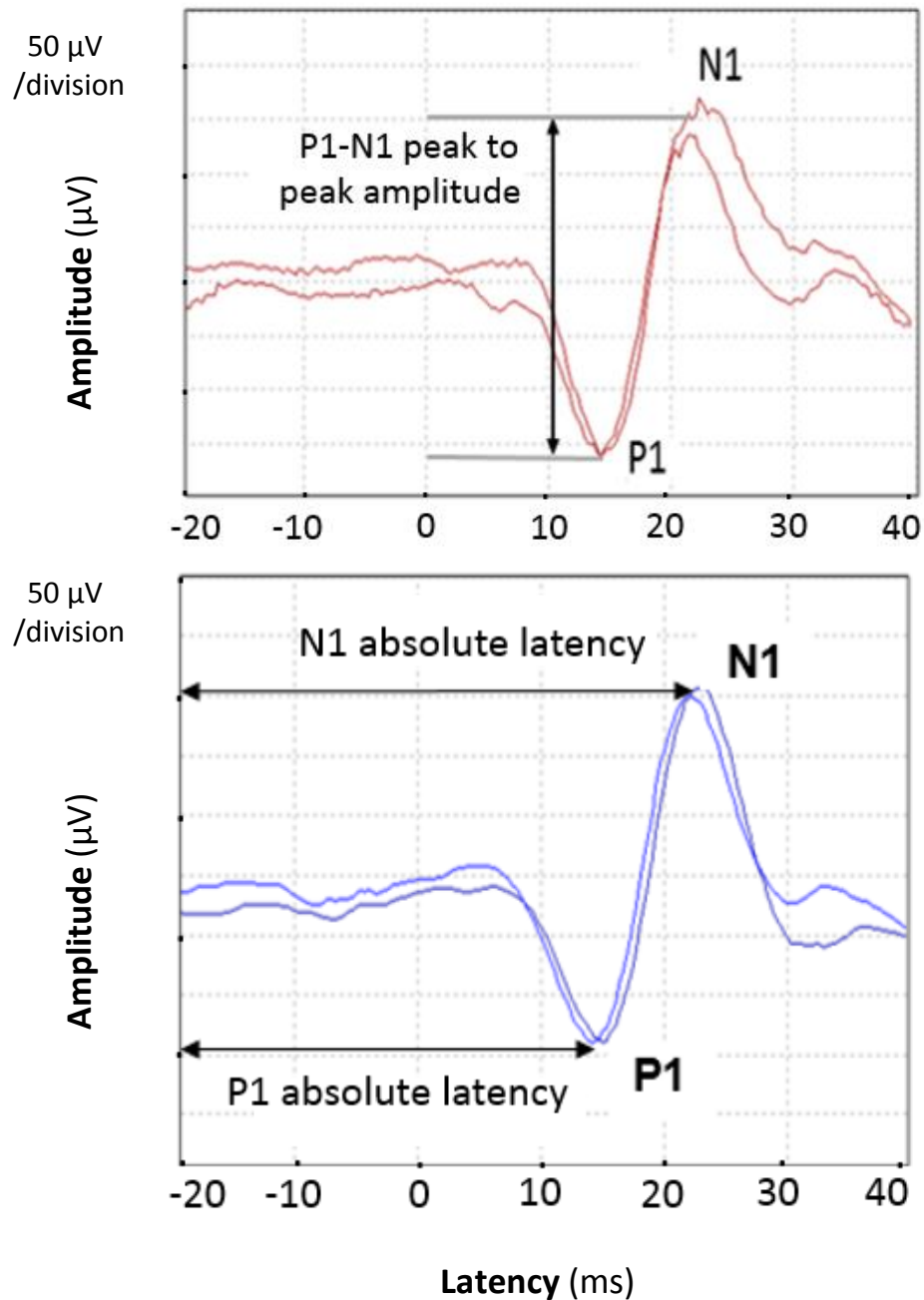
<b>cVEMP stimulus and recording parameters</b>	
Number of channels	1 or 2
Amplifier gain	5000 Hz
Band pass filter	Low pass (5 - 30 Hz) high pass (1000 – 3000 Hz)
Recording epoch	100 ms
Stimulus rate	5 Hz
Stimulus type	400 – 600 Hz tone burst (duration: up to 7 ms) or 0.1 clicks
Sample rate	2500 – 10,000 Hz
Stimulus intensity level	120 -135 dB pSPL– (maximum 140 dB pSPL)
Artifact rejection	Off
Stimulus gating	Blackman weighted
Number of sweeps	100 – 250

Hz: hertz, ms: milliseconds, pSPL: peak sound pressure level.

### 1.6.3 Data analysis and clinical interpretation of cVEMP

cVEMP response is characterized by a biphasic positive-negative waveform labelled P1-N1 or P13-N23 based on their respective latencies in milliseconds (ms). Similar to other evoked potentials, when P1-N1 waveform is detected, the response should be replicated to ensure waveform reproducibility. Analysis of cVEMP is usually based on the presence or absence of the response. If the response is present, then the following measures are used to interpret cVEMP normality: peak absolute latency for P1 and N1, P1-N1 peak to peak amplitude, cVEMP threshold, inter-aural latency difference and inter-aural amplitude asymmetry ratio (IAR). The mean latency of the positive peak (P1) is  $\approx 13$  ms and for the negative peak (N1) is  $\approx 23$  ms (Figure 1.4). P1 and N1 latencies have shown good test-retest reliability in cVEMP testing (Li et al., 1999; Versino et al., 2001).

P1-N1 peak to peak amplitude is defined as the relative amplitude to the baseline (calculated from the difference between P1 and N1 absolute amplitudes) and is measured in microvolts ( $\mu\text{V}$ ). Because of the well-known relationship of cVEMP response to voluntary muscular effort, the literature has documented a wide range of inter-subject (between subjects) and intra-subject (within the same subject) normal cVEMP amplitude variabilities. For example, Akin et al. (2003) reported cVEMP amplitude values for 100 dB nHL clicks to be between 16 to 179  $\mu\text{V}$  and from 15 to 337  $\mu\text{V}$  for 500 Hz tone bursts at 90 dB nHL. Another group of investigators reported  $\approx 59$   $\mu\text{V}$  to 280  $\mu\text{V}$  for 500 Hz tone bursts with the use of self-monitoring of EMG by a visual biofeedback (Vanspauwen et al., 2009; Janky and Shepard, 2009; Park et al., 2010; Maes et al., 2010; de Oliveira Barreto et al., 2011; Akin et al., 2012; van Tilburg et al., 2014). A biofeedback method provides the subject with an ongoing measure of muscle contraction or EMG level. The EMG activity is transformed into a visual target and displayed on a screen for the subject to observe in real time during recording. This form of feedback enables the subject to compare his or her muscle contraction level or EMG level to a preset target level and thus, can help both the subject and the tester ensure that the applied EMG activity is within the predefined target range.



**Figure 1.4 Typical cVEMPs response waveform obtained from adult subject with normal audio-vestibular function.** The bi-phasic P1-N1 waveform was recorded twice in each ear to ensure waveform reproducibility. Red tracing/top (right ear), blue tracing/bottom (left ear).

One way of solving cVEMP intra-subject amplitude variability is to use amplitude asymmetry measures commonly known as inter-aural amplitude asymmetry ratio (IAR) instead of absolute amplitude measures. IAR is the difference in amplitude between the right and the left sides, whichever is larger, and is expressed as a percentage. IAR is calculated using the following formula:

$$\text{IAR} = \frac{[AL - AS]}{[AL + AS]} \times 100 \quad (\text{Equation 1.1})$$

IAR = Inter-aural amplitude asymmetry ratio

AL = the larger P1-N1 amplitude ( $\mu\text{V}$ )

AS = the smaller P1-N1 amplitude ( $\mu\text{V}$ )

Normal mean value for IAR ranges from  $\approx 20$  to 40 % depending on the cVEMP protocol used and whether there is a visual biofeedback system used during cVEMP testing or not (Li et al., 1999; Brantberg and Fransson, 2001; Akin et al., 2003; Bogle et al., 2013; McCaslin et al., 2013). It should be highlighted here that IAR measurement does not solve the cVEMP amplitude variability problem and amplitude instability should be controlled by other effective means to ensure that approximately equal muscular tension between test sessions or across sides is applied during cVEMP recording. Another cVEMP measure is cVEMP threshold, which is the lowest sound intensity level at which P1-N1 waveform can be detected and successfully reproduced. It can be obtained by using the ascending (increase sound intensity level in 5 dB steps) and descending (reduce sound intensity level in 10 dB steps) techniques until the response is identified. It is unlikely that cVEMP can be recorded near or below 75 or 80 dB nHL (Streubel, 2001). The cVEMP threshold obtained from individuals with normal audio-vestibular function ranges from 75 to 105 dB nHL for click stimuli (Colebatch et al., 1994a; Lim et al., 1995; Ochi et al., 2001; Welgampola and Colebatch, 2001b; Akin et al., 2003). Similar ranges have been reported for tone burst-evoked cVEMP (Isaradisaikul et al., 2008). However, some studies reported that tone burst stimuli require lower stimulus intensities and thus, result in lower cVEMP thresholds (Welgampola and Colebatch, 2001a).



The clinical utility of cVEMP threshold has been demonstrated in cases of superior canal dehiscence (SCD) where the part of the temporal bone overlying the superior semicircular canal is thin or completely absent, and other third window pathologies (Brantberg et al., 1999; Zuniga et al., 2013). These studies found that the affected side in patients diagnosed with these pathologies will often show a more reduced cVEMP threshold (below 75 or 80 dB nHL) than would normally be expected. Therefore, ideally, it would always be desirable to obtain cVEMP threshold for patients with symptoms indicative of these disorders (e.g. SCD). In order to do this, cVEMP testing would have to be repeated several times to determine the exact threshold and this would be a lengthy process to carry out, which might require multiple sessions for each patient. More importantly, the threshold searching process would expose patients to repeated high stimulus levels that might be uncomfortable for some patients, especially those with increased sound sensitivity. In fact, some studies found that the use of high stimulus levels in cVEMP testing may alter cochlear function by reducing DPOAE amplitudes in normal individuals with no history of audio-vestibular disorders (Krause et al., 2013; Strömberg et al., 2016) and may result as well in subjective auditory symptoms, such as tinnitus, muffled hearing, ear pressure and otalgia (Krause et al., 2013). For this reason, unless SCD or other third window pathologies are suspected, obtaining cVEMP responses at one sufficiently high sound intensity level (90 to 100 dB nHL) is preferable.

When a cVEMP response is present and reproducible, the response parameters should be compared with their corresponding normative data. The upper normal limit (mean + 2 SD) is commonly used to judge normality of cVEMP response parameters (McCaslin and Jacobson, 2016). If P1/N1 latency values exceed the upper normal limit, then the response is labelled as abnormally delayed or prolonged. If P1-N1 peak to peak amplitude values are less than the lower end of the normal range, the response is labelled as abnormally reduced or small. If the amplitude exceeds the upper normal limit then the response is regarded as an abnormally large cVEMP response. The same criteria apply to the rest of the cVEMP response parameters. In summary, although both latency and amplitude parameters have been routinely measured in cVEMP recording, the clinical interpretation of most abnormal vestibular pathologies is typically based on the response rate (i.e. presence/absence) and also on the amount of amplitude differences

between the right and left ears as an indication of the likely side of pathology. However, the wide range reported for cVEMP amplitude values in normal subjects limits the clinical utility of amplitude measure unless a method is introduced during cVEMP recording to ensure approximately equal muscle contraction effort has been taking place across tested sides. Several methods and techniques to reduce SCM muscle variability have been described in the literature. A description of these methods/techniques is provided in the following section (section 1.6.4).

#### **1.6.4 Factors affecting cVEMP response**

Although the cVEMP bi-phasic waveform response (P1-N1) in the normal population has been described by numerous studies over the last decade, the response is still being investigated because it is influenced by several factors. The factors which can affect cVEMP response can be divided into four categories a) stimulus-related factors and b) subject-related factors c) method/procedure-related factors and d) pathological factors. The following sub-sections provide more details about the influence of each of these factors on cVEMP response characteristics.

##### ***a) Stimulus-related factors***

cVEMP response is influenced by a number of stimulus factors, such as the stimulus level, type, frequency, duration and mode of stimulation (air conduction versus bone conduction). cVEMP amplitude varies as a function of stimulus level. As stimulus level increases, there is a corresponding increase in cVEMP amplitude. In contrast, P1 and N1 latencies are not affected by stimulus level (Colebatch et al., 1994a; Lim et al., 1995; Ochi et al., 2001; Akin et al., 2003; Wit and Kingma, 2006). cVEMPs evoked by tone bursts have longer latencies and larger amplitudes compared to responses obtained by clicks (Akin et al., 2003; Cheng et al., 2003; Wu et al., 2007). Stimulus frequency also has an influence on cVEMP amplitude and threshold. Tone burst stimulation between 500 to 1000 Hz produces the largest cVEMP amplitudes and the lowest cVEMP thresholds with 500 Hz being the best frequency of stimulation (Murofushi et al., 1999; Welgampola and Colebatch, 2001a; Akin et al., 2003; Akin et al., 2004; Janky and Shepard, 2009). The

finding that 500 Hz tone burst was the optimal auditory stimulus to generate cVEMP is consistent with the neurophysiologic findings obtained from human and animal studies, which suggests that the inferior vestibular nerve is most responsive between 500 to 1000 Hz (McCue and Guinan, 1995) and that is why 500 Hz tone burst is currently the stimulus of choice to record cVEMP in most clinical settings.

The finding of the vestibular system being more sensitive to lower frequencies compared to higher frequencies suggests that the vestibular system has a broad frequency tuning, unlike the auditory system which is finely tuned. The low frequency tuning characteristics of cVEMP responses were explained by the mass-spring damping properties of the saccule itself rather than the transmission properties of the vestibule (Todd et al., 2000). Changes in tone burst duration or rise/fall time also affect cVEMP latency and amplitude measures. Welgampola and Colebatch (2001a), Cheng and Murofushi (2001a; 2001b) demonstrated an increase in cVEMP latency and amplitude when the rise/fall time of tone burst stimuli was increased from 1 to 7 ms. cVEMP stimulus is commonly delivered through air conduction via headphones or insert phones. However, air conducted stimuli require the conductive mechanisms (outer ear and middle ear) to be free from obstruction, such as impacted wax, middle ear pathology and conductive hearing loss (Bath et al., 1999).

Alternatively, cVEMPs can be successfully obtained in these cases by using bone conduction stimuli (clicks or tone bursts) delivered to the inner ear via a bone vibrator (Sheykholeslami et al., 2000; Yang and Young, 2003; McNerney and Burkard, 2011) or tendon taps delivered to the forehead and mastoid (Halmagyi et al., 1995; Brantberg et al., 2008). However, it should be noted that cVEMP responses obtained by bone-conducted stimuli have lower thresholds (30 to 35 dB nHL) (Welgampola et al., 2003) and lower tone burst optimal frequency (200 to 250 Hz) compared to those obtained by air-conducted stimuli (Sheykholeslami et al., 2000; Welgampola et al., 2003; Miyamoto et al., 2006). In addition, the anatomical origin of cVEMP responses obtained using bone conduction stimuli is also different from those obtained using air conduction stimuli. Curthoys et al. (2006) found that bone-conducted responses obtained at 500 Hz stimulated irregular otolith neurons, primarily in the superior vestibular nerve and

utricle macula in guinea pigs. Electrical/galvanic stimulation can also be used to evoke cVEMP (Watson et al., 1998; Murofushi et al., 2002). Galvanic evoked cVEMP are thought to originate from irregular vestibular afferents arising from all vestibular receptors (Kim and Curthoys, 2004). Meyer et al. (2015) conducted a systematic review and meta-analysis of 66 cVEMP normative data publications and confirmed the influence of stimulus parameters on cVEMP response.

### ***b) Subject-related factors***

Several studies have described age-related changes in cVEMP response parameters. The primary noted changes were a significant decrease in amplitude, an increase in threshold and a prolongation of P1 and N1 latencies in individuals over the age of 60 (Basta et al., 2005b; Lee et al., 2008b; Janky and Shepard, 2009; Maes et al., 2010; Tourtillott et al., 2010; Akin et al., 2011b; McCaslin et al., 2013). Studies which have compared cVEMP amplitude levels of normal subjects at different age groups found that the smaller cVEMP amplitudes found in the older groups were more likely caused by age-related changes in both the SCM muscle and vestibular system (Akin et al., 2011b; McCaslin et al., 2013). Su et al. (2004) found bilateral absent cVEMP responses in 40 % of neurologically and otologically intact individuals aged between 60 and 75 years. A similar finding was reported by Janky and Shepard (2009). Thus, the presence of a measurable cVEMP response decreases with increasing age, so age should always be considered when interpreting cVEMP responses in patients over the age of 60.

As mentioned earlier, the majority of studies suggest that frequencies around 500 Hz produce the largest cVEMP amplitude and the lowest cVEMP threshold. Further exploration of cVEMP responses using different age groups revealed that age-related changes in the vestibular system may alter this optimal frequency. cVEMP response of 39 participants with different age groups (youngest = 18 to 39 years, middle age = 40 to 59 years, oldest > 60 years of age) were investigated to determine the effects of age on the cVEMP optimal frequency (Piker et al., 2013). The study showed that 750 kHz was the optimal frequency to obtain cVEMP in the youngest group while in the oldest group, 1000 Hz was the optimal frequency. These findings suggest that the vestibular system might change its tuning frequency with increasing age and thus, when assessing patients

older than 60 years of age, higher frequencies (700 or 1000 Hz) might yield better cVEMPs responses. The above described cVEMP age-related changes are consistent with the well-known documented degenerative changes in the vestibular system due to the aging process (Johnsson, 1971; Park et al., 2001). In fact, several temporal bone studies conducted in humans showed a significant reduction in saccular hair cells in individuals over 70 years of age compared to controls (Rosenhall, 1973; Rosenhall and Rubin, 1975; Rauch et al., 2001).

Conversely, the effect of gender on cVEMP response parameters is less understood. A number of studies explored gender differences in cVEMP findings. Brantberg and Fransson (2001) found that P1 latency in response to click stimuli was earlier in females compared to males. These studies suggested that the observed shorter latencies in females were most likely due to the reduced vestibular response time, similar to the reduced cochlear response time in auditory brainstem response observed in females (Allison et al., 1983; Don et al., 1994; Watson, 1996). In contrast, Lee et al. (2008b) studied cVEMP responses of 194 normal subjects (98 males and 96 females) and found that females had significantly higher amplitudes and more prolonged N1 latencies compared to males. The study proposed that their female participants may have cooperated more than their male participants, resulting in greater muscle contraction and hence larger amplitudes. However, it is not clear from Lee's study how participants' cooperation level was assessed during testing and thus, an explanation for why females had higher cVEMP amplitude compared to males and why also females had longer N1 latencies in this study is lacking.

A positive correlation between neck length and cVEMP latencies both in adults and children was also reported in the literature. Some investigators explained this by the longer neural transmission time needed for the evoked potentials to travel in individuals with longer necks (Chang et al., 2007). A positive correlation between subcutaneous thickness (i.e. the amount of tissue between the muscle and the recording electrode) and cVEMP amplitude also has been documented (Farina et al., 2002; Chang et al., 2007). The authors of these studies suggested that structural differences, such as neck length, muscle thickness, head size and conduction velocity might explain why cVEMP

latency and amplitude measures might sometimes vary among subjects with different age groups or different gender. On the other hand, a number of studies did not show any gender effect in their cVEMP findings (Ochi and Ohashi, 2003; Akin et al., 2003; Basta et al., 2005b; Basta et al., 2007; Lee et al., 2008b; de Oliveira Barreto et al., 2011). For example, Akin et al. (2011b) found no gender effect for variable SCM muscle contraction levels obtained from cVEMP responses of 48 individuals. The subjects were divided into two age groups: the young group had 24 adults aged between 22 to 31 years and the old group had 24 adults aged between 61 to 86 years. However, Akin's study found a gender effect in the findings of the young group for the EMG levels recorded at maximum contraction levels. It could be that one source of variation in cVEMP findings between males and females is the natural variations in their muscular systems (i.e. males have stronger muscles compared to females). Thus, unlike the effect of age on cVEMP response parameters, gender-related differences in cVEMPs are still controversial and not yet fully understood and more data are needed to support the potential effect of gender on cVEMP characteristics.

### ***c) Method/procedure-related factors***

#### *SCM muscle contraction levels*

As explained earlier, in order for an inhibitory myogenic potential to be recorded, the muscle at the recording site should be contracted and as expected this is true for cVEMPs. The amplitude of the average cVEMP responses has been shown to increase with an increase in the mean level of tonic muscle activation. As a result of that, large cVEMP amplitude variation between subjects has been documented in individuals with normal audio-vestibular function (i.e. inter-subject variability) and also within the same subject (i.e. intra-subject variability; between ears (inter-aural variability) and between several tests (test-retest variability)) (Colebatch et al., 1994a; Lim et al., 1995; Bath et al., 1998; Akin et al., 2004). If cVEMP amplitude is greatly affected by voluntary muscular effort, then clinicians should ensure that enough muscle contraction is taking place during cVEMP recording, otherwise, absent or reduced cVEMP might result due to insufficient EMG levels rather than a true vestibular pathology. This can be done by standardizing the cVEMP protocol by applying a particular method or procedure that

can minimize amplitude differences across sides and across recordings. Achieving suitable patient positioning which enables creation of sufficient muscular tension in SCM muscle is one of the suggestions in the literature. More information about muscle activation procedures used in cVEMP testing is provided in the following sub-section.

### *SCM muscle activation procedure*

Mainly, there are two muscle activation procedures suggested in the literature to activate SCM muscle during cVEMP recording: head rotation (HR) procedure (Colebatch et al., 1994a; Murofushi et al., 2001; Basta et al., 2005b; Lee et al., 2008b; de Oliveira Barreto et al., 2011) and head elevation (HE) procedure (Wu et al., 1999; Welgampola and Colebatch, 2001a; Welgampola and Colebatch, 2001b; Murofushi et al., 2004). In the HR procedure, the patient is rotating his/her head sideways towards one shoulder with head down trying to approach the shoulder with the chin. In the HE procedure, the patient is lying supine and raising the head from the bed/pillow about 30° from the horizontal plane with the head maintained in the midline position. The HR procedure can be done with the patient either in a sitting position or a supine position, while the HE procedure can only be done with the patient in a supine position. Thus, basically, there are three muscle activation procedures: HR-sitting (HR-S), HR (supine) and HE (supine). The most commonly investigated procedures in cVEMP testing are the HE (supine) and the HR-S procedures.

Positioning of the head in the HE procedure enables simultaneous bilateral cVEMP recording because SCM muscles from both sides are contracted. Hence, the HE procedure saves time because it allows bilateral cVEMP recording. In contrast, the HR procedure allows only unilateral recording because only one SCM muscle from one side is contracted. A number of reports support the use of HR (supine) procedure because of the high EMG activity associated with this procedure (Wang and Young, 2006; Isaradisaikul et al., 2008; McCaslin et al., 2013). However, pain, discomfort and fatigue have been reported with the HR (supine) procedure (Wang and Young, 2006; Isaacson et al., 2006; Bogle et al., 2013). Only a few studies have investigated the effect of muscle activation procedure on cVEMP parameters (Wang and Young, 2006; Ozdek et al., 2009; Tseng et al., 2013; Sánchez-Andrade et al., 2014). A systematic review and meta-analysis

of 66 published papers was done to determine the effect of various stimulus parameters and recording methods including the above discussed SCM muscle activation procedures (Meyer et al., 2015). The results showed that the HE (supine) was the most commonly used procedure with both click-evoked and tone-burst evoked cVEMP testing. Moreover, the study revealed that SCM muscle activation procedure had a significant effect on all cVEMP response parameters.

Hence, current evidence suggests that activating SCM muscle using either the HE (supine) or the HR-S is capable of producing robust cVEMP responses in normal subjects. However, a relatively recent study found that the HR-S produced significantly larger amplitudes in normal subjects compared to the HE (supine) procedure and thus, suggest that the HR-S procedure is the most appropriate procedure to obtain cVEMP responses (Sánchez-Andrade et al., 2014). Furthermore, the HR-S procedure involves less muscular strain and hence, results in less pain and discomfort reported by patients compared to other procedures, such as the HE (supine) procedure (Wang and Young, 2006; Sánchez-Andrade et al., 2014). Although the pros and cons of each of the muscle activation procedures have been highlighted by the above mentioned studies, though are limited, the most effective procedure to activate SCM during cVEMP testing has not been determined yet. In addition to the muscle activation procedure, the patient must sustain the same tension level throughout the recording to minimize possible amplitude differences. This can be achieved by applying an external method or technique that helps the patient to monitor and standardize the EMG levels' variability encountered during cVEMP recording. More information about these methods/techniques is provided in the following sub-section.

#### *Monitoring and standardizing EMG levels*

Although it has been agreed that an appropriate positioning of the head and neck during cVEMP recording is critical to obtain a reliable and repeatable cVEMP response, the main cause of cVEMP intra-subject amplitude variability comes from the variations in tonic EMG activities. This is caused largely by the inability of the patient to generate equal and consistent amounts of muscular contraction on both right and left sides during cVEMP recording (i.e. inter-aural amplitude variability). Hence, in conjunction with the SCM



muscle activation procedure, which is an essential step to generate muscular contraction in cVEMP testing, two approaches have been suggested to overcome cVEMP intra-subject amplitude variability 1) self-monitoring of muscle contraction levels by the use of visual targets which are known as *Visual Biofeedback Methods* and 2) mathematical correction, commonly known as *Amplitude Normalization*.

So far, two visual biofeedback methods have been described in the literature; the *Electromyogenic Monitoring (EMGM) Method* and the *Blood Pressure Manometer (BPM) Method*. These methods employ self-monitoring of muscle contraction levels, which can be viewed by both the patient and the tester through the use of a biofeedback mechanism. The aim of these methods is to help the subject to monitor the amount of muscle contraction levels to ensure equal muscle tensions are exerted from both sides or between several test sessions. The EMGM method provides the patient with real time viewing and monitoring of EMG levels through an EMG monitor (Colebatch and Halrnagyi, 1992). The patient is given a predefined EMG range (minimum and maximum target EMG numbers) and asked to maintain an EMG level during cVEMP recording within that range. On the other hand, the BPM method does not require EMG recording. Alternatively, in this method, the patient is required to hold an inflated blood pressure cuff between the jaw and the hand and to press against it to increase the muscle tension and at the same time monitor a pre-determined target on a blood pressure manometer (Vanspauwen et al., 2006a).

Amplitude normalization, which also sometimes referred to as *Amplitude Correction*, is a technique that requires recording of EMG activity, like the EMGM method, but does not provide the patient or the tester with any means of monitoring SCM muscle contraction levels. Rather, a mathematical correction or normalization is used to quantify right/left ears amplitude differences and subject to subject variations (Colebatch et al., 1994a; Welgampola and Colebatch, 2001a; Colebatch, 2009). For clarity purposes, from now on, this technique will be referred to as amplitude normalization. Because amplitude normalization is a data analysis technique and not a method or a procedure by itself, it can be combined with any method or procedure (i.e. EMGM, BPM, HR-S). More details about the nature and application of the EMGM

method, the BPM method and the amplitude normalization technique in cVEMP testing are provided in the following chapter (Chapter 2, section 2.3).

There is a general consensus among studies that controlling EMG levels during cVEMP testing is essential. However, the optimal approach to achieve this is not yet determined. A number of studies support the use of BPM (Vanspauwen et al., 2006a; Vanspauwen et al., 2006b; Suh et al., 2009) and EMGM (Akin et al., 2004; Akin et al., 2011b; McCaslin et al., 2014) methods in cVEMP testing as means to control amplitude variability. Although these studies suggest that self-monitoring biofeedback methods seem to be acceptable and attractive tools to use with patients, it is currently unknown to what extent these methods affect cVEMP response parameters and ultimately inter-subject and intra-subject variability. It has not been determined also if these methods have equal effect on cVEMP data or whether one method is superior in performance to the other or not. In the same way, although the importance of monitoring EMG activity during cVEMP recording via several methodologies was supported in the recently published guidelines for cVEMP, the optimal method to control SCM muscle variability was not addressed (Papathanasiou et al., 2014).

The same is also true for amplitude normalization. While several reports have shown that using this technique is effective in reducing cVEMP amplitude variability (Lee et al., 2008a; Colebatch, 2009; McCaslin et al., 2013; McCaslin et al., 2014; van Tilburg et al., 2014), others have shown that this technique had no effect on cVEMP data and therefore do not advocate its application (Ochi et al., 2001; Bogle et al., 2013). Thus, the exact role of amplitude normalization technique in controlling cVEMP amplitude variability is controversial. In addition, very few studies have attempted to compare cVEMP data established by EMGM, BPM or amplitude normalization (Lee et al., 2008a; McCaslin et al., 2013; McCaslin et al., 2014). All the available investigations have either looked at each methodology separately or only compared one or two of them but not all of them in a single study. To the best of the author's knowledge, there has been no published work that compared cVEMP data across all of these methodologies. Hence, the study described in Chapter 2 aimed to investigate the effect of these methodologies on cVEMP response parameters in a large group of normal adults and determine an

optimal methodology for recording cVEMP, which will be utilized in subsequent chapters.

#### ***d) Pathological factors***

The diagnostic utility of cVEMP has been examined for various audio-vestibular disorders. Outer and/or middle ear conditions can easily affect cVEMP responses because of the well-known effect of these conditions in reducing the transmitted sound energy delivered to the inner ear (Bath et al., 1999). Consequently, several studies have shown that cVEMP responses can be reduced or absent in the presence of outer and/or middle ear pathologies (Halmagyi et al., 1994; Kurzyrna et al., 2005; Wang and Lee, 2007). These findings are consistent with preserved cVEMP responses evoked by bone conduction or forehead tapping in patients with conductive hearing loss because the stimulus is bypassing the middle ear cavity (Sheykhholeslami et al., 2001; Welgampola et al., 2003; Yang and Young, 2003). Hence, it is always important to confirm the integrity of the outer and middle ears before cVEMP recording by conducting otoscopic examination and middle ear function testing. In addition, patients with intact vestibular organs but with significant neuromuscular diseases can have absent or abnormal cVEMP, so the integrity of patient's neuromuscular system must be ensured before conducting cVEMP.

As explained earlier, cVEMP presence is independent of cochlear function and thus, can be recorded in the presence of variable degrees of sensorineural hearing loss even with profound degree of hearing loss (Colebatch et al., 1994a; Ozeki et al., 1999; Wu and Young, 2002). Since cVEMP reflects the integrity of the sacculo-collic reflex pathway, absent or asymmetrical cVEMP response should be considered as an indication of a lesion anywhere along this pathway. The presence of air-conducted cVEMPs at low thresholds (below 75 or 80 dB nHL) or very large cVEMP amplitude suggests the presence of superior SCD (Brantberg et al., 1999; Minor, 2005; Zuniga et al., 2013). Absent or reduced cVEMP amplitude with normal cVEMP latencies have been reported in  $\approx 80\%$  of vestibular schwannoma cases (Murofushi et al., 1998; Patko et al., 2003; Ernst et al., 2006). Similar cVEMP findings have been reported in patients diagnosed with vestibular neuritis (Murofushi et al., 1996b; Ochi et al., 2003). Absent cVEMP, reduced

amplitude and/or latency prolongation were reported in patients suffering from posterior benign paroxysmal positional vertigo (Murofushi et al., 1996b; Akkuzu et al., 2006; Hong et al., 2008b). Some investigators reported prolonged cVEMP latencies in cases of brainstem lesions and other retrolabyrinth impairments, such as multiple sclerosis (Shimizu et al., 2000; Murofushi et al., 2001; Rosengren et al., 2011; Gazioglu and Boz, 2012). However, it should be noted that diseases of the central nervous system including multiple sclerosis could produce abnormal cVEMP findings even if the peripheral vestibular organs are functionally intact (McCaslin and Jacobson, 2016), so the clinical usefulness of cVEMP in many central pathologies is not yet fully understood. Abnormal cVEMP findings have also been demonstrated in Meniere's disease or endolymphatic hydrops (Waele et al., 1999; Rauch et al., 2004; Ogido et al., 2009). Air-conducted cVEMPs were found absent in 55 % of ears affected by Meniere's disease (Waele et al., 1999). Seo et al. (2003) observed enlarged cVEMP amplitude in 40 % of patients with Meniere's disease. Another study found that ears affected by Meniere's disease had increased cVEMP threshold and altered tuning at 500 Hz compared to normal ears (Rauch et al., 2004). The demonstrated cVEMP variability among cases of Meniere's disease could be explained by the fluctuating nature of this disease, the stage or time course of the disease and whether cVEMP was recorded during the attack or not. Promising cVEMP findings have also been shown in some brainstem disorders (Rosengren et al., 2011).

In summary, it is important to take the following into consideration while performing and interpreting cVEMPs a) cVEMP responses should be obtained using an appropriate recording protocol, which includes a sufficient stimulation level b) cVEMP response in normal subjects over the age of 60 should be interpreted with caution because responses could be small or absent in that age group c) although normative data for cVEMP response parameters have been widely published in the literature, due to differences in stimulus and recording techniques among studies, it is highly recommended that each clinical site obtain its own age and gender-matched norms for cVEMP to ensure accurate test interpretation and finally d) middle ear pathology and/or a conductive hearing loss should be ruled out before performing cVEMP as they can cause absent or reduced cVEMP responses.

Over the last decade, clinical applications of cVEMP testing have been expanding and the clinical value of cVEMP in the evaluation of several vestibular disorders is gradually growing. Nevertheless, larger scale studies are needed to describe cVEMP characteristics in many peripheral, audio-vestibular and central disorders. One of the new clinical applications of cVEMP is the area of noise-induced vestibular dysfunction. However, the great majority of research has been directed towards the effects of noise exposure on the cochlea and its consequences on the auditory mechanism and less attention has been given to possible effects of noise on the human vestibular system. This has motivated the author of the present thesis to explore vestibular consequences resulting from noise exposure in more depth. The assumption that noise exposure might not only cause adverse effects to the cochlea but also might cause some vestibular involvement came from the fact that both the cochlea and the vestibular system are in close anatomic proximity, they have common embryological origin, they share the membranous labyrinth, they have similar hair cell ultra-structures, they share a common arterial blood supply via the same end artery and surely that the vestibular hair cells are also sensitive to sound (Damiano and Rabbitt, 1996; Rabbitt et al., 1996). This all suggests that it is very possible that excessive noise exposure could damage not only the auditory system, but also the vestibular system. More about the evidence of noise-induced audio-vestibular damage and the use of cVEMP to evaluate possible vestibular involvement in individuals affected by noise exposure is provided in the following sections

## 1.7 Adverse effects of noise exposure on the peripheral audio-vestibular system

### 1.7.1 Occupational noise exposure: a brief summary

Sound is a form of energy that is transmitted by pressure vibration, which the human ear can detect. Sound, including speech, conveys vital information to humans. Whereas sound is a sensory perception, noise is an undesired sound. In some situations and in certain places, common everyday sounds start to interfere with communication and everyday routine tasks. An example of that are loud sounds. Loud sounds may be considered as noise, especially if we are trying to work on a task that requires high concentration or if we want to go to sleep. When this happens, sound becomes noise because it is unwanted. However, loud sounds may not necessarily always be undesired. For instance, when we listen to loud music, because it is a pleasurable sound, we do not consider it as noise. The National Institute for Occupational Health and Safety (NIOSH), which is a federal agency responsible for the prevention of work-related injuries in the United States, defined noise as any unwarranted disturbance within a useful frequency band (NIOSH, 1998). Thus, sound is a desired signal and sound becomes noise if it is loud, disruptive, unpleasant or unwanted, so the difference between sound and noise depends on the person and the circumstances.

Today, noise is considered one of the greatest occupational and environmental health hazards (WHO, 2008). A considerable number of studies have demonstrated that repeated exposure to high levels of noise can result in adverse health effects (Passchier-Vermeer and Passchier, 2000; Stansfeld and Matheson, 2003; Ising and Kruppa, 2004). Of these, the most extensively investigated ones are the effects on the human inner ear system and thus, hearing. Since the current thesis is exploring the impact of noise on human's inner ear system, it is important at this stage to provide a clear definition for some of the terms, which will be used frequently in this thesis, such as noise exposure, noise damage and other noise-related terms. *Noise exposure* can be defined as the state of being in contact or close proximity to elevated noise levels for an extended period of time. Repeated long-term exposure to elevated noise levels in the worksite is commonly

referred to as *Occupational or Industrial Noise Exposure*. Correspondingly, *Industrial Noise*, or *Occupational Noise*, is the amount of acoustical energy (noise) received by an employee's ear system while they are working. However, repeated exposure to elevated noise levels during common everyday life activities is known as *Environmental Noise Exposure*. Traffic, transportation and household appliances are common examples of environmental noise sources. Repeated exposure to elevated levels of noise during leisure activities like music playing or listening is also another kind of noise exposure commonly known as *Recreational Noise Exposure*. Generally, *Noise Damage* can be defined as health consequences of regular exposure to consistently elevated noise levels. A comprehensive source of noise and noise-related terminologies can be found in [Stach \(2003\)](#). Because this thesis is concerned about the adverse effects of occupational noise exposure on the human inner ear system, whenever the terms "noise exposure" and "noise damage" are mentioned, they imply the adverse effects of occupational noise on the peripheral audio-vestibular system.

Hearing impairment resulting from repeated long-term exposure to elevated noise levels is commonly known as *Noise-induced Hearing Loss (NIHL)*. NIHL is the most common sensorineural hearing loss after presbycusis (a similar kind of hearing loss caused by the aging process) and the second most self-reported occupational illness in the United States ([Rosenhall et al., 1990](#); [NIOSH, 2010](#)). More information about NIHL is provided in the next section (1.7.2). According to NIOSH, approximately 30 million people in the United States are exposed to noise on a routine basis with the most frequently occurring noise exposure occurring in the worksite ([NIOSH, 2010](#)). In Germany and other developed countries, 4-5 million people are thought to be exposed to hazardous noise ([Burkhart et al., 1993](#)). In Britain, it is estimated that 153,000 men and 26,000 women aged 35 to 64 years have severe hearing difficulties caused by noise in the worksite ([Palmer et al., 2002](#)). The worldwide estimates of the number of people affected by hearing loss increased from 120 million in 1995 ([Wang et al., 2001](#); [WHO, 2001](#)) to 250 million in 2004 ([Smith, 2004](#)) and a large proportion of these cases may be related to occupational noise exposure. Therefore, preventing the health outcomes of occupational noise exposure is a major national and international health priority.

Studies conducted in several developing countries revealed that a large number of people in the Kingdom of Saudi Arabia (Ahmed et al., 2001b), United Arab Emirates (Gomes et al., 2002), Kuwait (Koushki et al., 2004), Turkey (Atmaca et al., 2005), Pakistan (Ashraf et al., 2009) and Egypt (Ali, 2011) are exposed regularly to high levels of noise. The available data suggest that noise exposure in many developing countries is higher due to lack of governmental noise control bylaws and hearing conservation programmes (Pathak and Tripathi, 2008). A survey conducted among 78 industrial factories in Saudi Arabia revealed that 86 % of the surveyed worksites exceeded the 85 dBA (A-weighted) limit in at least part of the factory and 12 % of them exceeded this limit in the entire factory (Alldrisi et al., 1990). A subsequent study showed that workers in 20 industrial factories at Jeddah city in Saudi Arabia were exposed to significant noise levels in their worksites (Noweir and Jamil, 2003). Hence, occupational noise exposure in Saudi Arabia is starting to be recognized as a major health and governmental concern

It is well recognized that people working in military and industrial environments are exposed to significant noise levels (Johnson, 1991; Eleftheriou, 2002; Humes et al., 2006; Saunders and Griest, 2009; Yong and Wang, 2015). Military personnel are exposed to high sound intensity levels produced by explosions, artillery, jet aircraft, shooting, rifle fire and other heavy machinery. Industrial workers like engineers and technicians are exposed mainly to machinery noise, such as fans, blowers, electric motors, transformers, air vents and gas jets. It is often difficult to ensure adequate noise control because it is not always feasible to predict the noise source and noise level, especially in the military. More information about occupational noise-induced hearing loss can be found in the recent task force statement on occupational noise-induced hearing loss released by the American College of Occupational and Environmental Medicine (ACOEM, 2012). In order to assess the risk of noise exposure, noise levels are measured using the A-weighting scale, which weights frequencies based on the sensitivity of the human ear. The A-weighting scale measures noise levels using sound pressure levels, which are given in units of dB(A). Ideally, noise levels are measured using a sound level meter, which is a hand-held instrument with a sensitive microphone that responds to changes in air pressure caused by sound waves. Sound level meters are effective to quantify different kinds of noise, especially those which are relatively constant. However, in places where



individuals tend to move around, which is particularly true for many working personnel, or where the noise intensity tends to fluctuate over time, it becomes problematic to conduct an accurate measurement of noise levels just with a simple hand-held sound level meter. Alternatively, noise exposure can be estimated more accurately by *Noise Dosimetry*. This involves small portable devices that can be attached to the person's body, with the microphone mounted close to the person's head.

Sometimes, the nature of some studies precluded noise level measurements, either by sound level meters or even personal monitoring devices like noise dosimeters, due to lack of instrumentation or the diversity of noisy activities/occupations in the lives of the subjects, which would make the performance of these procedures impossible. Alternatively, self-reported data or noise surveys can provide useful alternative methods to estimate the noise levels the individual is exposed to and thus, can provide useful information on risks from noise exposure. Because the individual may be exposed to noise for only part of the day, or part of the week or for only a certain number of hours in a day, this reduces the individual's risk from noise exposure. Therefore, risk is dependent on the total A-weighting energy reaching the ear. It is possible to assess the individual's daily noise exposure levels by the level of a noise that, if present for a nominal working day of 8 hours, contains the same energy as the pattern of noise when it actually occurs. In addition, one could estimate the cumulative noise exposure by collecting information about the noise energy the individual is exposed to over his/her lifetime, which is commonly known as a *Lifetime Noise Exposure* (Lutman and Spencer, 1991; Smith et al., 2000; Lutman et al., 2008). Such information is useful to determine the effects of individuals' personal noise exposure on their other important measurement outcomes, such as hearing thresholds, cochlear function, vestibular function and self-reported symptoms.

In an attempt to limit noise exposure, regulations and guidelines have been established worldwide. The National Institute for Occupational Safety and Health (NIOSH, 1998), defined 85 dB(A) as the maximum acceptable A-weighted sound pressure level averaged across an 8-hour workday. The Occupational Safety and Health Administration (OSHA) in the United States uses 90 dB(A) as the maximum allowable noise exposure level

(OSHA, 1983). The European Agency for Safety and Health at Work and the European Union (EU) adopted a maximum of 87 dB(A) per 8-hour workday as a noise exposure limit criterion (EU, 2003). The maximum noise exposure levels established by these regulatory agencies are known as the *Permissible Exposure Limit* (PEL). These recommended standards state that exposure to sounds equal to or above these limits is considered hazardous and puts exposed individuals at high risk of developing NIHL. In addition, workers are required to use hearing protection devices if they are exposed to noise beyond these limits.

Although a PEL of 85 dB(A) per 8-hour workday has found acceptance in most countries, some countries with developing economies are using a slightly different PEL (90 dB(A)/8-hour workday) in their noise exposure regulation (Alldrisi et al., 1990; Shaikh, 1999; Ahmed et al., 2001b; Fuente and Hickson, 2011). It is important to point out here that if the recommended PEL is 8 hours exposure at 85 dB(A) but the noise level the worker is exposed to increases beyond this recommended PEL, then there is a 3 dB exchange rate, meaning that the amount of time a person can be exposed to a certain noise level to receive the same dose is cut in half. For instance, if the person is exposed to a noise level of 88 dB(A), then the maximum allowable daily noise dose of 100 % in this case is 4 hours. The World Health Organization (WHO, 2008) has recommended a 24 hour PEL of 70 dB(A) with a 3 dB exchange rate, which is equivalent to 8 hours exposure at 75 dB(A) with no noise exposure allowed for the other 16 hours per day. Despite the existence of international occupational noise guidelines, the literature suggests that a large number of working personnel including soldiers and technicians in different parts of the world are still exposed to significant amounts of noise. Therefore, investigators should continue to engage these professions in research to understand the long-term implications of noise exposure on these personnel. The effects of noise exposure on those two working groups (military and technicians) are further investigated in the second study of this thesis. As noted at the start of this section, excessive noise exposure causes hearing loss. However, the damage is not restricted to the auditory portion of the inner ear (i.e. cochlea). Significant noise exposure might also impair the vestibular portion of the inner ear and result in vestibular disturbances. More details about the

evidence of noise effects on the peripheral audio-vestibular system are provided in the following section.

### **1.7.2 Effects of noise exposure on the peripheral audio-vestibular system**

The cochlea transforms the mechanical energy conducted by the outer and middle ear into neural impulses and this is done by the sensory hair cells embedded in the basilar membrane within the Organ of Corti. Hence, cochlear function depends on the structural integrity of the hair cells. The normal human cochlea has roughly 12,000 outer hair cells (OHCs) and 4000 inner hair cells (IHCs). With excessive noise exposure, the cochlea undergoes a variety of physical changes, such as broken tip links between OHCs stereocilia, loss of contact between the stereocilia and the tectorial membrane, swelling of the auditory nerve fibres and reduction in cochlear blood flow (Henderson and Hamernik, 1995). Because OHCs have high metabolic activity associated with electromotility, they are more vulnerable to damage compared to IHCs. Hence, the primary cochlear site of lesion following significant noise exposure is death of OHCs (Henderson et al., 2006). As noise exposure continues and hearing loss progresses, additional damage to IHCs and auditory nerve fibres occurs. When OHCs are damaged due to intense noise exposure, they do not regenerate and a permanent sensorineural hearing loss results. Initial damage to the OHCs tends to occur in the basal turn of the cochlea which corresponds to the frequency region of 3 to 6 kHz (Clark and Bohne, 1999). The damage appears first, and most often, for the 4 kHz frequency region and is shown in the audiogram as a dip or notch commonly known as the *Audiometric Notch or Noise Notch* (McBride and Williams, 2001a; McBride and Williams, 2001b). The 4 kHz notch tends to be considered as a benchmark for noise exposure. However, the notch could be seen as well at other frequencies, such as 3 or 6 kHz (Coles et al., 2000). The exact location of the notch depends on the frequency of the damaging noise and the length of the ear canal (Shotland, 1996).

There are several acoustic variables that make sound potentially damaging to the inner ear. The leading factor is the sound intensity level. In other words, the higher the noise level, the more damage would be expected to take place in the cochlea. The other

contributing factor to noise damage is the length of noise exposure, in that the longer the length of noise exposure, the more noise damage is expected to occur in the cochlea. Hence, the level and the length of noise exposure are the two most important key variables to consider in estimating the amount of noise damage. The rate of NIHL is greatest during the first 12 years of exposure and it slows down as the hearing loss progresses (Rosenhall et al., 1990). In addition, the spectrum of the sound influences cochlear noise damage. The fact that the basal turn of the cochlea is most sensitive to sound makes high frequency sounds more damaging to the cochlea compared to low frequency sounds. Experimental animal studies have shown that regardless of the frequency content of the noise exposure, long-term, constant or steady-state noise has a more detrimental effect on the cochlea compared to short-term or intermittent noise of a similar sound intensity level (Ward, 1991; Pourbakht and Yamasoba, 2003).

As mentioned earlier, the most common manifestation of noise-induced peripheral damage is Noise-induced Hearing Loss (NIHL). NIHL is usually characterized by a slowly progressive hearing loss that develops from repeated exposure to noise over time. Early physical changes in the cochlea as a result of noise exposure result in a reversible sensorineural hearing loss, commonly known as Noise-induced Temporary Threshold Shift (NITTS) and in most cases, these cochlear changes are not permanent and the hearing threshold returns to the pre-exposure baseline (Wang et al., 2002). In NITTS, hearing thresholds begin to decline after minutes to hours from noise exposure and might continue to decline for about 12 to 24 hours. However, the recovery time of NITTS might be several weeks, depending on the initial noise exposure severity. If the recovery from NITTS is incomplete, which is often caused by long-term repeated exposure to moderately intense noise levels of roughly 75 to 78 dB(A) to 132 dB pSPL, then hearing thresholds stabilize at an elevated level, resulting in an irreversible sensorineural hearing loss commonly known as Noise-induced Permanent Threshold Shift (Lieberman and Dodds, 1984).

Another picture of noise damage commonly seen is when the ear encounters a single, sudden and intense acoustic event (e.g. blasts, such as explosions, gun/rifle shooting and hunting), that can also cause damage to the auditory system and result in a very similar kind of hearing loss usually, referred to as *Acoustic Trauma*. However, the clinical picture of acoustic trauma is quite different from NIHL. Acoustic trauma is characterized by a marked sudden decrease in hearing sensitivity resulting in an audiogram with a 4 kHz notch or a steeply sloping high frequency hearing loss. In most instances, the damage caused by acoustic trauma is irreversible. Additional auditory effects associated with noise exposure include tinnitus, hyperacusis, aural fullness and muffled speech. More information about NIHL and acoustic trauma can be found in [Sliwinska-Kowalska and Davis \(2012\)](#). Although both NIHL and acoustic trauma have significant effect on individuals' auditory mechanism, the focus of this review is only on NIHL because in most circumstances, the noise exposure sound field is typically diffused and sudden extremely high acoustic events leading to acoustic trauma happen only in special less frequent situations.

Numerous studies have attempted to describe the mechanism of noise-induced cochlear damage and there is a general consensus in the literature that the mechanism of noise-induced cochlear damage falls into two main categories: direct mechanical damage and metabolic damage in the cochlea. Mechanical damage, which is commonly seen in acoustic trauma, causes direct and substantial physical disruption of structural elements in the Organ of Corti. Noise-induced mechanical damage can affect a wide range of cochlear structures, such as the OHCs, IHCs, supporting cells and tectorial membrane. In severe cases, this mechanical damage can cause massive destruction, leaving holes in the cochlear partition, allowing the perilymph and endolymph to mix. However, noise-induced metabolic damage is more likely to occur during and following long-term noise exposure leading to NIHL. Metabolic damage produces potentially toxic reactions and induces cell death. Several investigations showed that metabolic overstimulation in the inner ear can lead to the release of reactive oxygen species and toxic free radicals caused by ischemic mechanisms, glutamate excitotoxicity and endogenous antioxidant system reduction resulting in mitochondrial damage, membrane lipid per-oxidation, neural apoptosis and release of pro-apoptotic factors

causing cell death (Henderson et al., 1994; Ohlemiller et al., 1999; Yamashita et al., 2004). A comprehensive review of the cellular basis of NIHL, anatomical effects of noise exposure and the role of oxidative stress in hair cell death can be found in Henderson et al. (2006).

In addition, animal studies showed that the underlying mechanism giving rise to NITTS and NIHL is markedly different (Nordmann et al., 2000; Wang et al., 2002). Noise-induced permanent threshold shift results from destruction of cochlear hair cells or damage to mechano-sensory hair bundles (Liberman and Dodds, 1984). Other forms of damage have been also observed following noise-induced permanent threshold shift, such as focal loss of hair cells especially IHCs and corresponding nerve fiber degeneration (Nordmann et al., 2000). In contrast, there is no hair cell death, both inner and outer, in NITTS. Instead, other changes have been reported, such as swelling of cochlear nerve terminals at hair cell synapse giving rise to glutamate excitotoxicity (Spendlin, 1971; Liberman and Mulroy, 1982; Robertson, 1983), collapsed pillar cells and detachment of OHC stereocilia from the tectorial membrane (Nordmann et al., 2000). As mentioned previously, a full recovery from decreased hearing after NITTS within 24 or 48 hours and of a maximum by 2 to 3 weeks is possible and this notion has been accepted for many years. Some experiments even showed that most swollen cochlear nerve terminals in noise-exposed guinea pigs degenerate then regenerate within a few days (Puel et al., 1998; Pujol and PUEL, 1999). However, this possible full recovery from NITTS without any adverse consequences has been called into question by further recent animal studies done on mice. Kujawa and Liberman (2006) found that a complete reversible NITTS may leave the noise-exposed ear with long-term nerve degeneration. The study showed that noise exposure caused loss of spiral ganglion cells and the cell bodies of the cochlear afferent neurons contacting hair cells and this could occur several months post-exposure and can progress for years. The findings of this study also suggest that spiral damage caused by noise exposure early in life made mice more susceptible to age-related hearing loss. A subsequent study by the same authors demonstrated similar findings (Kujawa and Liberman, 2009). The study was done also on mice models and found that acoustic overexposure causing moderate, but completely reversible threshold elevation, might cause acute loss of approximately 50

% of the auditory nerve terminals and delayed degeneration of the cochlear nerve, even if cochlear hair cells remain and recover normal function. Similar findings were observed in noise-exposed guinea pigs (Lin et al., 2011). Hence, the findings of the above discussed animal studies suggest that noise-exposed ears, which suffered from NITTS might develop a diffused neuronal loss despite the presence of normal functioning OHCs and restored normal behavioural thresholds and if this is likely to be common to all mammalian ears, then it would be expected to happen as well in noise-exposed human ears. These observations are important as they indicate that reversible changes in the human ear resulting from excessive noise exposure might lead to irreversible peripheral neurodegeneration. This peripheral damage is well-known to affect signal processing at higher cortical levels and ultimately cause problems in difficult listening situations, where speech signals are often compromised by background noise levels.

A second important and adverse consequence of noise exposure is the possibility of damage to the vestibular structures in the inner ear. An extensive number of studies have demonstrated noise-induced vestibular damage in animal models. One of the first experimental studies which provided histological evidence of vestibular damage in animal models following noise exposure was the one carried out by McCabe and Lawrence (1958). The investigators of this study observed a collapse of the saccule and a destruction of otoconia and otolithic membrane in noise exposed guinea pigs. The study also showed that semicircular canals and utricle were unaffected. However, a subsequent study done by Mangabeira-Albernaz et al. (1959) showed that the effect of noise on the vestibular system of guinea pigs was seen in all vestibular system structures. Ylikoski (1987) found damage in the cochlea and vestibular organs of guinea pigs after exposing them to impulse noise (rifle shots) presented at 158 dB SPL. Ylikoski reported that the damage was mostly observed in the crista of the ampulla and in the utricular and saccular maculae. Another group of investigators extended Ylikoski's work and re-examined the effect of impulse noise on the vestibular system in rats (Perez et al., 2002). The rats were exposed to ten gunshots generating impulse noise at high intensity levels of approximately 160 dB SPL. The rats were evaluated using auditory brainstem response (ABR) and VEMPs at different times (2 to 4 hours, 1 week and 6 weeks) post-exposure. The study findings revealed absent and elevated ABR responses

and a significant reduction in amplitude and latency prolongation of VEMP responses, which suggest cochlear and vestibular noise damage. The study concluded that intense impulse noise exposure caused clear functional damage to the vestibular end organs, mainly the otolith organs, in rats.

Some investigations went one step further and examined the effect of different noise characteristics (i.e. noise type: steady state/continuous, intermittent/impulsive, duration of noise exposure) on the vestibular system. For example, [Hsu et al. \(2008\)](#) looked at the effect of continuous broadband white noise presented at 115 dB SPL on the peripheral auditory and vestibular systems of guinea pigs using cVEMP and ABR. The study classified the guinea pigs into three groups: 1) the short-term noise exposure group (N = 15, duration of noise exposure = 30 minutes) 2) the long-term noise exposure group (N= 9, duration of noise exposure = 40 hours) and 3) the control group (N = 2, no noise exposure). The study found that 70 % of the ears, which had short-term noise exposure had temporary cVEMP loss which recovered in 90 % of ears within two days. Likewise, 97 % of the short-term noise exposure group had temporary threshold shifts in ABR immediately after exposure, which were resolved within four days. In contrast, ten days following noise exposure, 78 % of the long-term noise exposure group had permanent cVEMP loss and 83 % of them had ABR threshold shifts. Interestingly, morphological examination of the short-term noise exposure group revealed intact hair cells, supporting cells, saccular macula, otolith membrane and vestibular nerve fibres. In contrast, marked changes (i.e. signs of distribution and atrophy in cell bodies of hair cells in the saccular macula) were observed in the long-term noise exposure group. Hence, the experimental findings of Hsu's study not only provided evidence for saccular damage due to long term noise exposure in guinea pigs, but also suggested that the exhibited temporary or permanent functional loss in the saccule following noise exposure may reflect temporary or permanent threshold shifts in hearing.

A similar study found that after exposing guinea pigs to continuous noise (4 kHz octave band) presented at 120 dB SPL for 6 hours, the following morphological changes were noted: degeneration of the epithelial cells and separation of their layers, marked crystalolysis (the dissolution or disruption of cells) and stromal cell apoptosis (a process



of death in connective tissue cells)(Akdogan et al., 2009). In the same study, a second group of guinea pigs were exposed to intermittent noise presented at the same level (120 dB SPL) for 12 hours. While similar morphological changes were noted in the intermittent noise exposure group, the changes were less obvious in this group compared to the continuous noise exposure group. In brief, the literature has provided substantial evidence for noise-induced damage to animals' vestibular system and the above discussed investigations have attempted to clarify where and how noise induces damage in the vestibular system. There is an agreement that noise-induced vestibular damage occurs mainly in the otolith organs, specifically the saccule. However, the exact mechanism by which noise affects the vestibular system and results in this damage is still unclear. Because the cochlea and the vestibular system both share a common arterial blood supply, it has been suggested that hypoxia due to noise exposure may induce metabolic changes in both cochlear and vestibular mechanisms, leading to noise-induced cochlear and vestibular damage (Fetoni et al., 2009). Hence, from an anatomical and physiological point of view, the close proximity of the saccule to the cochlea and to the stapes footplate, which is the entrance point of sound energy, makes the saccule prone to damage from noise (see Figure 1.2). This all supports the supposition that the noise levels which can cause damage to the cochlea may also affect the vestibular system, particularly the saccule. For the same reasons outlined above, it is likely that the mechanism of noise-induced vestibular damage might greatly resemble that of noise-induced cochlear damage. Finally, the established evidence of saccular origin to cVEMP response and the derived evidence of noise-induced vestibular damage from animal experimental studies all suggest that saccular damage demonstrated by abnormal cVEMP responses could indicate possible noise-induced saccular dysfunction.

With regard to noise-induced vestibular dysfunction in humans, several early investigations demonstrated that noise-exposed patients presenting with NIHL had vestibular disturbances (Dickson and Chadwick, 1951; Man et al., 1980; Kemink and Graham, 1985; Ylikoski et al., 1988). Subsequent studies demonstrated that people affected by long-term noise exposure, in addition to their cochlear damage, had vestibular abnormalities (Kilburn et al., 1992; Manabe et al., 1995). For example, Kilburn's study found hearing loss and balance deficits indicated by body sways

measures in 78 noise-exposed construction workers. In Manabe's study, 36 NIHL patients with and without vertigo complaints were evaluated using electrocochleography and caloric testing. The study found reduced caloric responses and increased summing potential/action potential ratio in the NIHL patients with vertigo complaints. In a more recent study, [Golz et al. \(2001\)](#) reported abnormal findings in videonystagmography and vestibular symptoms in 258 Israeli veterans presenting with history of occupational noise exposure. However, the abnormal findings of this study were reported only in subjects with asymmetrical hearing loss.

Conversely, some studies found that the vestibular findings (i.e. body sway measures) of individuals affected by NIHL were similar to those of controls ([Era and Heikkinen, 1985](#); [Juntunen et al., 1987](#); [Era, 1988](#); [Pyykkö et al., 1989](#)). The fact that these studies utilized either ocular-motor tests, caloric testing or postural control measures, most of which are not significantly affected by otolith dysfunction and this might explain why results were controversial across these studies. In addition, the evidence that noise exposure had no apparent effect on semicircular canal function explains also why the use of routine vestibular measures was probably not helpful to identify noise-induced vestibular lesions in the studies discussed above and in more recent studies ([Wuyts et al., 2007](#); [Lang and McConn Walsh, 2010](#)). The fact that cVEMP originates from the same vestibular structure, which is most likely to be damaged by noise exposure (i.e. the saccule), makes cVEMP an appropriate diagnostic tool to evaluate noise-induced vestibular damage. The following two sections (1.7.3 and 1.7.4) review the common diagnostic test procedures available to evaluate NIHL and the investigations which have used cVEMP to diagnose noise-induced saccular dysfunction.

### 1.7.3 Assessment of noise-induced auditory dysfunction

*Pure Tone Audiometry (PTA)* is routinely carried out to diagnose NIHL. NIHL usually expresses itself by a typical pure tone audiogram. Figure 1.5 shows an example of a typical audiometric configuration for early NIHL. The classical NIHL audiogram shows an elevation of thresholds in the high frequency region between 3 and 6 kHz with better hearing at 2 kHz and below and at 8 kHz and above (i.e. audiometric notch). NIHL usually progresses over 10 to 15 years of noise exposure and the progression of hearing loss tends to slow down thereafter. At early stages, the hearing loss is usually around 40 to 60 dB HL and with further noise exposure, hearing loss might extend to lower and higher frequencies, so the audiometric notch becomes deeper and broader, and the degree of hearing loss might exceed 60 dB HL.

As hearing loss worsens, the noise-exposed individual starts to have speech discrimination difficulties in quiet and noisy situations. Usually hearing loss in NIHL occurs in both ears. However, the degree and configuration of hearing loss might not necessarily be equal (i.e. symmetrical) between the two ears especially if the noise exposure conditions favoured one side of the head more than the other. Then asymmetrical hearing loss would occur. A common example of this condition occurs in rifle or gun shooting, where the device is closer to one ear than the other. It is also possible to have a sudden asymmetrical hearing loss in cases of acoustic trauma where the sound blast affects the ear closest to the explosion (Shupak et al., 1993; Van Campen et al., 1999; Hoffer et al., 2010).

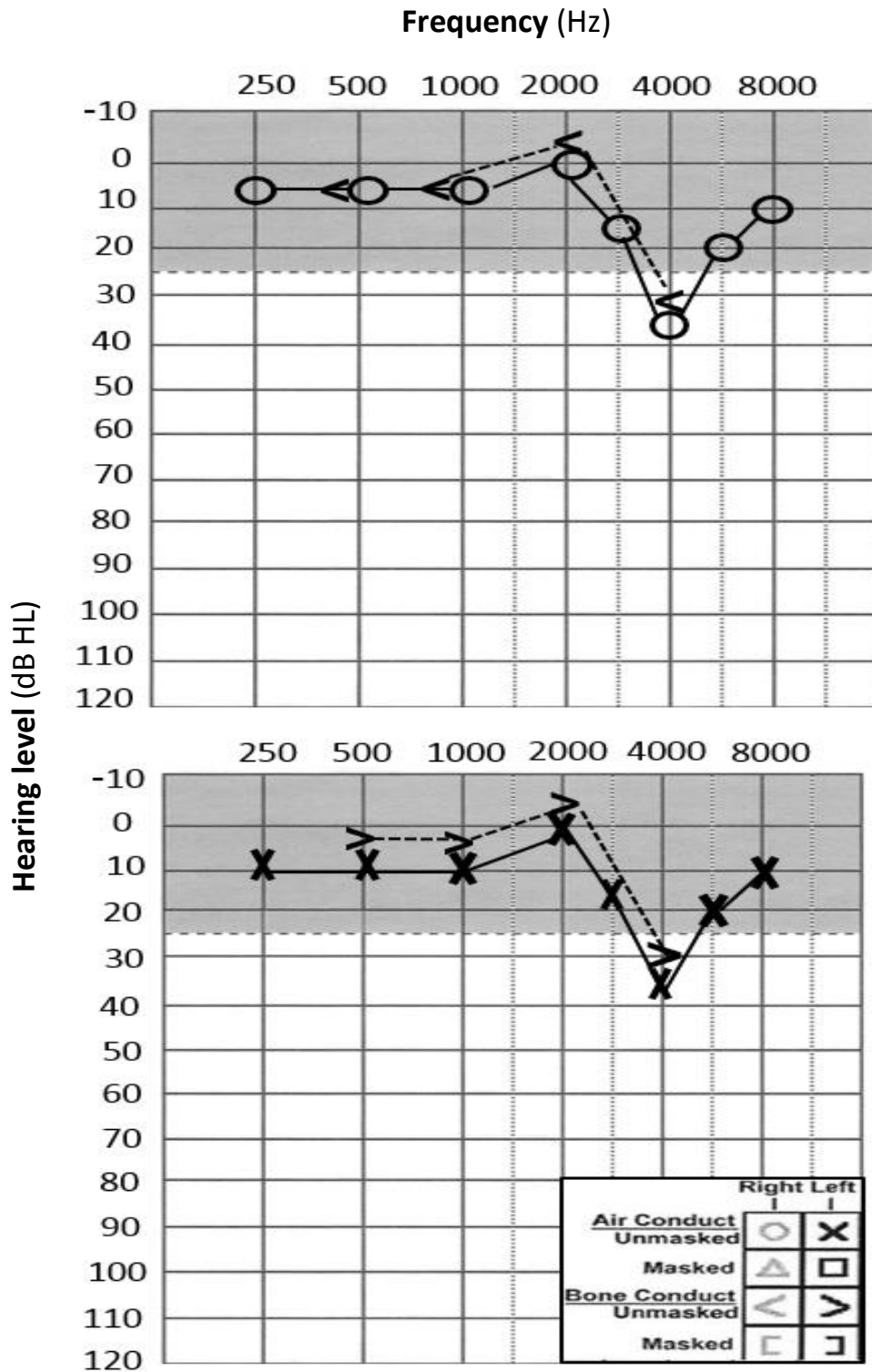


Figure 1.5 Typical audiometric configuration for early noise-induced hearing loss (NIHL).

In conventional PTA procedure, behavioural thresholds in response to pure tone stimuli are obtained for frequencies between 0.25 and 8 kHz. However, since NIHL mostly affects high frequencies ( $\geq 4$  kHz), sometimes this routine audiometry fails to identify the hearing loss if it occurs beyond 8 kHz. Thus, other procedures have been suggested in the literature to improve the early diagnosis of NIHL. For example, *High Frequency Pure Tone Audiometry* which is also referred to as *Extended High Frequency Audiometry* involves testing at additional higher frequencies (i.e. 10 kHz, 12 kHz, 14 kHz and 16 kHz) compared to the routine PTA. A number of reports showed that high frequency audiometry is more sensitive than the conventional PTA and thus, could be useful in the early detection of NIHL (Ahmed et al., 2001a; Porto et al., 2003; Mehrparvar et al., 2011). Although high frequency audiometry is currently being utilized in some clinical settings, conventional PTA is still the standard means of diagnosing NIHL in most clinics.

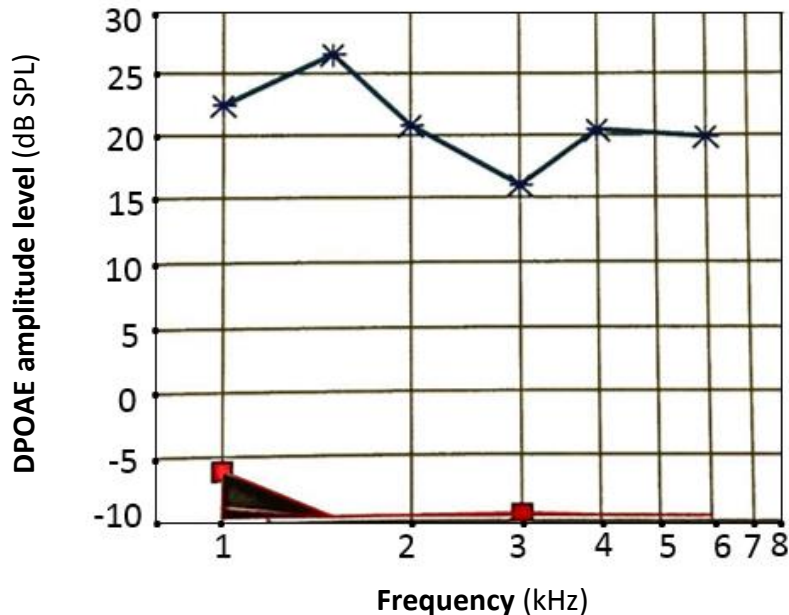
An appropriate alternative procedure to behavioural audiometric testing to detect NIHL in its early stages is *Otoacoustic Emissions* (OAEs) (Miller and Marshall, 2007). OAEs are low level signals that can be recorded by a sensitive microphone placed in the external auditory canal. OAE is a non-invasive objective procedure that reflects the integrity of the cochlea, mainly the OHC function. Loss of IHC does not appear to affect the presence of OAE (Liberman et al., 1997). While behavioural thresholds reflect the status of the entire peripheral auditory system, OAEs involve a wide range of stimulus frequencies and are by-products of the displacement of sensory hair cells at the basilar membrane. OAEs can be recorded only if the OHCs which correspond to OAE stimulus frequency are intact. The presence of robust OAE responses indicates normal OHC function. Correspondingly, normal hearing individuals exposed to excessive amounts of noise tend to have lower OAE than those who also have normal hearing but without such exposure. Hence, OAE may be potentially used to predict susceptibility to future noise-induced cochlear damage (Griest and Bishop, 1998).

*Distortion Product Otoacoustic Emissions* (DPOAEs) are a sub-type of OAEs, and are a product of a non-linear intermodulation between two pure tones inside the cochlea which then generates several new acoustic frequency components travelling in the ear canal and are picked up by a miniature microphone mounted in an ear canal probe

(Kemp, 2002). Since DPOAE will be used in one of the studies described in this thesis, a general and brief introduction about DPOAE measurement is provided here. DPOAEs are responses generated when the cochlea is stimulated simultaneously by two pure tone frequencies called "primaries". The frequencies of the primaries are conventionally designated as " $f_1$ " and " $f_2$ " ( $f_1 < f_2$ ). The intensity levels used for the primaries are usually 55-65 dB SPL ( $L_1 = 65$ ,  $L_2 = 55$  dB SPL) and the frequency separation of the two primaries described as the  $f_2/f_1$  ratio, which influences the DPOAE level, is also specified ( $f_2/f_1$  ratio = 1.2). For the intermodulation DPOAE component to be generated, the  $f_1$  and  $f_2$  have to be close to each other. The interaction of these two primaries at the basilar membrane in the cochlea results in a cochlear output at other discrete frequencies, which are mathematically related to the frequencies of the primaries. Then DPOAE can be measured using narrowband filtering centered at the frequency of interest. The cochlea then generates a long series of components, which are not present in the input stimuli, and these components are called *Distortion Product (DP)*. The most commonly measured DP component in clinical practice is  $2f_1-f_2$ . The  $2f_1-f_2$  DPOAE has the largest level in human and other mammalian normal hearing ears compared to other DPOAEs (Harris et al., 1989; Gaskill and Brown, 1990).

Hence, DPOAEs measured in the ear canal are a combination of energy from a non-linear distortion component, which originates at the region of overlap between the two primaries, and a reflection component originating from the region of the DPOAE frequency. For clinical purposes, DPOAE amplitudes are plotted as a function of the primary tone frequency (the most commonly used is  $f_2$  frequency) and the resulting graph is called a "DP-gram". Figure 1.6 is an example of a DP-gram obtained from an adult left ear with normal cochlear function. Further information about DPOAE measurement can be found in Dhar and Hall (2011). DPOAEs are preferable to use compared to the other sub-type of OAEs (i.e. Transient-evoked Otoacoustic Emissions "TEOAEs") because they permit testing for higher frequency regions in the cochlea up to 6 kHz and can be measured in ears with greater hearing loss (Axelsson and Sandh, 1985; Post and Dickerson, 2010; Lee, 2012). DPOAE is currently being utilized in clinical diagnosis and monitoring of patients suffering from noise exposure because it is capable of detecting early noise-induced cochlear changes before they become evident in

routine PTA. Several advantages have been identified for OAE. First, it is an objective test that does not require the patient's behavioural participation, whereas audiometry is a subjective behavioural test that requires a considerable amount of cooperation from the patient. Second, OAE procedure is faster to perform and does not require testing in a sound-treated room like PTA. Hence, OAEs have been proposed as early indicators of NIHL in industrial and military settings (Marshall and Heller, 1998; Miller et al., 2006). However, OAEs are likely to be absent or reduced in amplitude with insufficient stimulus level, greater than mild to moderate hearing losses (i.e. 15 to 40 or 45 dB HL) and abnormal outer or middle ear function (Hall, 2000). When combining PTA and OAE results to diagnose NIHL, it is important to highlight that the literature has shown variable results regarding the consistency between the two procedures. While some reports demonstrated the existence of an association between DPOAE and/or TEOAE and PTA thresholds in cases of NIHL (Reshef et al., 1993; Attias et al., 1995; Attias et al., 1998), the established level of association was variable, ranging from poor to moderate. Thus, the precise relationship between PTA and OAE is not yet clear.



**Figure 1.6** Example of DPOAE measured from the left ear canal of a 30 years old normal-hearing adult using DP-gram. DP-gram represents DPOAE amplitude levels in dB SPL as a function of the primary tone frequency ( $f_2$ ). The top line with crossed symbols indicates DPOAE level measured in dB SPL and the bottom shaded area with square symbols indicate noise levels in dB SPL.

#### **1.7.4 Assessment of noise-induced saccular dysfunction by cervical vestibular evoked myogenic potentials (cVEMP)**

cVEMP has been utilized in both animal and human studies to investigate the possibility of vestibular damage as a result of excessive noise exposure. As explained earlier, evidence from neurophysiologic studies of animals suggests that the saccule is the area in the vestibular system most likely affected as a result of excessive noise exposure. However, the extent of this damage cannot be assessed by most routine vestibular measures, because they do not evaluate otolith function. On the other hand, because cVEMPs appear to originate from the saccule and inferior vestibular nerve and are independent of cochlear integrity, it has been suggested as a potential technique to explore noise-induced vestibular dysfunction. A limited number of investigations used cVEMP to investigate noise-induced saccular damage in patients affected by NIHL (Wang et al., 2006; Wang and Young, 2007; Wu and Young, 2009; Kumar et al., 2010; Akin et al., 2012; Tseng and Young, 2013). Although most of these studies reported that cVEMP abnormalities in NIHL patients were in the form of absent responses, delayed P1/N1 latencies and reduced response amplitude, the cVEMP characteristics reported by these studies were variable.

Although anatomic and physiologic similarities between the cochlea and the vestibular system support potential damage of the vestibular system secondary to NIHL and the literature indicates a relationship between noise-induced cochlear damage and noise-induced saccular damage measured by cVEMP, the mechanism or the order of damage between the two systems are not yet known. In other words, it is still unknown if vestibular dysfunction as a result of noise only occurs in conjunction with cochlear damage or NIHL. The possibility that saccular dysfunction occurs before cochlear damage or hearing loss as indicated by routine clinical testing also has not been investigated yet. In order to address this, the audio-vestibular function of individuals with and without cochlear damage or hearing loss due to noise exposure is investigated in this thesis using cVEMP as a measure of saccular function and PTA and DPOAE as measures of cochlear function.



In summary, the evidence of saccular abnormality in individuals affected by NIHL is gradually growing in the literature. Nevertheless, the present evidence is still controversial. A great part of this is due to the fact this vestibulopathy has been largely overlooked in favour of the noise effects on hearing. As indicated at the start of this chapter, including patients' perspectives in the overall process of vestibular assessment is critical. Given that vestibular dysfunction can significantly affect balance control, which is well-known to have adverse effects on individuals' quality of life, a detrimental effect of noise on vestibular function should be investigated. The following section reviews current investigations which have employed self-reported data to investigate possible vestibular disturbances in individuals affected by noise exposure.

#### **1.7.5 Assessment of noise-induced audio-saccular dysfunction using self-reported data**

A number of authors have demonstrated the importance of using self-reported data with individuals affected by noise exposure (Bogoch et al., 2005; Jokitulppo et al., 2006a; Widén et al., 2006; Holmes et al., 2007; Rawool and Colligon-Wayne, 2008). Self-reported data obtained from noise-exposed individuals could include a wide variety of useful information, such as the auditory effects, noise associated symptoms like tinnitus, perception and awareness of potential noise hazards, personal experiences in noisy worksites, estimations of noise exposure levels and attitudes towards hearing protection (Scherer et al., 2007; Hong et al., 2008a; Muhr and Rosenhall, 2010; Hoffer et al., 2010). All this information is useful to know because it helps to understand how much noise has an impact on individuals' life. This information is needed also to design and implement hearing conservation programmes in areas with potential noise hazards. Furthermore, integration of self-reported data with data obtained from diagnostic measures, such as pure tone audiometry and direct physical noise measurements could facilitate the clinical diagnosis of noise-exposed patients and also improve our understanding of the underlying manifestations of noise exposure.

Although few data have been collected in terms of noise-induced vestibular symptoms (Golz et al., 2001; Cassandro et al., 2003; Atmaca et al., 2005; Akin et al., 2012;

Raghunath et al., 2012), the evidence of noise-induced saccular damage is gradually emerging through cVEMP studies. If saccular abnormality evident by abnormal cVEMP has been documented, then it should act similarly to other peripheral vestibular abnormalities and manifest itself as subjective symptoms reported by these individuals as disequilibrium or imbalance. However, the reported incidence of vestibular symptoms with or without the existence of NIHL in these studies was highly variable (16 to 60 %) and the symptoms were not clearly described. Some of these studies, in addition to reporting vestibular symptoms from NIHL cases, demonstrated saccular damage as well by cVEMP (Cassandro et al., 2003; Akin et al., 2012). Nevertheless, the majority of these studies reported only the presence or absence of vestibular symptoms without discussing or describing the symptoms in details probably because they did not use a detailed questionnaire to obtain information on the symptoms. In addition, these studies did not provide details on how these symptoms might be indicative of saccular damage and how they might be differentiated from other otolith lesions (i.e. utricle lesions) or semicircular canal lesions. Thus, these studies discussed noise-induced vestibular symptoms in general without relating them to saccular damage.

A study found that approximately half (49 %) of their investigated participants with asymmetrical NIHL reported noise-induced vestibular symptoms Akin's et al. (2012). The symptoms most commonly reported by their participants were lightheadedness followed by imbalance and then vertigo. The low reported incidence of vertigo in this study is consistent with intact semicircular canal function in noise-exposed individuals. A similar finding was obtained by Farrell and Rine (2014). In this study, 14 patients suffering from vestibular symptoms due to variable vestibular pathologies were investigated using several vestibular procedures including cVEMP. The study found that patients with abnormal otolith function did not report any rotatory symptoms. It should be noted that the otolith dysfunction involvement in the participants of this study was not related to noise. Although it would be expected that all otolith organs' dysfunctions would behave similarly and produce similar (non-rotary) symptoms, until the literature describes symptoms specifically reported by individuals diagnosed with noise-induced saccular dysfunctions (cVEMP abnormalities), this remains an assumption that needs further investigation. Furthermore, because the possibility of saccular dysfunction

before or without the involvement of cochlear damage or NIHL has not been determined yet, then the existence of such pathology should be explored as well. This was demonstrated by [Raghunath et al. \(2012\)](#). The investigators in this study looked at the frequency of vestibular symptoms among 20 factory workers with a history of long-term occupational noise exposure, work-related physical activity and no NIHL using dizziness questionnaires. The study revealed normal PTA findings, reduced TEOAEs, vestibular symptoms and tinnitus in the investigated group. However, the identified vestibular symptoms in this study cannot be attributed to saccular damage because saccular function testing (i.e. cVEMP) was not done. Thus, given the research gaps demonstrated in the literature discussed above, the present thesis aimed to investigate vestibular symptoms, particularly those related to saccular damage, in noise-exposed individuals with and without NIHL in more depth.

## **1.8 Summary**

Although the use of cVEMP has been advocated to evaluate saccular function, the high variability in cVEMP amplitude measures has been a limitation in clinical interpretation of cVEMP data. Several approaches have been described in the literature to overcome SCM muscle contraction variability during cVEMP recording. However, the effects of these approaches on cVEMP response parameters were examined in separate studies with different protocols and different groups. A comparison of all the available methodologies to control cVEMP amplitude variability has not been done in one single study. Consequently, the available data are controversial and unclear. Hence, there is a need to conduct a study that compares cVEMP data in a normal population utilizing all these methodologies. Adding cVEMP testing to the existing vestibular test batteries has expanded investigators' understanding of otolith lesions including noise-induced saccular dysfunction. Although the close proximity and the anatomic similarity between the auditory system and the vestibular system supports the existence of a relationship between NIHL and noise-induced saccular damage, only few studies have examined cVEMP characteristics among noise-exposed individuals. Despite that the order of damage between cochlear dysfunction or NIHL and saccular dysfunction resulting from noise exposure is still unknown, all the available cVEMP data were collected only from

cases of NIHL and no systematic data have been collected yet from noise-exposed individuals without cochlear damage or NIHL. Thus, the possibility that developing early saccular dysfunction as a result of noise exposure before cochlear damage or hearing loss needs further exploration. Furthermore, the associated symptoms resulting from this noise-induced vestibulopathy have not been investigated yet. The available studies did not discuss noise-induced symptoms in relation to their potential site of damage (i.e. saccular damage) either because no cVEMP data were obtained in the same study or simply because the assessment tools used did not include enough questions to allow detailed descriptions of these symptoms. Thus, the purpose of the present thesis is to overcome these research gaps by exploring saccular damage and symptoms among noise-exposed individuals with and without cochlear damage or hearing loss.

### **1.9 Aim of the work described in this thesis**

Whilst the weight of the arguments presented in this chapter indicates that saccular dysfunction, demonstrated by abnormal cVEMP findings, is evident in individuals affected by NIHL, only few studies have described the characteristics of cVEMP response parameters in such a population. Furthermore, most of the existing studies did not use the optimal cVEMP protocol to control amplitude variability, which might have accounted for the inconsistency among these studies. The possibility of an early saccular dysfunction without noise-induced cochlear damage or before it becomes evident in PTA or OAE has not been investigated yet. There is also very limited data on vestibular symptoms associated with such vestibulopathy. After consideration of the available literature, the aim of the work described in this thesis was to address the overarching research question: *“Does noise exposure affect vestibular function?”*. Thirteen hypotheses were derived from this question. Since cVEMP is the only available clinical test to evaluate saccular function, it is necessary to ensure that the selected methodology to record cVEMP is an optimal one before using it to examine the other hypotheses. Thus, the optimal methodology to stabilize cVEMP amplitude data are examined in the following chapter – Chapter 2. The findings obtained in Chapter 2 served as the basis of the cVEMP protocol used in Chapter 3. Three hypotheses were tested in Chapter 2:

- i. If both biofeedback methods (BPM and EMGM) are equally effective in controlling SCM muscle contraction variability in cVEMP testing, then there will be no difference in cVEMP response parameters (P1 absolute latency, N1 absolute latency and P1-N1 peak to peak amplitude) obtained by these two biofeedback methods.
- ii. The combined use of both a biofeedback method (BPM or EMGM) and an amplitude normalization technique will stabilize cVEMP inter-aural amplitude variability and produce lower inter-aural amplitude asymmetry ratios (IARs).
- iii. The combined use of both a biofeedback method (BPM or EMGM) and an amplitude normalization technique will stabilize cVEMP inter-subject amplitude variability and produce lower standard deviation (SD) values.

To examine these hypotheses, cVEMP data were obtained from a large number of normal individuals using two biofeedback methods (BPM and EMGM) and one data analysis technique (amplitude normalization). cVEMP responses were obtained under several testing conditions and response parameters were contrasted across testing conditions. The core experimental study needed to examine the major thesis question "*Does noise exposure affect vestibular function?*" is presented in Chapter 3. The three main hypotheses tested in Chapter 3 were:

- i) If noise exposure affects saccular function, then cVEMP findings of noise-exposed individuals with NIHL would demonstrate:
  - a) A higher abnormal/absent cVEMP rate compared to those obtained from individuals with normal audio-vestibular function without a history of noise exposure (controls).
  - b) A longer P1 latency compared to those obtained from controls.
  - c) A longer N1 latency compared to those obtained from controls.
  - d) A reduced P1-N1 peak to peak amplitude compared to those obtained from controls.
- ii) If long-term noise exposure can cause early vestibular dysfunction and cVEMP is sensitive to detect such damage, even if noise-exposed individuals still have normal hearing evident by routine clinical testing, then, *noise-exposed individuals with normal hearing (NH group)* would demonstrate:
  - a) A higher abnormal/absent cVEMP rate compared to those obtained from controls.
  - b) A longer P1 latency compared to those obtained from controls.
  - c) A longer N1 latency compared to those obtained from controls.
  - d) A reduced P1-N1 peak to peak amplitude compared to those obtained from controls.

iii) Because the literature has provided evidence for noise-induced saccular damage mainly in individuals with NIHL, it can be hypothesized that noise-exposed individuals with documented NIHL are more likely to develop noise-induced saccular damage compared to noise-exposed individuals with normal hearing (NH group). Hence, the *NIHL group* would demonstrate:

- a) A higher abnormal/absent cVEMP rate compared to those obtained from the noise-exposed NH group.
- b) A longer P1 latency compared to those obtained from the noise-exposed NH group.
- c) A longer N1 latency compared to those obtained from the noise-exposed NH group.
- d) A reduced P1-N1 peak to peak amplitude compared to those obtained from the noise-exposed NH group.

To examine these hypotheses, cVEMP responses were collected from noise-exposed individuals with and without cochlear damage or NIHL and then results were compared with routine auditory function test results (PTA and DPOAE) to gain a full picture of the overall effect of noise exposure on the audio-vestibular system. In Chapter 4, the frequency and nature of vestibular symptoms reported from the noise-exposed individuals with normal hearing (NH group) and those with hearing loss (NIHL group), who were enrolled in the study described in Chapter 3, were investigated. The possibility of a relationship between the diagnostic test results obtained in Chapter 3 and the self-reported data obtained in Chapter 4 was also examined. The study reported in Chapter 4 also included an estimation of the cumulative noise exposure gained during the whole of the noise-exposed individual's personal lifetime. Hence, seven hypotheses were examined in Chapter 4:

- i. If vestibular dysfunction is related to noise exposure, then *the noise-exposed NIHL group* will report vestibular symptoms which reflect saccular dysfunction as a result of noise exposure.
- ii. If vestibular dysfunction is related to noise exposure and this occurs before hearing loss is detected by PTA, then *the noise-exposed group with normal hearing (NH group)* will report vestibular symptoms which reflect saccular dysfunction as a result of noise exposure.
- iii. If noise-induced audio-vestibular dysfunction can express itself as audio-vestibular manifestations, then an association would be expected between the self-reported

- audio-vestibular symptoms, reported in Chapter 4 and their (a) PTA findings (b) DPOAE findings (c) cVEMP findings, reported in Chapter 3.
- iv. If self-reported audio-vestibular symptoms are related to noise exposure, then an association would be expected between the self-reported audio-vestibular symptoms data and participants' estimated lifetime cumulative noise exposure data, reported Chapter 4.
  - v. If the identified audio-vestibular dysfunction is related to noise exposure, then a relationship would be expected between the hospital technicians' estimated lifetime cumulative noise exposure data, reported in Chapter 4 and their (a) PTA thresholds (b) DPOAE amplitudes (c) cVEMP response parameters, reported in Chapter 3.
  - vi. If the identified audio-vestibular dysfunction is related to noise exposure, then a relationship would be expected between the soldiers' estimated lifetime cumulative noise exposure data (rifles/machine guns), reported in Chapter 4 and their (a) PTA thresholds (b) DPOAE amplitudes (c) cVEMP response parameters, reported in Chapter 3.
  - vii. If the identified audio-vestibular dysfunction is related to noise exposure, then a relationship would be expected between the soldiers' estimated lifetime cumulative noise exposure data (light artillery/explosives), reported in Chapter 4 and their (a) PTA thresholds (b) DPOAE amplitudes (c) cVEMP response parameters, reported in Chapter 3.

To test these hypotheses, self-reported symptoms associated with noise exposure were obtained from the same noise-exposed sample investigated in Chapter 3. The exact rationale and reasoning for each of the above listed hypotheses are provided in the corresponding chapters. Although each of the three studies presented in Chapters 2, 3 and 4, was designed to test a particular research question, the overall data presented in these studies, will be combined and interpreted to determine the extent to which noise exposure can account for the observed abnormalities revealed by variable subjective and objective test procedures. In each of these chapters, the results are presented and discussed in relation to the specific hypothesis being assessed. In the last chapter (Chapter 5), the conclusions and the implications of the findings of each study are discussed together in relation to the primary research question.

## **Chapter 2**

**Cervical Vestibular Evoked Myogenic Potentials (cVEMP):  
determination of an optimal biofeedback method and  
data analysis technique using the head rotation-sitting  
procedure**



## 2.1 Introduction

The present chapter sets out the first experimental work of this thesis. It describes a study aimed at identifying the optimal methodology to control SCM muscle contraction variability in cVEMP testing using the head rotation-sitting (HR-S) as the muscle activation procedure. The chapter starts with an overview of the factors affecting cervical vestibular evoked myogenic potentials (cVEMPs) with focus on the recording methods and data analysis techniques available to control cVEMP amplitude variability. The literature which has compared cVEMP data across different methodologies is also reviewed. The literature review ends with identifying the research aim of the experimental work described in this chapter along with the hypotheses statements. This is followed by reporting the findings of the first study of this thesis.

## 2.2 Effect of sternocleidomastoid muscle contraction level on cervical vestibular evoked myogenic potential

cVEMPs are short latency EMG responses evoked by high level air conducted signals delivered to the ear. They are a product of a brief inhibition of the continuous EMG activity and therefore only present during sternocleidomastoid (SCM) muscle contraction and absent if the muscle is at rest (Colebatch et al., 1994a; Lim et al., 1995; Bath et al., 1998; Akin et al., 2004). cVEMP response is recorded from tonically contracted SCM muscles via surface electrodes. cVEMP measures the saccule-collic reflex and the response presence is dependent upon the integrity of the saccule and the inferior vestibular nerve (Colebatch and Halrnagyi, 1992; Colebatch et al., 1998; Colebatch and Rothwell, 2004; Wit and Kingma, 2006). As mentioned in Chapter 1 (section 1.6.4), the cVEMP response is influenced by a number of stimulus and recording parameters, such as stimulus type, stimulus mode, stimulus frequency and age. Because the cVEMP response is an inhibitory myogenic response, one of the major factors affecting it, particularly amplitude measure, is the level of muscle contraction. Over the last few years, cVEMP is increasingly being used as a clinical test of otolith function. Although the bi-phasic waveform (P1-N1) response in normal population has been extensively described in the literature over the last decade, utilizing amplitude measures

in clinical interpretation of cVEMP can be problematic, because it often becomes hard to distinguish between reduced cVEMP amplitude responses due to insufficient muscle contraction and those reduced due to vestibular pathology. As a result of this large amplitude variability, diagnostic interpretation of cVEMP response is typically based on whether the response is present or absent or on amplitude comparisons between the two ears, commonly known as the inter-aural amplitude asymmetry ratio (IAR). Calculation of IAR was described in Chapter 1 (section 1.6.3, Equation 1.1). Thus, in order to accurately interpret cVEMP findings using amplitude measure, it is vital to account for SCM muscle contraction levels during cVEMP recordings. The following section describes in details the methods and techniques developed to reduce the effect of SCM muscle contraction on cVEMP amplitude variability.

### **2.3 Methodological approaches to control the effect of sternocleidomastoid muscle contraction level on cVEMP amplitude variability**

Since SCM muscle contraction is a pre-requisite to obtain a cVEMP response, appropriate positioning of subjects to allow for muscle activation is an essential step in cVEMP recording. It has been shown that the procedure of activating SCM muscle has a significant effect on cVEMP response parameters (Meyer et al., 2015). In view of this, an attempt should always be made to achieve adequate muscle contraction during cVEMP recording by selecting an appropriate muscle activation procedure. As previously explained in Chapter 1 (section 1.6.4), the HE (supine) procedure has revealed the most robust cVEMP amplitudes (Zapala and Brey, 2004; Wang and Young, 2006; Isaradisaikul et al., 2008; Ozdek et al., 2009; McCaslin et al., 2013). However, the supine procedures require greater physical exertion by the patient because they involve lifting the head

from the supine position in contrast to the procedure administered in the sitting position and thus, are frequently associated with discomfort and muscular fatigue (Wang and Young, 2006; Isaacson et al., 2006; Bogle et al., 2013). The use of the supine procedures may also be contraindicated for many individuals with neck and back problems. Conversely, it has been shown that the HR-sitting (HR-S) procedure was more comfortable for patients to perform and demonstrated excellent test-retest reliability in normal subjects (Tseng et al., 2013). A subsequent study found that the HR-S procedure was the most appropriate testing procedure to obtain cVEMP responses evoked by tone burst stimuli in 60 normal subjects because it revealed the highest amplitude values compared to the HE (supine) procedure (Sánchez-Andrade et al., 2014).

Although the best procedure to activate SCM muscle during cVEMP testing remains undetermined, it seems that the literature favours the use of the HR-S procedure. However, because of limited studies done in this area, the optimal procedure to activate the SCM muscle in cVEMP testing has not been confirmed yet. A further approach to ensure sufficient and, importantly, consistent muscle contraction, is self-monitoring of muscle contraction levels through the use of a visual biofeedback mechanism. Visual biofeedback methods help the subject monitor the amount of muscle contraction to ensure equal muscle tension is exerted on both sides and between test sessions. The following sub-sections (2.3.1 and 2.3.2) provide more details about the two most commonly used visual biofeedback methods in cVEMP testing; Electromyogenic Monitoring (EMGM) Method and Blood Pressure Manometer (BPM) Method.

### 2.3.1 Visual biofeedback methods

#### *a) Electromyogenic monitoring (EMGM) method*

The use of EMGM method during cVEMP recording requires direct measurement and monitoring of the background EMG activities through an EMG monitor (Colebatch and Halrnagyi, 1992). The method is based on the assumption that if cVEMP amplitude is influenced by EMG level (Colebatch et al., 1994a; Lim et al., 1995; Welgampola and Colebatch, 2001a; Welgampola and Colebatch, 2001b; Akin et al., 2004), then achieving a constant EMG level during cVEMP recording should result in more stable cVEMP amplitude measurements across sides and between several recordings from the same side. In order to directly record and monitor EMG level from SCM muscles, special equipment may have to be used (i.e. a stand-alone EMG recording system) and an extra electrode placement has to be attached to the muscles while recording cVEMP (Wu et al., 1999; Todd et al., 2000; Cheng and Murofushi, 2001a; Murofushi, 2001; Akin et al., 2011b). Alternatively, an EMG recording feature is sometimes incorporated in the evoked potential recording system which performs cVEMP measurements (i.e. Interacoustics Eclipse evoked potential system) so simultaneous monitoring of EMG activities is performed during cVEMP recording. An EMG monitor display is shown on the same window as of the VEMP recording. The target EMG level is commonly shown between two markers which are usually colour coded. Both the tester and the subject can view the screen and the subject is asked to monitor the EMG level through the cVEMP recording screen and to adjust effort to maintain a level within a specified target EMG range (Akin et al., 2003; Akin et al., 2004; Ito et al., 2007; Wang et al., 2008). The experimental setup to perform EMGM method during cVEMP recording is shown in Figure 2.1.

In view of the known relationship between surface EMG levels and SCM contraction levels, the EMGM method has gained great attention from investigators. This method was used in conjunction with different SCM muscle activation procedures: HE (supine) (Wu et al., 1999; Cheng and Murofushi, 2001a; Murofushi, 2001; Young and Kuo, 2004; Su et al., 2004; Murofushi et al., 2004; Wang and Young, 2004; Murofushi et al., 2005; Wu et al., 2007); HR (supine) (Wu and Murofushi, 1999; Sheykholeslami et al., 2001; Murofushi et al., 2004; Murofushi et al., 2005) and HR-S (Murofushi et al., 2001; Takegoshi and Murofushi, 2003; Basta et al., 2005b; Lee et al., 2008b; de Oliveira Barreto et al., 2011; Akin et al., 2011b). These reports employed the EMGM method as the only means to control SCM contraction levels and reported reliable and repeatable cVEMP responses. However, these studies did not investigate the effectiveness of applying the EMGM method itself in cVEMP testing to stabilize or reduce cVEMP amplitude variability.

The only study the author is aware of that has evaluated the use of EMGM method in cVEMP testing was the one done by Isaradisaikul et al. (2008). In this study, the investigators examined the test-retest reliability of cVEMP responses in 20 normal subjects using the HR (supine) procedure applied in two testing conditions (with and without EMGM method). The study demonstrated similar cVEMP findings in both conditions and concluded that using the HR (supine) procedure without any monitoring method was as effective as using the EMGM method. However, the study had several limitations, such as the use of small sample size and a disproportionate ratio of male and female subjects (males = 6, females = 14). As explained in Chapter 1 (section 1.6.4), because limited data are available on the influence of gender on cVEMP response parameters, it would be sensible for investigators to include an approximately equal number of males and females until the effect of gender on cVEMP data is clarified.

Furthermore, the study also indicated that one of their participants was excluded from the study because he/she had no cVEMP in the second session without providing an explanation of why the response was absent in the second session but present in the first session.



**Figure 2.1 cVEMP recorded from participant's right ear using electromyogenic monitoring (EMGM) method.** The Figure shows cVEMP obtained using the HR-sitting (HR-S) procedure (the participant is turning the head to the contralateral shoulder "left side" to contract the right SCM muscle). The participant monitors his EMG level on the screen and asked to adjust muscular effort to maintain a level within a specified target EMG range. A red bar demonstrates that the applied muscular contraction is not sufficient and the participant is not reaching the target EMG level. A green bar demonstrates sufficient muscular contraction and that the participant is reaching the target EMG level.

***b) Blood pressure manometer (BPM) method***

The BPM method is similar to the EMGM method in that it is a biofeedback method which requires the subject to use a certain tool to monitor the muscle contraction level during cVEMP testing. However, the technology that allows simultaneous monitoring of EMG activity while performing cVEMP is still not readily available in many standard clinical settings and therefore, there was a need to establish an alternative readily available tool. Thus, the BPM method was developed by [Vanspauwen et al. \(2006a\)](#). The BPM method only requires a simple blood pressure manometer with a hand-held cuff. This piece of equipment is affordable and readily available in most clinical settings. The subject sits comfortably in a chair and holds a hand-held pre-inflated blood pressure cuff between the jaw and the hand and presses against it (not squeezing it) to increase the muscle tension while turning the head to one side (away from the test ear to the contralateral shoulder) to watch the BPM (Figure 2.2). The pushing task will increase the pressure applied to the cuff and this will increase the contraction of the contralateral SCM muscle. During muscle contraction, the subject is instructed to maintain a pre-determined target level throughout cVEMP recording and can monitor the target on the BPM screen during testing. Inflating the blood pressure cuff to a 20 mmHg is usually enough to obtain a cushion to push against. It is important to note here that in order to apply this method, the SCM muscle should be activated only by the HR-S procedure because practically, this method cannot be performed with the subject in a supine position (i.e. HR/supine OR HE/supine). Therefore, every time the BPM method is mentioned, the reader should assume that the HR-S procedure was used.

In addition, the tester can monitor how the subject is performing and provide re-instructions to apply more or less muscular effort as needed in order to maintain the target. The BPM method requires clear instructions to the subject and often the tester needs to re-position the subject's head, chin and hand to achieve the appropriate position. Training prior to actual recording and rest breaks between recordings are recommended because participants need to be comfortable while performing the test and training prior to actual recording allows them to find the most comfortable position. The experimental setup to perform the BPM method during cVEMPs testing is shown in Figure 2.2. The BPM method was first described by [Vanspauwen et al. \(2006a\)](#). In this

study, the effect of BPM method use on cVEMP inter-aural amplitude variability (differences between the right and left ears) was evaluated in two groups of healthy adults (group 1 = 15 subjects, group 2 = 12 subjects). cVEMP data were obtained from both groups with and without the use of the BPM method, so one group used the method and the other group did not. The investigators of this study also aimed to examine if EMG levels measured just before cVEMP recording can be used as an indicator of EMG activity levels during recording. Results showed statistically non-significant differences between EMG levels obtained before and during cVEMP testing with the use of the BPM method. Findings also revealed that cVEMP amplitude variability was significantly reduced with the application of the BPM method. Overall, the study findings supported that the use of the BPM method during cVEMP testing facilitated constant SCM contraction levels throughout testing and thus, suggested that this method could be used to improve cVEMP inter-aural amplitude reliability. Despite these findings, it is not possible to conclude definitively from this study that the biofeedback method was solely responsible for the reduced amplitude variability because the biofeedback-no biofeedback comparison data were obtained from two different test groups.

A subsequent investigation of the BPM method was carried out by [Vanspauwen et al. \(2006b\)](#). cVEMPs were obtained from 15 healthy subjects with the use of the BPM method using a range of cuff pressures (30, 40 and 50 mmHg). Differences in amplitude data between these three test conditions were examined. The study revealed no left-right cVEMP amplitude differences for all the three cuff pressures. The study suggested that a minimum cuff pressure of 40 mmHg which indicates a minimum SCM contraction level is required to evoke cVEMP responses in normal population. The study concluded that although the BPM method helped to yield comparable right and left cVEMP



amplitudes in study subjects, amplitude differences between the two sides will still exist in cVEMP measurements due to anatomical and biological differences between the two sides. Although the study re-supports the usability of the BPM method in cVEMP testing, it still does not provide evidence whether this method is optimal to control cVEMP amplitude variability, because no comparison was made with other methods, such as the EMGM method.



**Figure 2.2 cVEMP recorded from participant's right ear using the blood pressure manometer (BPM) method.** The Figure shows cVEMP obtained using head rotation-sitting (HR-S) procedure (the participant is turning head to the contralateral shoulder "left side" to contract right SCM muscle). The participant is wearing the inflated blood pressure cuff on the left hand and pushing the cuff against the jaw and cheek while monitoring the muscle contraction level through the cuff pressure needle at the BPM screen.

Vanspauwen et al. (2006a; 2006b) originally demonstrated that it is possible to keep the SCM muscle contraction level fairly constant with the use of the BPM method. Nevertheless, a subsequent report by the same group of investigators suggested that applying the same cuff pressure on both sides while performing the BPM method in cVEMP testing does not necessarily result in the same contraction level (Vanspauwen et al., 2009). The study suggested that it is difficult to interpret possible right-left ear amplitude differences if the cVEMP procedure did not involve a direct measure of SCM muscle contraction levels like the EMGM method. A further examination of the BPM method was carried out by Suh et al. (2009). The investigators in this study compared cVEMP data across three testing conditions (with the use of BPM method, HR-S procedure alone and HR-supine procedure alone). The study showed that the condition which revealed the highest cVEMP amplitude was the HR (supine) procedure alone condition. The study also showed that although the IAR data were the same for all the three tested conditions, cVEMP data obtained using the BPM method demonstrated the lowest IAR values, with smaller variations compared to other conditions. The study demonstrated as well that cVEMP data obtained with the HR (supine) procedure alone condition correlated well with the BPM method condition data. In contrast, cVEMP data obtained in the HR-S alone condition had a poor correlation with the cVEMP data obtained in the other conditions. Therefore, the study suggested the application of a biofeedback method in cVEMP testing whenever the HR-S procedure is used.

As explained previously in Chapter 1 (section 1.6.4), the muscle tension resulting from rotating the head is obviously less than that obtained by elevating the head. Therefore, although the HE (supine) procedure might be able to produce the highest amplitude data, it does not necessarily result in stabilized IAR data. On the other hand, the BPM method condition used in Suh's study resulted in a reduced IAR data compared to the

data obtained without applying any biofeedback method and this suggests that the application of a biofeedback method like BPM could result in robust cVEMP amplitude data without compromising the stability of IAR measures. Several other studies have reported the successful use of BPM method while recording cVEMP responses from normal individuals in various age groups (Maes et al., 2009; Janky and Shepard, 2009; Maes et al., 2010; Tourtillott et al., 2010). However, none of these studies examined the effect of the BPM method on cVEMP amplitude variability. Hence, the majority of published studies included the BPM or the EMGM method in their cVEMP protocol without investigating the effect of these methods on reducing cVEMP amplitude variability or whether it is the optimal method or not.

### **2.3.2 Amplitude normalization technique**

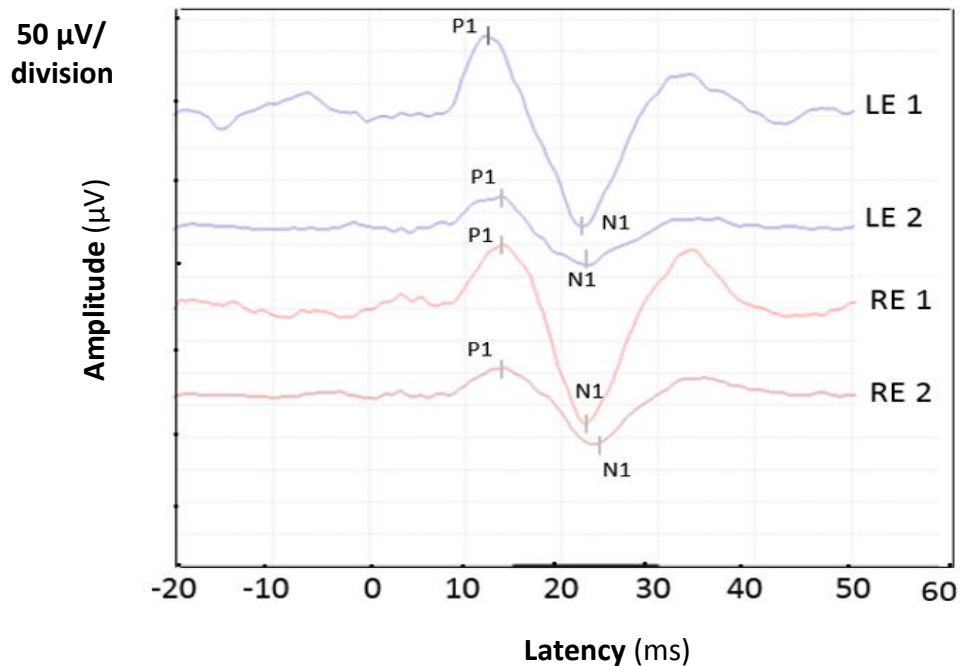
It may be that an EMG recording and monitoring feature is not available or subjects are incapable of producing approximately equal amounts of muscular effort from the right and left SCM muscles due to, for example, differences in muscular integrity between the two sides or fatigue. In this case, a third approach has been suggested which involves recording EMG activity (similar to the EMGM method) but without visual monitoring of EMG levels. Instead, suitable evoked potential recording equipment can be set up to automatically perform a mathematical correction to “normalize” the cVEMP waveform and quantify right/left sides amplitude differences and between-subject variations. This technique is commonly known as *Amplitude Normalization or Amplitude Correction* (Colebatch et al., 1994a; Welgampola and Colebatch, 2001b). In this technique, the background EMG activity estimate is recorded and then the mean rectified activity (the root mean square amplitude value) is measured over a pre-stimulus interval of 20 ms.

This value, known as the *Pre-stimulus EMG Estimate*, is then averaged and used to normalize the raw non-normalized amplitude to produce the *Normalized Amplitude*. The new normalized waveform, which is the normalized amplitude value, is expressed as a ratio and is the product of the following calculation:

$$\text{cVEMP normalized amplitude} = \frac{\text{P1-N1 non-normalized amplitude}}{\text{Pre-stimulus EMG estimate}} \quad (\text{Equation 2.1})$$

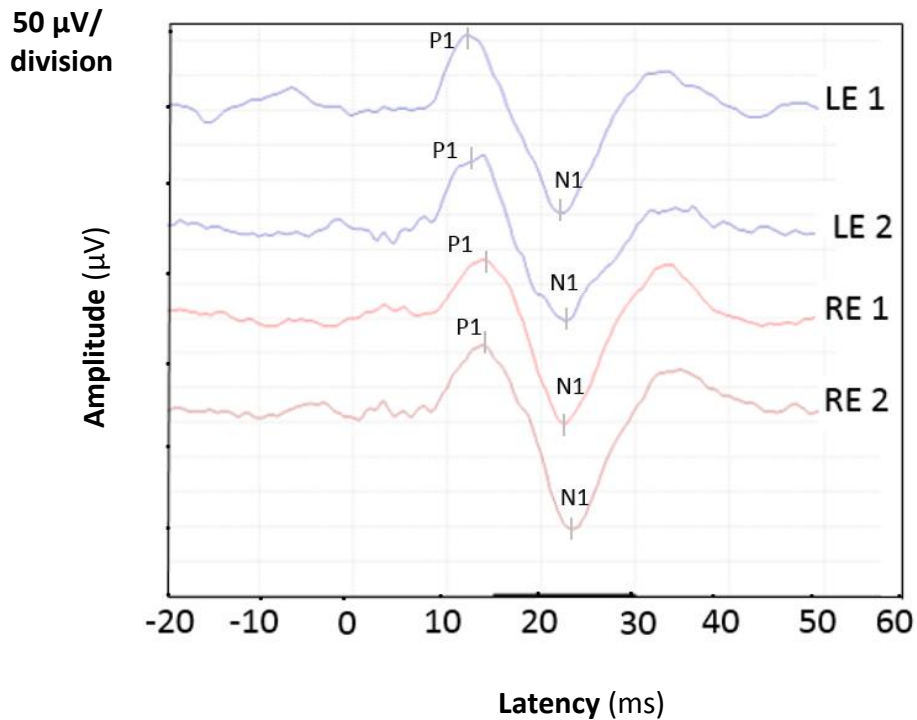
Some researchers (Colebatch et al., 1994a; Colebatch and Rothwell, 2004) hold that the amplitude normalization technique decreases amplitude variability arising from changes in muscle contraction over time, allowing better comparison of within and between subject's data. It is important to note here that the two amplitude parameters are expressed in different units and thus, their values should not be directly compared; the non-normalized amplitude is expressed in microvolts ( $\mu\text{V}$ ) and the normalized amplitude is expressed as a ratio. Alternatively, IARs calculated from each parameter (i.e. normalized and non-normalized IAR) can be calculated and then compared. Studies that have used amplitude normalization in cVEMP testing (Colebatch et al., 1994a; Ochi et al., 2001; Colebatch and Rothwell, 2004; Lee et al., 2008a) describe two ways to calculate the normalized amplitude. In the first calculation, the averaged pre-stimulus EMG is rectified as a noise estimate. Then this pre-stimulus estimate is divided into the signal-averaged peak to peak cVEMP amplitude, creating the cVEMP normalized amplitude value. In this calculation, cVEMP normalized amplitude is expressed against averaged pre-stimulus EMG providing an estimated signal to noise ratio (SNR) for the recording (Lee et al., 2008a). SNR is a measure used to compare the level of a desired signal to the level of background noise and is defined as the ratio of signal power to the noise power, often expressed in decibels (dB).

In the second calculation, real time simultaneous collection of both rectified and unrectified EMG recordings is conducted then the pre-stimulus section of the rectified epoch (root mean square "RMS" amplitude value) is averaged to create the pre-stimulus EMG estimate. In contrast, in the first calculation, the mean pre-stimulus EMG estimate is calculated for all epochs included in the average. The pre-stimulus EMG estimate is then divided into the signal-averaged peak to peak amplitude to generate the normalized cVEMP value (Colebatch et al., 1994a; Ochi et al., 2001; Colebatch and Rothwell, 2004). So in the second calculation, cVEMP amplitude is expressed as a proportion of the averaged amount of rectified pre-stimulus EMG activity performed during the average. The second calculation is more commonly reported and is known as the *Normalized Amplitude*. Figures 2.3 and 2.4 show differences in cVEMP responses obtained twice for a single individual using non-normalized then normalized amplitude recordings. The large difference obtained for test-retest non-normalized amplitude measurement for the same subject shown in Figure 2.3 is most likely caused by variability in muscle contraction levels between the first and the second recordings of the same ear. In Figure 2.4, this large amplitude variability observed between recordings of the same ear diminished after the non-normalized amplitude was divided by the pre-stimulus EMG estimate or, in other words, the application of amplitude normalization technique.



LE 1 & RE 1: the first recorded waveforms	LE 2 & RE 2: the second recorded waveforms
LE: left ear (blue traces)	RE: right ear (red traces)

**Figure 2.3 Normal cVEMP response waveforms obtained twice for a single individual without amplitude normalization.** The first (LE 1 & RE 1) and the second (LE 2 & RE 2) waveforms were obtained in response to 500 Hz tone burst stimuli presented at 95 dB nHL without amplitude normalization. The responses are repeatable (1 & 2) such that the responses are present with similar latencies. However, amplitude varies (first waveforms showed higher non-normalized amplitude values compared to second waveforms) resulting in high test-retest cVEMP amplitude variability for the same person. Note that the four waveforms were recorded under the same stimulus and recording conditions. *The figure was modified and taken from the Eclipse Platform Operation Manual (EP 25, software version 4.3.0.1.7, Page 3.45) after permission from Interacoustics (Interacoustics, Assens, Denmark).*



<b>LE 1 &amp; RE 1:</b> the first recorded waveforms	<b>LE 2 &amp; RE 2:</b> the second recorded waveforms
<b>LE:</b> left ear (blue traces)	<b>RE:</b> right ear (red traces)

**Figure 2.4 Normal cVEMP response waveform obtained twice for a single individual using amplitude normalization.** The first (LE 1 & RE 1) and the second (LE 2 & RE 2) waveforms were obtained in response to 500 Hz tone burst stimuli presented at 95 dB nHL using amplitude normalization. After taking into account the mean level of pre-stimulus background EMG activity as a baseline, the four recorded cVEMP responses become approximately even, resulting in significantly reduced variability for test-retest cVEMP amplitude measurements for the same subject. Note that the four waveforms were recorded under the same stimulus and recording conditions. *The figure was modified and taken from the Eclipse Platform Operation Manual (EP 25, software version 4.3.0.1.7, Page 3.46) after permission from Interacoustics (Interacoustics, Assens, Denmark).*

Although the use of amplitude normalization with cVEMP testing has been reported by several investigations, the exact effect of this technique on cVEMP amplitude variability is not yet clear. For example, test-retest variability of cVEMP response parameters responses was evaluated in 10 normal subjects using click stimuli, the HR-S procedure and amplitude normalization (Ochi et al., 2001). The study compared non-normalized with normalized amplitude data and found that the normalized responses did not significantly reduce cVEMP intra-subject (test-retest) variability. The investigators suggested that it is not necessary to adjust cVEMP raw amplitude data using this technique, especially if the subject is able to attain sufficient muscle contraction effort during recording. Another study examined both normalized and non-normalized cVEMP data from 70 healthy adults ranging in age from 25 to 85 years (Welgampola and Colebatch, 2001a). Although the investigators of this study reported both normalized and non-normalized IARs, differences between the two measures were not tested statistically and the effect of normalized data on cVEMP amplitude variability (both inter-subject and intra-subject variability) was not examined. The study only showed that cVEMP non-normalized amplitudes were less reproducible and produced wider ranges compared to normalized data.

Bogle et al. (2013) looked at the effects of using amplitude normalization on cVEMP amplitude and IAR variability in 10 healthy adults between the ages of 25 and 61. cVEMP responses were collected at three muscle contraction levels (maximum, moderate and minimum) measured by pre-stimulus EMG estimates. The study found that the relationship between cVEMP amplitude and muscle contraction was not always proportional. Rather, for most cases, when muscle contraction increased, the normalized amplitude increased and then once the pre-stimulus EMG estimate reached a certain threshold, cVEMP amplitude rapidly increased and then saturated. It was observed also in this study that increasing the level of muscle contraction will reduce the signal to noise ratio (SNR) which adds to amplitude variability. The study suggested that the EMG levels needed to achieve maximum contraction level, the range of EMG values and the point of saturation varied across sides for every subject and across subjects. The findings of this study also supported the importance of controlling muscle contraction variability across sides before applying this technique. The authors of



Bogle's study explained that amplitude normalization technique was unable to alter their results significantly because this technique is based on the assumption that cVEMP amplitude and muscle contraction levels have a perfect linear relationship and their study results violated this assumption.

Following on that, [Kim et al. \(2013\)](#) conducted a similar study where they examined the effect of amplitude normalization on IARs in 20 normal subjects. cVEMP responses were collected and IARs were compared across three different muscle contraction levels. To create the three muscle contraction levels, participants were asked to rotate their heads while lying supine (HR-supine procedure) and follow three head location point targets on the ceiling (0°, 15°, 30° and 45°). The study found that amplitude normalization was able to correct the muscle contraction variability across sides only if the IAR fell between  $\approx 23$  to 45 %. In other words, the study found that if IAR values were below or above this range, this technique had no apparent effect on cVEMP data. The study concluded that although amplitude normalization could help to overcome cVEMP amplitude variability across sides, the technique is not perfect and does not work well in every case, especially if differences in muscle contraction levels are very high. Considering the findings obtained by both Bogle's and Kim's studies, it seems that the IAR limit specified by Kim's study, where amplitude normalization was found useful, might reflect the cVEMP amplitude saturation observed in Bogle's study. Because it is difficult to predict the exact amount of muscle contraction asymmetry each subject will demonstrate and also the point of amplitude saturation for every single person, it eventually becomes difficult to predict how the amplitude normalization will behave.

To summarize, although a number of studies utilized the amplitude normalization technique in cVEMP recording in an effort to stabilize amplitude measures between sides and between different test sessions for the same subject, it is still unclear how much this technique influences cVEMP results. Part of this uncertainty arises also from the difficulty of conducting an accurate comparison among the existing studies because of the methodological differences. However, all of the above mentioned studies, including Bogle's and Kim's studies, used only amplitude normalization without applying any other method to control cVEMP amplitude variability (i.e. biofeedback method).

Hence, the present study will investigate the influence of the amplitude normalization technique by comparing cVEMP non-normalized and normalized amplitude data in normal population while at the same time controlling potential amplitude side variability by using a biofeedback method.

## **2.4 Comparison of cVEMP data obtained by different methodological approaches to control cVEMP amplitude variability**

The research that describes and compares several methodological approaches (SCM muscle activation procedures, biofeedback methods and amplitude normalization technique), devised to control SCM muscle contraction variability is limited. To the best of the author's knowledge, only three investigations have done such a comparison. The first study was carried out by [Lee et al. \(2008a\)](#). In this study, the investigators compared mean IAR data for 22 normal subjects obtained in four testing conditions (1 = no method, only HR-supine procedure, 2 = HR-supine with amplitude normalization, 3 = only BPM method, 4 = both BPM and amplitude normalization). Findings showed that IAR data were similar across the two non-normalized conditions (conditions 1 and 3). However, statistically significant differences were noted between non-normalized and normalized IAR data (conditions 1, 3 and 2, 4) as well as between the two normalized IAR data (conditions 2 and 4). The study concluded that normalized cVEMP data resulted in more reliable IAR and supported the importance of choosing an appropriate SCM muscle activation procedure. However, the study did not discuss the influence of the BPM method on non-normalized and normalized IAR data. Lee's and colleagues findings implied that if no biofeedback method was used while activating SCM muscle during cVEMP recording, muscle variation across sides would likely result. Normalizing amplitude data would lower the IAR in this case, because the muscle contraction asymmetry between the two sides is high. On the other hand, less muscle variation across sides occurred with the use of the BPM method and that is probably why the amplitude normalization technique in this condition did not reveal any statistically significant differences.

The second study was conducted by [McCaslin et al \(2013\)](#). In this study, cVEMP responses were obtained by activating the SCM muscle while the subject was in a semi-recumbent position with head turned away from the stimulated ear and elevated at the same time (combined HR/HE). cVEMP responses and IAR ratios were calculated under four testing conditions (1 = control condition/no method, 2 = EMGM method, 3 = amplitude normalization, 4 = both EMGM and amplitude normalization). The study found that IAR data for all subjects were not altered with the use of visual targets (i.e. EMGM) or amplitude normalization technique, which was consistent with the previous findings of [Lee et al. \(2008a\)](#). Thus, both McCaslin's and Lee's studies were in line with the earlier work of [Ochi et al. \(2001\)](#) mentioned in the previous section (section 2.3.2). The non-linear relationship between cVEMP amplitude and EMG Levels demonstrated in [Bogle et al. \(2013\)](#) and [Kim et al. \(2013\)](#) studies provided a reasonable explanation of why amplitude normalization technique is not always able to stabilize cVEMP amplitude or IAR.

The third study was carried out by [McCaslin et al. \(2014\)](#). In this study, the effect of amplitude normalization on cVEMP data of 20 normal subjects was examined using the HR (supine) procedure and the EMGM method to control SCM muscle variability. Both normalized and non-normalized data were obtained at various EMG levels. The study revealed that the growth function of cVEMP amplitude and EMG levels was not always linear, which is again in agreement with the findings of [Bogle et al. \(2013\)](#). However, McCaslin's study showed that normalized amplitude data did not change significantly with changes in EMG levels, whereas non-normalized amplitude level resulted in a significant increase when EMG levels were increased. The unpredicted and imprecise relationship between cVEMP amplitude and background EMG activities is the most likely source of variability between these studies. Thus, the available evidence regarding the effect of amplitude normalization on reducing cVEMP amplitude variability is still unclear and further investigation of this area is required to justify its use in cVEMP testing.

## **2.5 Summary**

There is a general consensus in the literature that in order to obtain reliable recordings and utilize amplitude measures in cVEMP clinical interpretation, it is critical to ensure sufficient SCM muscle contraction and control contraction variability during cVEMP recording. Although several methodologies have been described in the literature, limited data are available on the effectiveness of using these methods/techniques in reducing cVEMP amplitude variability. Although the biofeedback methods seem to be acceptable and attractive tools to use with subjects, it is currently unknown how much these methods affect inter-subject and intra-subject cVEMP amplitude variability. The same is true for amplitude normalization. While several studies showed that using this technique was effective in reducing cVEMP amplitude variability, others have shown that it had no effect on cVEMP data. Thus, the existing data provide no strong evidence to reject or strongly favour one method/technique to control cVEMP amplitude variability over the other. Although some studies have attempted to compare cVEMP data established by these methodologies, these studies have either looked at a single methodology or compared one or two of them. To the best of the author's knowledge, no study has conducted a comparison of cVEMP data for all of these methodologies (EMGM, BPM and amplitude normalization). The experimental work described in this chapter is the first one to provide such a comparison. Thus, the aim of the present study was to determine the optimal biofeedback method and data analysis technique in cVEMP testing using HR-S as SCM muscle activation procedure.

## **2.6 Aim of the work described in this chapter**

Whilst the weight of the arguments presented earlier in this chapter supports the need for controlling the variability of SCM muscle contraction levels during cVEMP recording and although a number of methodologies have been described in the literature, it is not clear yet which methodology is optimal. Hence, the aim of the study described in this chapter was to identify the optimal biofeedback method and data analysis technique for cVEMP using HR-S as a muscle activation procedure. Based on the current cVEMP literature, the optimal biofeedback method and data analysis technique will be one that

meets one or more of the following criteria: (a) demonstrates higher cVEMP non-normalized and/or normalized amplitude and EMG levels (b) results in the greatest reduction of cVEMP intra-subject amplitude variability by demonstrating lower cVEMP inter-aural amplitude asymmetry ratios (IARs) (c) results in the greatest reduction of cVEMP inter-subject amplitude variability by demonstrating lower standard deviation (SD) values.

First, it was hypothesized in this study that since both biofeedback methods involve monitoring the level of EMG and EMG activities, which are related to cVEMP amplitude levels, then a difference in cVEMP response parameters measured in this study (P1 absolute latency, N1 absolute latency and P1-N1 peak to peak amplitude) would not be expected. Second, since the design and the setup of both biofeedback methods (BPM and EMGM) facilitate the production of constant SCM contraction levels across the two tested sides (right ear and left ear) and because the amplitude normalization technique is believed to correct muscle contraction variability across sides arising from changes in muscle contraction over time, then it was hypothesized that the combined use of both biofeedback methods (BPM or EMGM) and amplitude normalization will stabilize cVEMP inter-aural amplitude variability and produce lower IARs. Third, these methods (biofeedback methods) and techniques (amplitude normalization) are expected to give more uniform amplitude levels, not only between sides but also between subjects. It was therefore hypothesized that the combined use of these methods and this technique will reduce the expected large inter-subject cVEMP amplitude variation obtained from the study's cohort when measured by standard deviation (SD). The following is a summary list of this study's hypotheses:

- i. If both biofeedback methods (BPM and EMGM) are equally effective in controlling SCM muscle contraction variability in cVEMP testing, then there will be no difference in cVEMP response parameters (P1 absolute latency, N1 absolute latency and P1-N1 peak to peak amplitude) obtained by these two biofeedback methods.
- ii. The combined use of both, a biofeedback method (BPM or EMGM) and an amplitude normalization technique will stabilize cVEMP inter-aural amplitude variability and produce lower inter-aural amplitude asymmetry ratios (IARs).

- iii. The combined use of both, a biofeedback method (BPM or EMGM) and an amplitude normalization technique will stabilize cVEMP inter-subject amplitude variability and produce lower SDs.

To examine these hypotheses, cVEMP data were obtained from a large number of healthy individuals using the HR-S as a SCM muscle activation procedure and two biofeedback methods (BPM and EMGM) in combination with and without one data analysis technique (amplitude normalization). cVEMP response parameters were compared across all testing conditions (EMGM/non-normalized amplitude, EMGM/normalized amplitude, BPM/non-normalized amplitude and BPM/normalized amplitude). Findings obtained in this study were compared with previous investigations which have used, but not compared, similar cVEMP protocols. Furthermore, because structural and physiological differences in skeletomuscular system between males and females could possibly have an influence on cVEMP findings (inter-subject amplitude variability) obtained by different biofeedback methods, gender was taken into account during data analysis.

## **2.7 Methodology**

### **2.7.1 Participants**

Initially, 137 participants were enrolled in the study. Forty seven participants were excluded: 34 participants had incomplete data, nine participants had abnormal audiograms, one participant had an absent cVEMP in one ear and three had abnormally reduced cVEMPs with poor waveform reproducibility. Hence, the participants included in the study were 90 adults (total number of ears = 180) ranging in age from 19 to 45 years (mean age =  $25.40 \pm 5.54$  years). Participants consisted of 50 females ranging in age from 22 to 45 years (mean age =  $26.68 \pm 5.25$  years) and 40 males ranging in age from 19 to 42 years (mean age =  $23.80 \pm 5.53$  years). All participants had bilateral normal hearing sensitivity and normal middle ear function on the days of testing. cVEMP responses were evoked by 500 Hz tone burst stimulus presented at 95 dB nHL using two

biofeedback methods (BPM and EMGM). In addition, normalized and non-normalized amplitude values were calculated for all obtained responses.

Four ethical approvals were obtained to conduct this experiment; one from the School of Healthcare Research Ethics Committee (SHREC/RP/225) at the University of Leeds, Leeds, UK and three from local ethical committees (Institutional Review Board "IRB" and Research Committee) at King Abdullah International Medical Research Centre (KAIMRC-Ref no. RC 12/017) and IRB at King Khalid University Hospital (KKUH- Ref no. E-14-1070) in Riyadh, Saudi Arabia. The participants were recruited from the ENT department at King Abdulaziz Medical City (National Guard Hospital) and the department of Health Rehabilitation Sciences at College of Applied Medical Sciences in King Saud University. Prior to testing, all participants were provided with an information sheet which explained the overall aim of the study, what they were required to do, possible risks, discomforts and benefits from participation, confidentiality of data, how to get more information about participants' research rights and how to get more information about the study. Written informed consent was obtained from all participants. Because the study involved Arabic and non-Arabic speaking participants, the consent forms and the information sheets were made available in two languages (Arabic and English). Prior to testing, the investigator obtained a case history from all participants to make sure that all the enrolled participants fulfilled the following conditions:

- i. Unremarkable outer and middle ear structures as determined by otoscopic examination
- ii. No history of head trauma in order to rule out cochlear and/or vestibular trauma
- iii. No history of previous ear surgery
- iv. No history of cochlear, vestibular or neurologic disease
- v. No recent history of vestibular signs and symptoms (i.e. vertigo, dizziness, instability, oscillopsia or tinnitus)
- vi. No history of musculoskeletal diseases or neck problems
- vii. Not taking prescription medication at the time of conducting measurements (i.e. vestibular suppressant medications)
- viii. No history of short or long-term or recent leisure or occupational noise exposure.

In addition, all participants had to fulfil the following audiological inclusion criteria:

- i. Bilateral normal hearing sensitivity defined by normal pure tone air conduction thresholds ( $\leq 25$  dB hearing level (dB HL) at 0.25, 0.5, 1, 2, 3, 4, 6 and 8 kHz). Audiometric difference between pure tone air conduction and bone conduction thresholds across all test frequencies was less than 10 dB.
- ii. Bilateral normal middle ear function defined by normal middle ear pressure and compliance when measured by tympanometry. Type A tympanogram was required (middle ear pressure within  $\pm 50$  daPa and compliance between 0.3 to 1.5 ml “equivalent volume”).

### 2.7.2 Test procedures

A full case history; medical, audiological and vestibular, leisure and occupational noise exposure history, was obtained orally by the investigator from all participants. Otoloscopic examination was performed for all participants to rule out any outer or middle ear abnormalities. Tympanometry (Grason-Stadler (GSI) TymStar, Viasys Healthcare Corp., USA) was also performed for all participants using standard clinical procedure to ensure normal middle ear function. To confirm that all participants had bilateral normal hearing sensitivity, air and bone conduction pure tone audiometry screening (at 25 dB HL) at octave and half-octave frequencies between 0.25 to 8 kHz (GSI 61 Clinical audiometer, Viasys Healthcare Corp., USA) was carried out in a sound-treated room meeting the standards of the American National Standards Institute (ANSI, 2004) and using the clinical procedure for manual pure tone audiometry recommended by the American Speech-Language-Hearing Association (ASHA, 1997; ASHA, 2005).

cVEMP measurements and EMG recording and monitoring were performed using an Interacoustics Eclipse auditory evoked potential system (EP 25, software version 4.3.0.1.7, Interacoustics, Assens, Denmark). cVEMP responses were recorded from SCM muscles using disposable silver-silver chloride surface electrodes (Ambu, Viasys, Madison, WI) positioned midway between the mastoid process and sternoclavicular junction on both sides of the neck (Rosengren et al., 2010). Prior to electrode placement,



the skin was cleaned and scrubbed with an impedance lowering gel. The active electrode (non-inverting) was placed above the sternum; the reference electrode (inverting) was placed on the ipsilateral tested midpoint of the SCM muscle, and the common electrode was placed on the lower forehead. Electrodes were placed at symmetrical sites over the midpoint of each SCM muscle (see Figure 1.3, Chapter 1). Impedance at each electrode site was  $\leq 5 \text{ K}\Omega$  and the inter-electrode impedance was within  $3 \text{ K}\Omega$ . cVEMP responses were obtained from each ear separately (monaural stimulation) using 500 Hz tone bursts delivered at 95 dB nHL (normal hearing level, equivalent to 125 dB SPL) through insert phones (Biologic Corp., Mundelein, IL, USA). Stimuli were presented at a rate of 5 per second. The tone burst had a one-cycle rise time, a two-cycle plateau and a one-cycle fall time. The stimulus was gated with a Blackman-weighting function. A band-pass filter of 10 Hz to 1500 Hz was used during data collection. Artifact rejection was disabled. The amplifier gain was 5 kHz and the recording epoch was 53 ms. A total of 200 single samples per averaging block were collected with each averaging block replicated at least once. The results of the two most replicable runs were averaged, providing the final response from which the cVEMP response parameters were calculated. Data were collected for each ear separately in every testing condition. A single channel recording was used throughout all testing conditions. These stimulus and recording parameters have been shown to produce reliable cVEMP in normal human subjects (Wu et al., 1999; Murofushi, 2001; Cheng and Murofushi, 2001a; Wang and Young, 2004).

Prior to cVEMP data collection, stimulus intensity level was calibrated using peak to peak equivalent SPL according to recommended calibration procedures suggested by the literature (Rosengren et al., 2009; Papathanasiou et al., 2014). Calibration of the sound delivery system was done by a 2-cc coupler (calibration Kit, Interacoustics). The Eclipse uses the ISO/DIS 389-6 standard for calibrating cVEMP 500 Hz tone burst stimulus (peak sound pressure level 'peSPL' -> nHL equivalent to 28.5 dB). The calibration was performed by the manufacturing company prior to data collection and the transducer's output was monitored periodically. Testing was carried out in an electromagnetic-shielded room to minimize electromagnetic interference. Case history, screening and all test procedures were performed on the same day within a single session lasting approximately 45 minutes to one hour per participant.

The HR-S procedure was applied throughout all testing conditions. cVEMP testing was administered twice for each participant to obtain two sets of cVEMP data, one for the EMGM method and one for the BPM method. The two testing conditions were the same apart from the type of biofeedback method used. In the EMGM method, as described earlier in section 2.3.1, the participant used the same muscle activation position (HR-S) to activate the SCM muscle. The evoked potential system provides a visual cue to the participant in the form of a coloured bar. As the participant turns his/her head, the EMG monitor turns green if SCM activation is in the defined EMG range (a range of 30 to 50  $\mu\text{V}$ ) and red if the activation is below the defined EMG range. The participant was asked to maintain the bar in the target area (green area) throughout the recording. For both methods (BPM and EMGM), at least two consecutive cVEMP recordings from the same ear were performed to ensure response reproducibility. The results of both runs (trial 1 and trial 2) were averaged to provide the final response for analysis. For each recorded cVEMP response, a rest of five minutes was given between same-ear recordings to allow the participant to relax and avoid muscle fatigue. The starting ear and the type of biofeedback method used were alternated to address any order effect.

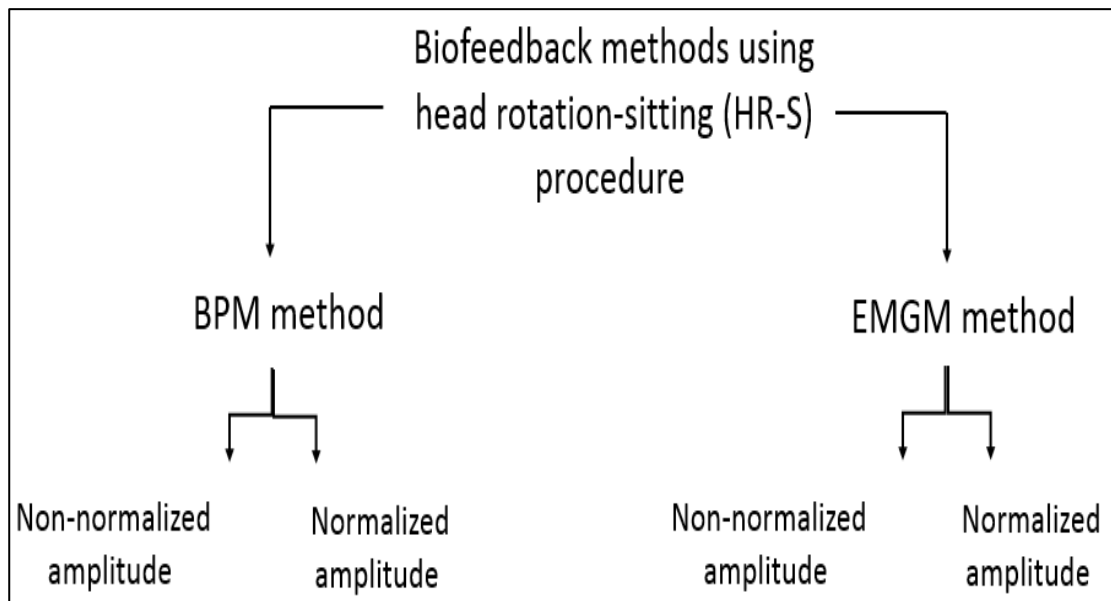
The BPM method used in this study was the one originally described by [Vanspauwen et al. \(2006a\)](#). The participant in this method was asked to push his or her jaw against a flat-hand-held pre-inflated cuff (at 20 mmHg) and to maintain a cuff pressure of approximately 40 mmHg (Heine Gamma XXL, Dharma Healthcare, Germany) while turning head away from the test ear to the contralateral shoulder as far as possible, lowering the chin slightly, thereby activating the ipsilateral SCM. The participant was asked to maintain this position throughout recording. A cuff pressure of 40 mmHg was chosen, because it has been found that a blood pressure target of 30 to 50 mmHg is usually sufficient to create good muscular contraction for cVEMP testing in normal subjects ([Vanspauwen et al., 2006b](#)). The cuff pressure level was monitored by both the participant and the investigator. Sometimes, the participant's head was adjusted by the investigator to ensure a similar head position and muscle contraction for all tested participants. Additionally, the participant was instructed not to compress the cuff with the hand while holding it, to avoid causing pressure fluctuations during recording. At the end of the assessment session, the participants were orally asked, "*if you were given the*

*option between the two methods; the BPM method and the EMGM method, which method would you choose?"* The purpose of asking this question was to find out which method was preferred by participants.

Since amplitude normalization is a data analysis technique rather than a method, it was available as an option in the evoked potential system for every recorded cVEMP waveform. Hence, both non-normalized and normalized amplitudes were automatically calculated by the software for each testing condition (EMGM and BPM) and there was no need to administer cVEMP testing for a third time to apply the amplitude normalization technique. The normalized amplitude response is calculated by dividing the mean RMS value of EMG levels for each recording by 20 ms pre-stimulus background EMG data (pre-stimulus EMG estimate). A detailed description of this technique was provided earlier in section 2.3.2. cVEMP testing was performed twice to administer the two biofeedback methods (EMGM and BPM) with and without normalization, so four cVEMP testing conditions were made available for analysis (EMGM/non-normalized amplitude, EMGM/normalized amplitude, BPM/non-normalized amplitude and BPM/normalized amplitude). Thus, a multivariate repeated measure design with two factors each with two levels was used to examine differences in cVEMP response parameters between the four testing conditions (see Figure 2.5).

cVEMP response rate defined as the number of present VEMP responses as a proportion of the total number of ears tested, was calculated for all included participants. For each biofeedback method, the cVEMP response parameters (P1 absolute latency, N1 absolute latency, inter-aural P1 latency difference, inter-aural N1 latency difference, non-normalized and normalized P1-N1 peak to peak amplitude) were calculated from the average of two responses (trial 1 and trial 2). P1 latency was defined as the initial positive polarity of the biphasic waveform that appears at  $\approx 13$  ms post-stimulus. N1 latency was defined as the subsequent negative polarity at  $\approx 23$  ms. P1 and N1 latencies were calculated from the stimulus onset at 0 ms to the maximal troughs and peaks forming the biphasic P1-N1 waveform. The Inter-aural latency difference for P1 and N1 was defined as the difference between absolute latencies for the right and left ears for

each peak (P1 and N1). An example of a typical cVEMP response waveform obtained from a healthy participant was provided earlier in Chapter 1 (Figure 1.4, section 1.6.3).



**Figure 2.5 Present study design.** The study employed a multivariate repeated measure design with two factors each with two levels to examine the effect of two biofeedback methods (BPM and EMGM) using head rotation-sitting (HR-S) procedure combined with and without one data analysis technique (amplitude normalization) on cVEMP response parameters.

A cVEMP response was only considered present and reliable if the following conditions were fulfilled: (a) the biphasic P1-N1 waveform was observed around the expected latencies of 13 and 23 ms (b) cVEMP waveform was reproducible in the second or third run and P1 and N1 of the second or third run occurred approximately in the same latencies of the first run. Conversely, cVEMPs were considered absent if the above mentioned conditions were not fulfilled. cVEMP amplitude was defined as the peak to peak P1-N1 amplitude in microvolts ( $\mu\text{V}$ ) relative to the baseline (calculated from the difference between P1 and N1 absolute amplitudes). In addition, the following cVEMP amplitude data were automatically calculated by the software; non-normalized amplitude, normalized amplitude and pre-stimulus EMG estimate. The non-normalized amplitude is the raw amplitude calculated in  $\mu\text{V}$ . The formula used to calculate the normalized amplitude is given in section 2.3.2 (Equation 2.1). While the non-normalized

amplitude and the pre-stimulus EMG estimate which is the 20 ms pre-stimulus mean background EMG levels are calculated in  $\mu\text{V}$ , the normalized amplitude is expressed as a ratio. Additionally, inter-aural amplitude asymmetry ratio (IAR) which is the difference in amplitude measurement between the two ears was calculated for each testing condition. IAR is expressed as a percentage and a certain formula is used to calculate it (see Chapter 1, Equation 1.1, section 1.6.3). Non-normalized and normalized IAR were both calculated. The upper limit for IAR in each method, which is the maximum normal range for IAR, both non-normalized and normalized, were calculated. The upper normal limits of IAR can be calculated using the following formula (mean of IAR for all participants + 1.96 x standard deviation 'SD') and are expressed in percentages. Since this calculated range of IAR was obtained from individuals with normal audio-vestibular function, it can be used as an additional useful response parameter to interpret cVEMP amplitude data.

### **2.7.3 Data Analysis**

Statistical analysis was carried out using IBM SPSS 21.0 software (SPSS Software, SPSS Inc., Chicago, IL, USA). Initially, data normality (Shapiro-Wilk) and equality of variances (Levene's test) assumptions were checked to determine the appropriate statistical tools to apply. To rule out any ear or side effect, cVEMP data were contrasted between the right and left ears. Differences in cVEMP response parameters between the two biofeedback methods as well as the effect of the amplitude normalization technique on cVEMP data for each biofeedback method (EMGM: normalized vs. non-normalized amplitude, BPM: normalized vs. non-normalized amplitude) were tested using non-parametric analysis (Wilcoxon Signed Rank test). For all analysis, an alpha level of ( $p < 0.05$ ) was used to determine significance. While IAR was considered as a measure of intra-subject amplitude variability because it gives indication for intra-aural amplitude variability, the calculated SD value for each mean response parameter was considered as an indicator of inter-subject amplitude variability. Because participants were of different genders (50 males and 40 females), cVEMP data were contrasted between male and female groups to determine any gender effect. Since the majority of cVEMP data showed a positive skewed distribution, median values were reported because they more

accurately represent non-normally distributed data. However, to facilitate comparison with published literature, mean values are reported as well in this study. Although cVEMP data were right-skewed (mean values were larger than median values), mean and median values were not appreciably different because the degree of skewness was not heavy. Hence, any effect on using mean or median values on the interpretation of this data would be very minimal.

## **2.8 Results**

### **2.8.1 cVEMP response parameters obtained by two biofeedback methods with and without amplitude normalization**

cVEMP responses were present in all the tested 180 ears (100 % response rate). Initially, cVEMP responses were examined to rule out any ear effect (left ear: N= 90, right ear: N= 90). Normality measures (Shapiro Wilk statistical test) and equality of variances (Levene's test) suggested that the differences between right and left ears data were normally distributed and of similar variance. Therefore, a paired sample t-test showed statistically non-significant differences ( $p > 0.05$ ) between the right and left ears in all cVEMP latency and amplitude parameters for both biofeedback methods data. Thus, cVEMP data were combined and averaged between ears for each participant and used to perform descriptive statistics. Table 2.1 shows the mean, median and SD of cVEMP response parameters for both ears combined and for each biofeedback method. Table 2.2 shows the upper normal limits of IAR (non-normalized and normalized) for each method calculated using  $(\text{mean} + 1.96 \times \text{SD})$ . Figure 2.6 shows an example for one participant's cVEMP response.

**Table 2.1 cVEMP response parameters obtained from 180 ears (90 participants) using head rotation-sitting (HR-S) procedure and two visual biofeedback methods: blood pressure manometer (BPM) method and electromyogenic monitoring (EMGM) method with and without amplitude normalization technique. The presented values are for both ears combined.**

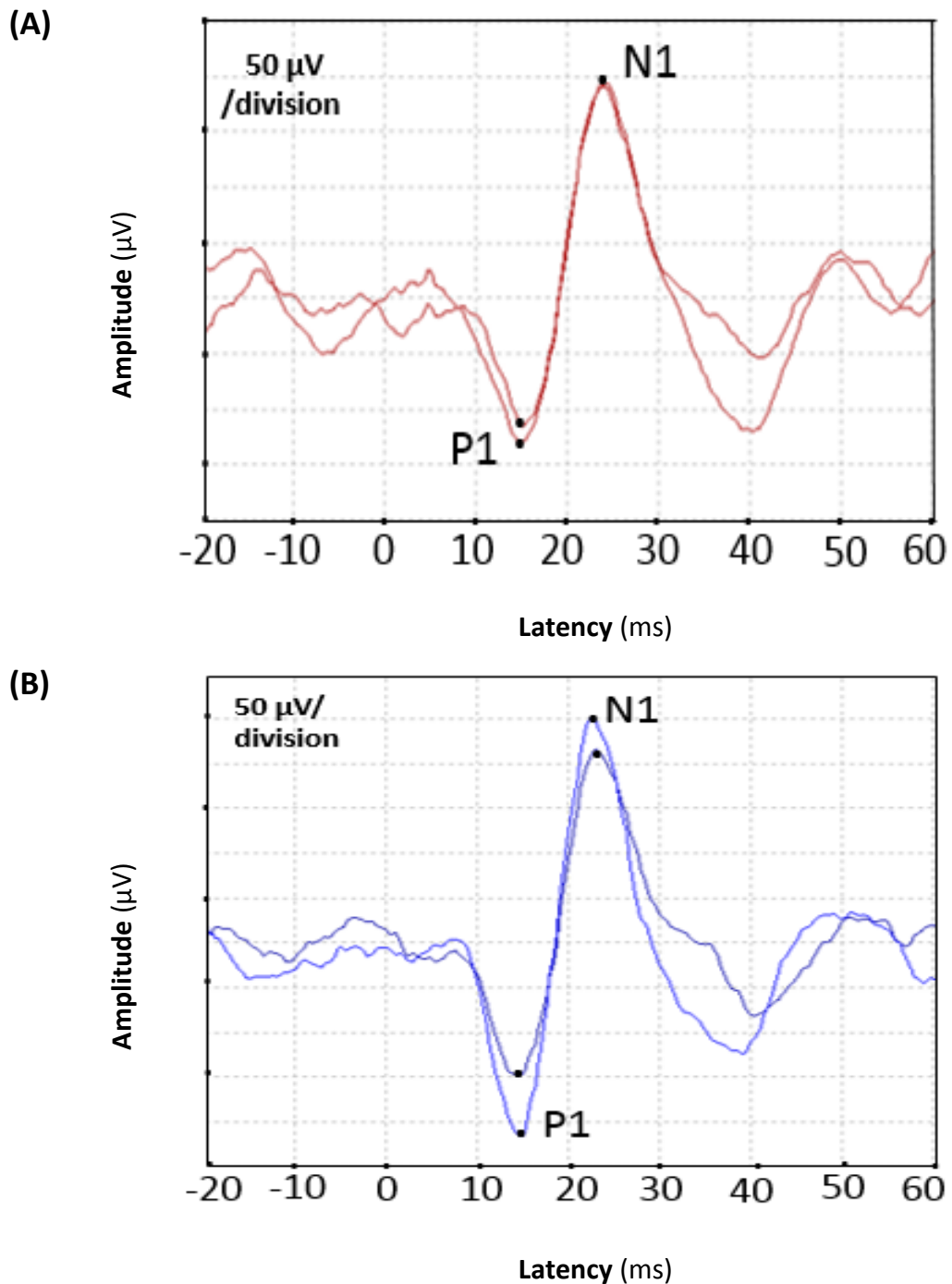
cVEMP response parameters (unit)	Visual biofeedback methods					
	BPM			EMGM		
	Mean	Median	SD	Mean	Median	SD
<b>P1 absolute latency (ms)</b>	15.8	15.4	2.0	15.9	15.5	2.1
<b>N1 absolute latency (ms)</b>	24.7	24.3	2.4	24.7	24.5	2.4
<b>Inter-aural P1 Latency difference (ms)</b>	1.2	0.8	0.9	1.3	1.3	0.9
<b>Inter-aural N1 latency difference (ms)</b>	1.5	1.1	1.3	1.5	1.2	1.2
<b>Non-normalized amplitude (<math>\mu\text{V}</math>)</b>	271.8	256.0	152.9	222.5	189.5	127.8
<b>Normalized amplitude (ratio)</b>	1.3	1.3	0.6	1.3	1.2	0.6
<b>Pre-stimulus EMG estimate (<math>\mu\text{V}</math>)</b>	212.8	196.6	80.1	174.8	170.2	51.6
<b>Non-normalized IAR (%)</b>	18.4	14.0	14.3	18.1	15.5	12.4
<b>Normalized IAR (%)</b>	17.2	14.0	12.6	18.2	16.5	12.1

IAR: inter-aural amplitude asymmetry ratio. ms= milliseconds.  $\mu\text{V}$  = microvolts.

**Table 2.2 Mean cVEMPs inter-aural amplitude asymmetry ratios (IARs) obtained for 90 participants (180 ears) using blood pressure manometer (BPM) method and electromyogenic monitoring (EMGM) method with and without amplitude normalization technique.** The table shows non-normalized and normalized IAR values and the corresponding calculated upper normal limits for IAR values.

<b>Visual biofeedback Method</b>	<b>IAR</b>	<b>Mean (%)</b>	<b>SD</b>	<b>IAR upper normal limits (%) (mean + 1.96 SD)</b>
<b>BPM</b>	non-normalized	18.40	14.32	44.50
	Normalized	17.22	12.55	41.83
<b>EMGM</b>	non-normalized	18.12	12.40	42.41
	Normalized	18.18	12.14	41.98



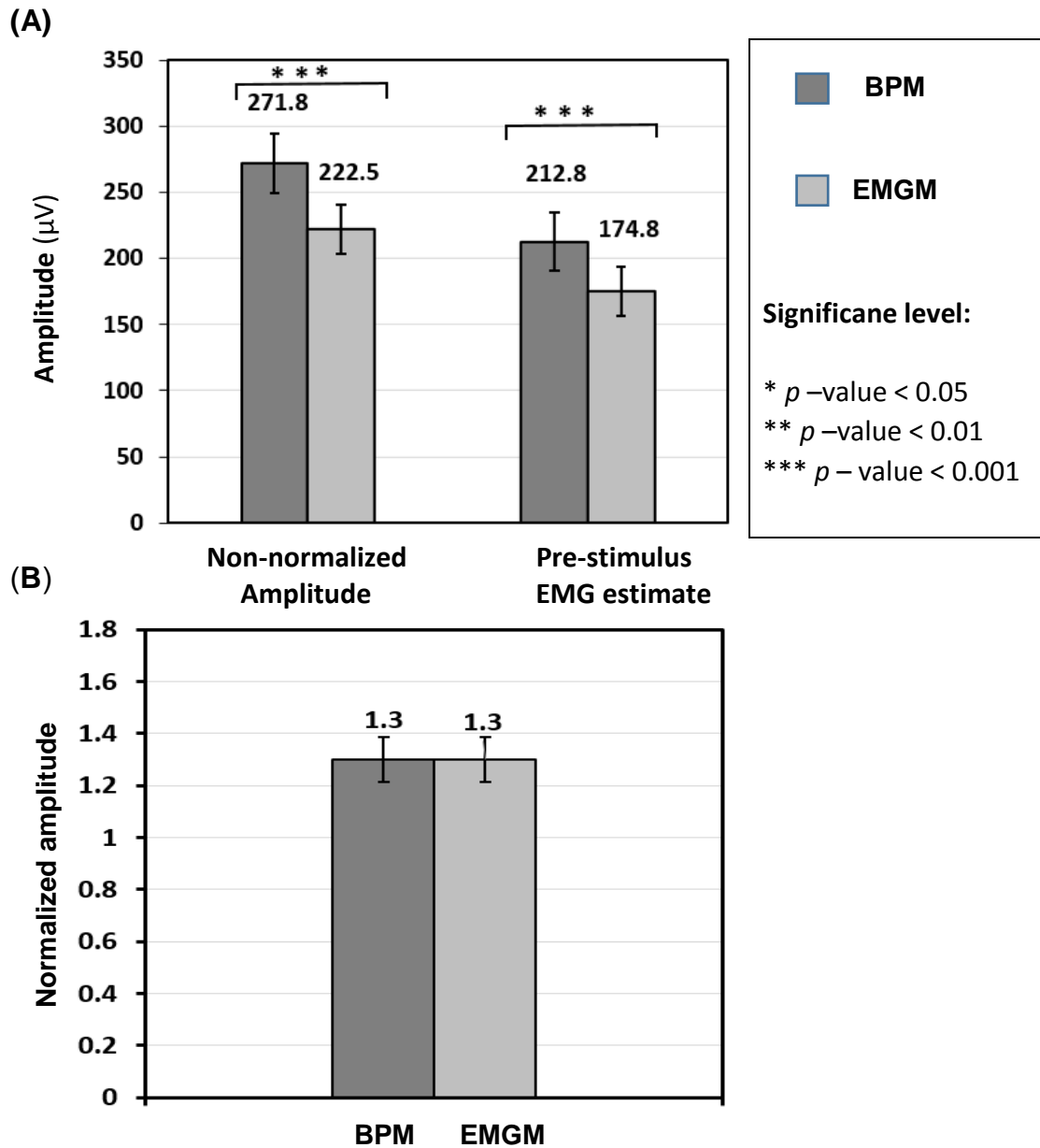


**Figure 2.6 Example cVEMP response waveform from one participant.** The participant is a 36 years old female with bilateral normal hearing sensitivity and normal middle ear function. Panel A (top/red) shows P1-N1 waveform for the right ear. Panel B (bottom/blue) shows P1-N1 waveform for the left ear. The presented P1-N1 waveforms were obtained using head rotation-sitting (HR-S) procedure, electromyogenic monitoring (EMGM) method without amplitude normalization. The two recorded waveforms in both panels indicate that the cVEMP response is replicable and repeatable in both ears.

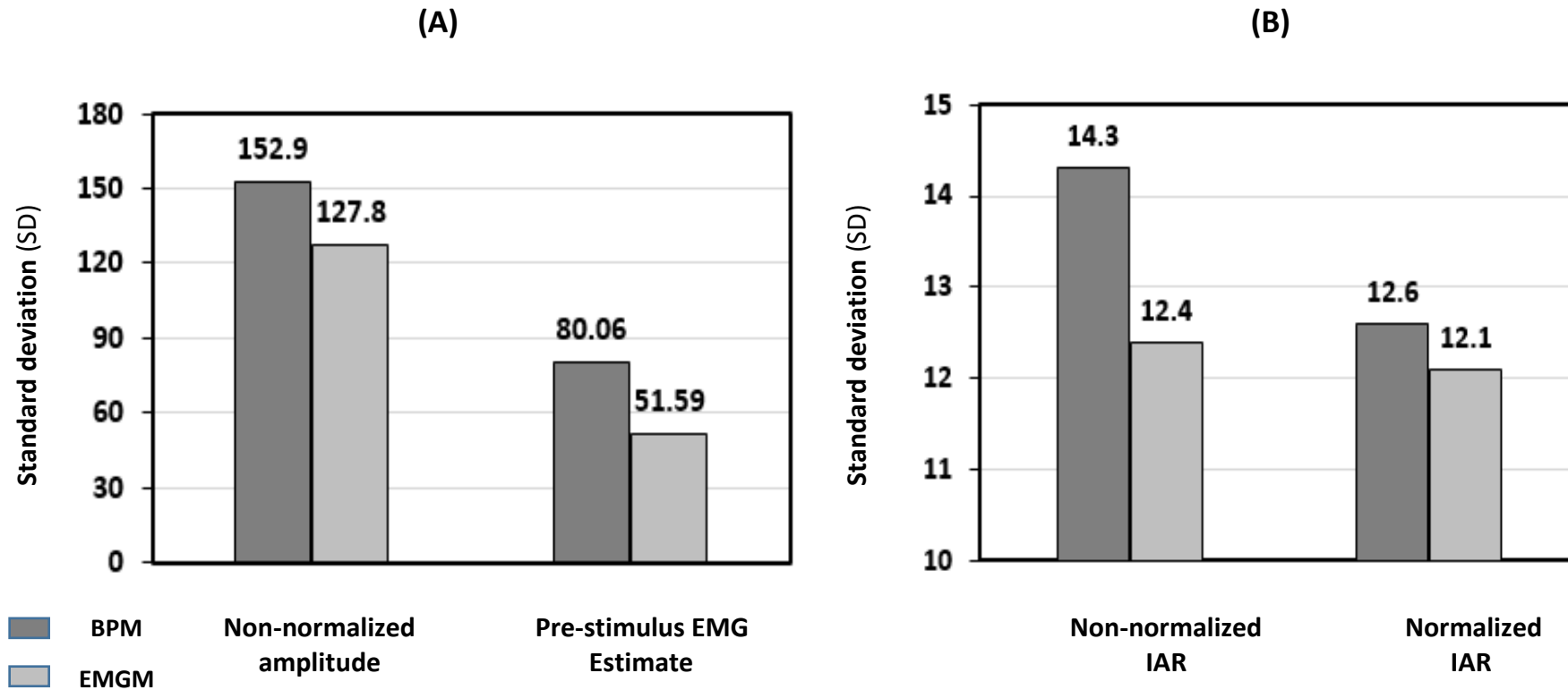
### 2.8.2 Effect of visual biofeedback methods on cVEMP amplitude data

Figure 2.7 shows statistically significant differences between cVEMP amplitude measures obtained by the BPM method and those obtained by the EMGM method. Results of Wilcoxon Signed Rank test showed that P1-N1 non-normalized amplitude and pre-stimulus EMG estimate were significantly higher ( $p < 0.001$ ) with the use of the BPM method compared to those obtained by the EMGM method (non-normalized amplitude: BPM =  $271.8 \pm 152.9$ , EMGM =  $222.5 \pm 127.8$ ,  $Z = -6.849$ ; pre-stimulus EMG estimate: BPM =  $212.8 \pm 80.1$ , EMGM =  $174.8 \pm 51.6$ ,  $Z = -7.146$ ,  $p < 0.001$  for both, Figure 2.7, Panel A). On the other hand, cVEMP normalized amplitudes were similar among the two biofeedback methods (normalized amplitude: both BPM and EMGM =  $1.3 \pm 0.6$ ,  $Z = -0.642$ ,  $p > 0.05$ , Figure 2.7, Panel B). When the SD of several cVEMP amplitude-related parameters (non-normalized amplitude, pre-stimulus EMG estimate, non-normalized IAR and normalized IAR) was compared across the two biofeedback methods, it was noted that the lowest SD values were produced by the EMGM method (Figure 2.8). Thus, the EMGM method appears to reduce cVEMP inter-subject amplitude variability in this cohort, as measured by SD, compared to the BPM method.

When the participants at the end of cVEMP assessment were asked to report which biofeedback method they personally preferred (BPM or EMGM), the great majority of participants ( $N = 82 = 91.1\%$ ) preferred the EMGM method and only a few participants ( $N = 8 = 8.9\%$ ) preferred the BPM method. One sample Chi-Square test (Goodness of Fit) showed that the difference observed in the personal preference of biofeedback methods was statistically significant ( $X^2 = 60.844$ ,  $p < 0.001$ ). Further, a Pearson's Chi-Square test of independence showed that gender had no influence on the personal method preference outcomes ( $X^2 = 1.159$ ,  $p > 0.05$ ).



**Figure 2.7** Bar graphs showing statistically significant differences ( $p < 0.001$ ) between two visual biofeedback methods (blood pressure manometer (BPM) method and electromyogenic monitoring (EMGM) method) obtained from 180 normal ears. The Differences were demonstrated by Wilcoxon Signed Rank Test for two cVEMP amplitude-related parameters. Panel A shows that the BPM method produced statistically significant higher cVEMP non-normalized amplitude and pre-stimulus EMG estimate compared to EMGM method. Panel B shows that the two biofeedback methods produced similar normalized amplitudes. These findings indicate that different biofeedback methods used in cVEMP testing to control variability of EMG levels might reveal different amplitude levels, particularly non-normalized data. Data labels indicate mean values and a 95 % confidence interval was used to calculate error bars.

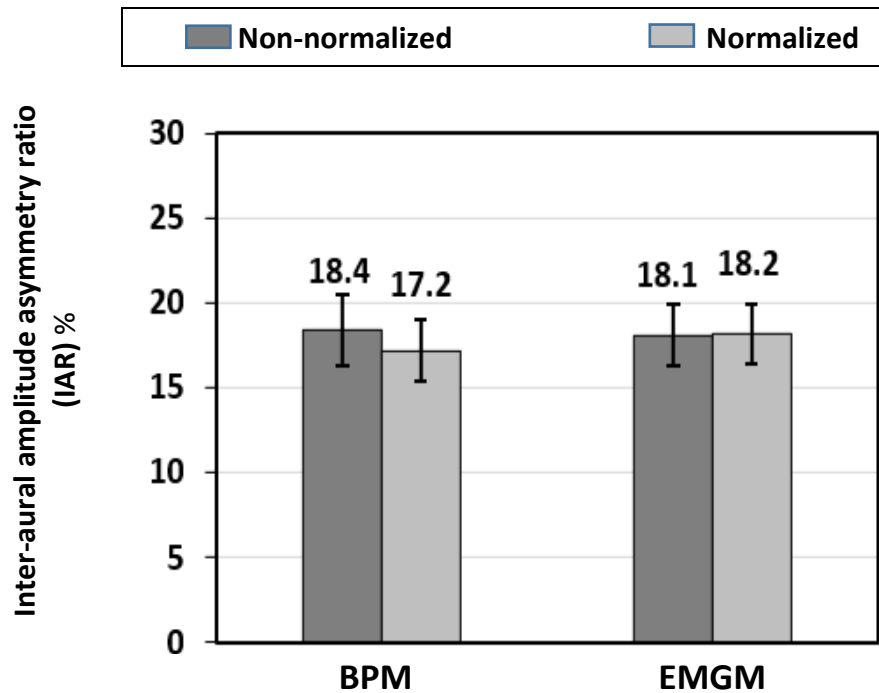


**Figure 2.8** Bar graphs comparing the standard deviation (SD) for several cVEMPs amplitude-related parameters obtained from 180 normal ears using two visual biofeedback methods. Panel A shows that electromyogenic monitoring (EMGM) method produced lower SD values for non-normalized amplitude and pre-stimulus EMG estimate. Panel B shows similar findings (EMGM method produced lower SD values for non-normalized and normalized inter-aural amplitude asymmetry ratios “IARs” compared to those obtained by the BPM method). These findings indicate that the EMGM method reduces cVEMP inter-subject amplitude variability, as measured by SD. Data labels indicate SD values.

### **2.8.3 Effect of the amplitude normalization technique on cVEMP inter-aural amplitude asymmetry ratio (IAR)**

As previously explained in section 2.7.3, inter-aural amplitude asymmetry ratio (IAR) was utilized as a measure of cVEMP intra-subject amplitude variability because it reflects inter-aural differences in amplitude for each subject. Figure 2.9 shows the difference between cVEMP non-normalized and normalized IAR obtained for two biofeedback methods (BPM; non-normalized IAR vs. normalized IAR, EMGM; non-normalized IAR vs. normalized IAR) tested by Wilcoxon Signed Rank Test. Results showed statistically non-significant differences between the non-normalized and the normalized IAR for both biofeedback methods data ( $p > 0.05$ ). Although the normalized IAR obtained with the BPM method demonstrated the lowest IAR mean (17.22 %), the difference between this condition and all the other conditions was statistically non-significant.

When the normal upper limits of IAR were calculated, in each biofeedback method, it ranged from  $\approx 42$  to  $45$  % for the non-normalized responses and  $\approx 42$  % for the normalized responses (see Table 2.2, section 2.8.1). The great majority of participants (EMGM: 96 %; BPM: 92 %) had normalized or non-normalized IARs which were equal or less than this range (42 – 45 %) while very few participants (4 to 8 %) had IAR values exceeding this range. Because the SD was utilized as an indicator of cVEMP inter-subject amplitude variability, the SD of the IAR measure obtained with and without the use of amplitude normalization was compared (non-normalized IAR vs. normalized IAR) for each administered biofeedback method (BPM and EMGM). Results showed that the lowest SD values were produced by the normalized IAR for both biofeedback methods (Figure 2.10). Hence, amplitude normalization reduces inter-subject amplitude variability because it produces lower SD values.



**Figure 2.9** Bar graphs showing statistically non-significant differences ( $p > 0.05$ ) between cVEMP non-normalized and normalized mean inter-aural amplitude asymmetry ratios (IARs) obtained by two visual biofeedback methods (BPM: blood pressure manometer method and EMGM: electromyogenic monitoring method). Differences were tested by Wilcoxon Signed Rank Test for 180 ears within each biofeedback method (EMGM/non-normalized IAR vs. EMGM/normalized IAR,  $Z = -0.444$ ; BPM/non-normalized IAR vs. BPM/normalized IAR,  $Z = -1.570$ ,  $p > 0.05$  for both). This finding indicate that amplitude normalization, when combined with a biofeedback method, had no effect on cVEMP inter-aural amplitude variability as measured by IAR. Data labels indicate mean values and 95 % confidence interval was used to calculate error bars.

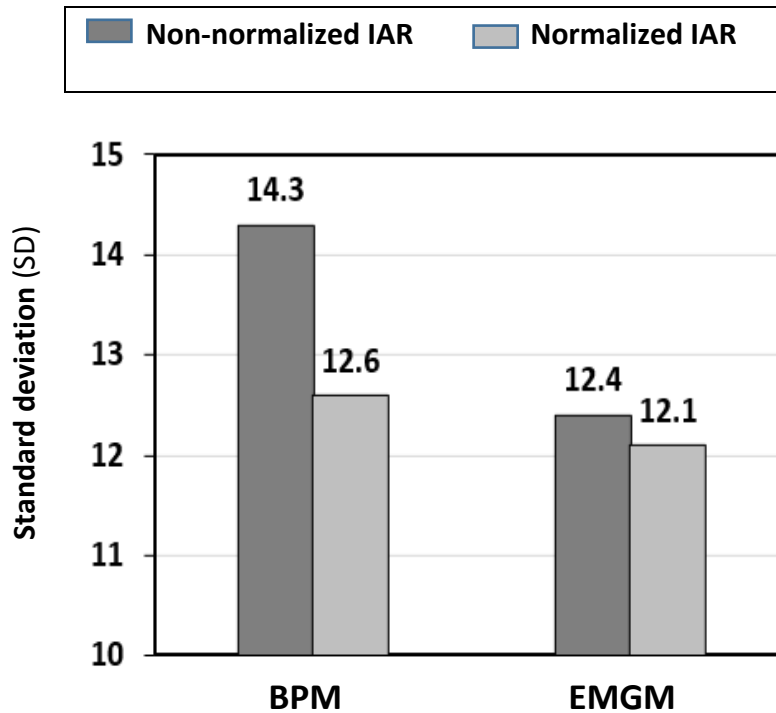


Figure 2.10 A bar graph comparing the standard deviation (SD) for cVEMP mean inter-aural amplitude asymmetry ratio (IAR) with and without amplitude normalization (non-normalized and normalized IAR) obtained from 90 normal participants (180 ears) using two visual biofeedback methods: blood pressure manometer (BPM) method and electromyogenic monitoring (EMGM) method. The figure shows that amplitude normalization, when combined with a biofeedback method, reduces cVEMP inter-subject amplitude variability, as measured by SD. Data labels indicate SD values.

#### 2.8.4 Effect of gender on cVEMP data

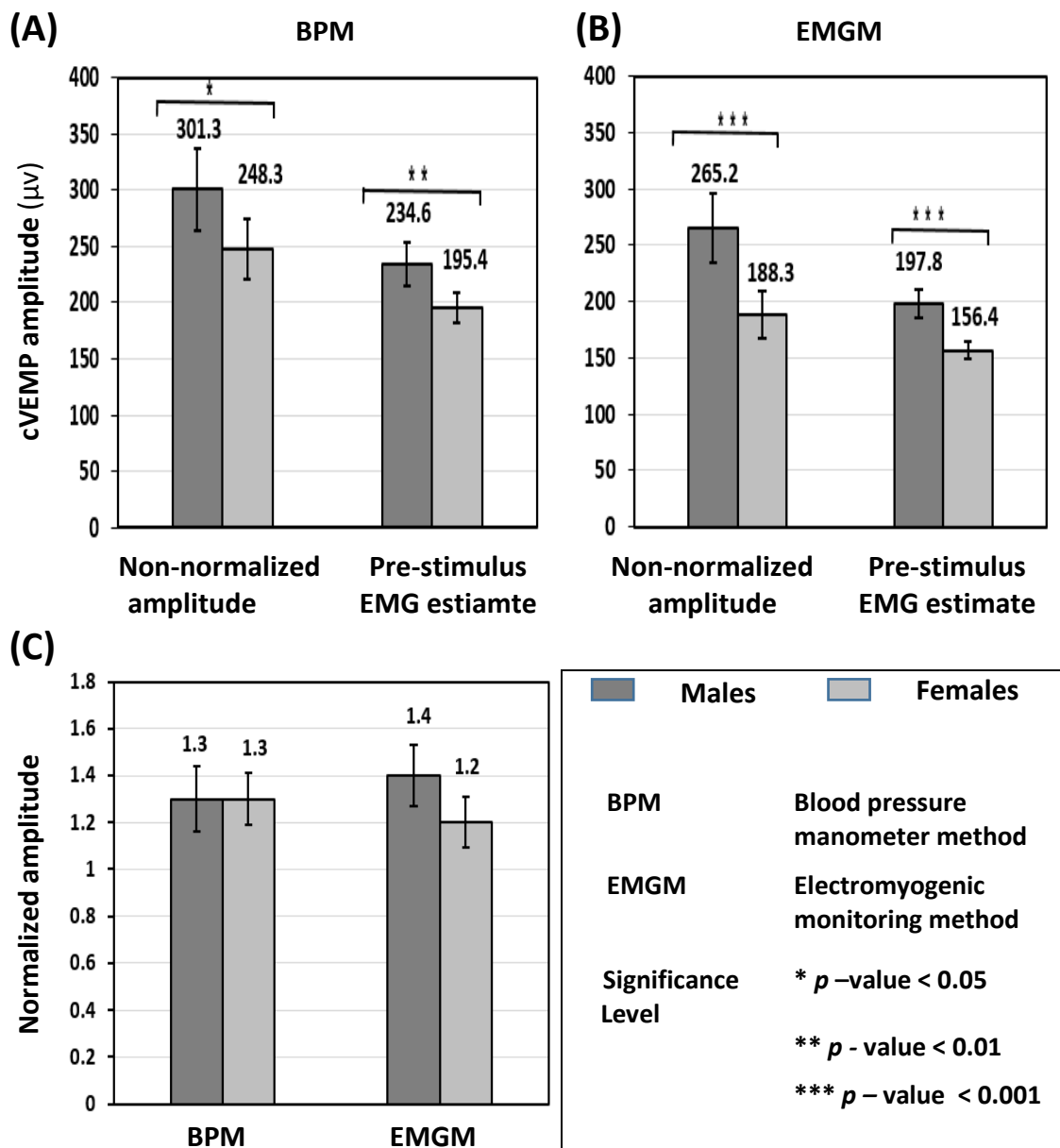
All cVEMP response parameters were analyzed to determine any gender effect on cVEMP data (40 males (M) = 80 ears, 50 females (F) = 100 ears). The Shapiro Wilk test suggested that the present cVEMP data for both genders were not normally distributed, so two comparative analysis were performed. First, the gender effect in cVEMP data was examined within each biofeedback method (BPM method: M vs. F; EMGM method: M vs. F) using Mann-Whitney  $U$  test. The first comparison revealed a statistically significant effect of gender obtained by both biofeedback methods in only cVEMP amplitude data obtained without amplitude normalization. Results showed that cVEMP non-normalized amplitude and pre-stimulus EMG estimate in males were significantly higher than those obtained in females ( $p < 0.05$ , see Table 2.3 and Figure 2.11, Panels A and B). After applying amplitude normalization, the gender effect was not observed, in that there were statistically non-significant differences between males and females in normalized amplitude data in both biofeedback methods data ( $p > 0.05$ , see Table 2.3 and Figure 2.11, Panel C).

Second, all cVEMP response parameters were tested within the same gender but across methods (BPM/M vs. EMGM/M, BPM/F vs. EMGM/F) using Wilcoxon Signed rank test. Similar results were observed for this comparison, in that a statistically significant effect of method was noted in cVEMP data without amplitude normalization. Results showed that non-normalized amplitude and pre-stimulus EMG estimate produced by the use of the BPM method were significantly higher in both male groups compared to those obtained by the EMGM method (BPM/M vs. EMGM/M (non-normalized amplitude):  $Z = -3.377$ , pre-stimulus EMG estimate:  $Z = -4.120$   $p < 0.001$  for both). Similar results were also observed for the female groups' comparison (BPM/F vs. EMGM/F (non-normalized amplitude):  $Z = -6.106$ , pre-stimulus EMG estimate:  $Z = -5.937$ ,  $p < 0.001$  for both). Although all these findings showed no gender or method effect on cVEMP data after amplitude normalization, a statistically significant difference between the two methods was noted in normalized amplitude data when the two female groups were compared (BPM/F vs. EMGM/F:  $Z = -2.082$ ,  $p < 0.05$ ).



**Table 2.3 Descriptive statistics (mean, median, SD) and Mann-Whitney  $U$  test showing a statistically significant effect of gender without amplitude normalization.** The gender effect was demonstrated in two cVEMP amplitude parameters; non-normalized amplitude and pre-stimulus EMG estimate in both visual biofeedback methods data (BPM and EMGM). Males produced significantly higher P1-N1 non-normalized amplitude and pre-stimulus EMG estimate compared to females in both biofeedback methods data. After applying amplitude normalization, there was statistically non-significant gender effect on cVEMP normalized amplitude data. N = number of participants.

cVEMP response parameters	Biofeedback method	Males (N = 40 = 80 ears)			Females (N = 50 = 100 ears)			Mann-Whitney $U$ Test (Z values)	p-value
		Mean	Median	SD	Mean	Median	SD		
Non-normalized amplitude ( $\mu\text{V}$ )	BPM	301.3	275.1	166.9	248.3	236.1	137.2	- 1.966	< 0.05
	EMGM	265.2	250.7	139.8	188.3	154.6	106.1	- 3.740	< 0.001
Pre-stimulus EMG estimate ( $\mu\text{V}$ )	BPM	234.6	226.8	88.1	195.4	183.9	68.6	- 3.020	< 0.01
	EMGM	197.8	194.9	56.1	156.4	156.2	39.2	- 5.262	< 0.001
Normalized amplitude (ratio)	BPM	1.3	1.2	0.63	1.3	1.3	0.57	-0.005	> 0.05
	EMGM	1.4	1.3	0.60	1.2	1.2	0.55	-1.500	> 0.05



**Figure 2.11** Bar graphs showing the effect of gender on cVEMP responses obtained from 90 adult participants with normal hearing (40 males = 80 ears, 50 females = 100 ears). Differences between the two gender groups were tested by Mann-Whitney  $U$  test. Panels A and B show a gender effect on cVEMP amplitude data without the use of amplitude normalization demonstrated in both biofeedback methods. After applying amplitude normalization, gender differences on cVEMP amplitude data in both biofeedback methods were statistically non-significant (Panel C). These findings indicate that males may produce higher amplitude values in cVEMP testing compared to females with the use of a visual biofeedback method, particularly without the use of amplitude normalization. Data labels indicate mean values and a 95 % confidence interval was used to calculate error bars.

## 2.9 Discussion

The aim of this study was to determine the optimal visual biofeedback method and data analysis technique in cVEMP testing in adults with normal audio-vestibular function using the HR-S muscle activation procedure. The study focuses on examining the currently advocated methods and techniques to control SCM muscle contraction variability in cVEMP testing. A repeated measures design was used to obtain cVEMP findings from 90 normal adults using two biofeedback methods: BPM and EMGM in conjunction with and without the use of amplitude normalization technique. Thus, the study had three main objectives. The first objective was to obtain cVEMP responses by two biofeedback methods to determine if there is any difference in cVEMP response parameters between the two methods. The second objective was to obtain non-normalized and normalized amplitude data for each biofeedback method and then compare findings within each method to determine how much influence amplitude normalization had on cVEMP intra-subject, particularly inter-aural and inter-subject amplitude variability.

### 2.9.1 Comparison of present study cVEMP data with previous investigations

The established cVEMP mean normative values of this study were comparable to those reported in the literature which made use of similar stimulus parameters and recording procedures. Table 2.4 provides a comparison between the present study common cVEMP response parameters and those of several other published studies. The mean absolute latency values obtained in the present study (P1/BPM: 15.82 ms; P1/EMGM: 15.86 ms; N1/BPM: 24.72 ms; N1/EMGM: 24.74 ms) fall within the mean range reported by these studies (P1: 14.2 – 15.98 ms; N1: 21.6 – 24.17 ms). Likewise, the mean non-normalized values reported in the present study (BPM: 271.8  $\mu$ V, EMGM: 222.5  $\mu$ V) fall within the mean ranges reported by the comparable studies (59.19 - 280  $\mu$ V). However, the obtained SD values for amplitude measures obtained in this study and all the other comparable studies suggest that cVEMP amplitude measures are far more variable than latency measures, which is consistent with present literature (Versino et al., 2001; Eleftheriadou and Koudounarakis, 2011). The wide range of normal cVEMP amplitude

values reported in the literature including those reported in this study is not unexpected since cVEMP amplitude measures are known to be influenced by several factors, such as muscle contraction level, age, anatomical differences among subjects, SCM muscle activation procedure, stimulus and recording parameters and electrode placement (see Chapter 1, section 1.6.4).

Although these factors have been shown to have an effect on cVEMP amplitude levels, there is a general consensus in the literature that variations in muscle contraction levels might be the main source of cVEMP amplitude variability. A systematic review and meta-analysis of 66 published cVEMP normative studies found significant differences not only in cVEMP amplitude-related parameters, but also in all the other response parameters with different methods to control SCM muscle contraction levels (Meyer et al., 2015). Thus, accurate comparison among the available cVEMP normative data is confounded by variation in cVEMP stimulus and recording protocols. Small differences among studies, such as differences in research groups and/or hardware differences might add also to this variability. Therefore, clinicians have to be cautious when attempting to utilize these normal values and, supported by the results presented here, it is recommended that each clinical setup obtains its own normative data based on its own protocol and equipment.

The normal non-normalized and normalized IAR ranges obtained in this study for both biofeedback methods (BPM: 18.4, 17.2 %; EMGM: 18.1, 18.2 %, respectively) fall within the IAR ratios reported in healthy individuals (0 to 40 %) regardless of the method used to control SCM muscle contraction variability (Jacobson and Shepard, 2016). Welgampola and Colebatch (2001a) reported 35 to 47 % as the IAR upper normal limit for subjects under 60 years of age with and without the use of amplitude normalization. Zapala and Brey (2004) reported 47 % in 21 subjects aged between 30 and 83. In a more recent study, McCaslin et al. (2013) reported 44 % with the use of HR (supine) procedure and 31 to 37 % when either EMGM or amplitude normalization was used. The upper normal limits for both non-normalized and normalized IAR data found in the present study were between  $\approx$  42 to 45 % for the BPM method and  $\approx$  42 % for the EMGM method which indicates that both are in good agreement with that reported in the literature.

**Table 2.4 Summary of cVEMP latency and amplitude values (means  $\pm$  1 SD) of this study and other studies which have used similar protocol.**

Methodological differences among studies (stimulus level and type of visual biofeedback method) are shown in the last two columns.

Study	N	Age (Yr.)	P1 Latency (ms)	N1 Latency (ms)	Non-normalized amplitude ( $\mu$ V)	Methodology	
						Stimulus level (dB nHL)	Visual biofeedback method
Present study	90	19 - 45	15.82 $\pm$ 2.02	24.72 $\pm$ 2.35	271.80 $\pm$ 152.98	95	BPM
			15.86 $\pm$ 2.07	24.74 $\pm$ 2.41	222.5 $\pm$ 127.75	95	EMGM
Van Tilburg et al. (2014)*	20	20 - 49	14.4 $\pm$ 2.3	21.8 $\pm$ 2.4	166.18 $\pm$ 150.56	93	EMGM
Akin et al. (2012)	14	25 - 63	15.0 $\pm$ 0.7	22.1 $\pm$ 1.7	79 $\pm$ 40	90	EMGM
De Oliveria Barreto et al. (2011)	78	18 - 31	14.15 $\pm$ 1.27	24.17 $\pm$ 2.05	59.19 $\pm$ 30.46	95	EMGM
Maes et al. (2010)**	51	18 - 55	14.50 $\pm$ 1.21	23.51 $\pm$ 2.0	147.05 $\pm$ 64.02	100	BPM
Park et al. (2010)	20	24 - 34	14.2 $\pm$ 1.34	21.6 $\pm$ 1.34	87.7 $\pm$ 47.38	95	BPM
Jankey and Shepard (2009)	28	20 - 49	15.98 $\pm$ 1.64	23.45 $\pm$ 2.20	65.59 $\pm$ 34.22	93	BPM
Vanspauwen et al. (2009)	54	20 - 33	15.4 $\pm$ 1.5	24.1 $\pm$ 2.0	280 $\pm$ 115	95	EMGM

Presented values are for both ears combined. N= number of participants, Yr. = year, ms = milliseconds,  $\mu$ V = microvolts. nHL: normal hearing level.

\* Mean values for 500 Hz tone burst stimulus were segregated from this study to match other studies' protocols. \*\*Mean values for the age group (18-55) were segregated from this study to match other studies' age groups.

Among all the studies listed in Table 2.4, the current study (BPM data) showed the highest inter-subject amplitude variability (i.e. largest SD). Since muscle contraction variability was controlled in this study, there must be other intrinsic factors playing a role in inflating the present study's SD values. The effect of age in this study is unlikely, because changes in cVEMP amplitude have been reported in the literature for subjects over the age of 60 and all present study participants were under this age. Due to insufficient numbers in age range groups; 18 to 30 years of age = 74 participants, 31 to 40 years of age = 14 participants, 41 to 50 years of age = 2 participants, the effect of age on cVEMP parameters could not be tested here and therefore the age variable was not pooled into any analysis. Another possible contributing factor is gender. Gender might have an interaction effect with methods used to control cVEMP amplitude variability. Further discussion about this is provided in section 2.9.3.

### **2.9.2 The optimal visual biofeedback method in cVEMP testing**

The findings of this study suggest that different biofeedback methods to control EMG levels might reveal different cVEMP response parameters. This is consistent with the findings of Meyer et al. (2015) discussed in the previous section (section 2.9.1). The present study observed differences between the two investigated biofeedback methods (BPM and EMGM) in non-normalized amplitude and pre-stimulus EMG estimate. Results showed that the BPM method produced higher mean values in these two amplitude-related parameters compared to those obtained using the EMGM method (see Figure 2.7, Panel A, section 2.8.2). The close agreement between non-normalized amplitude and pre-stimulus EMG estimate parameters is consistent with the well-documented relationship between cVEMP amplitude levels and muscle contraction activity measured by EMG levels (Lim et al., 1995; Akin et al., 2004; Akin et al., 2011b; Bogle et al., 2013). In addition, the lower amplitude values obtained by the EMGM method could be explained by the fact that the setup of this method itself does not influence the participant to exert as much muscular force and tension as it did in the BPM method (i.e. the BPM method involves a pushing task where the subject has to push cheek and jaw against the inflated blood pressure cuff). It could also be that there is a slight difference in head position between the two methods and the act of holding the inflated blood

pressure cuff in the BPM method creates a more optimal position to produce greater muscle contraction. The effect of five different head positions (upright, nose up, ear up, nose down and ear down), performed using the HR-S procedure without any feedback method, on cVEMP data was demonstrated in 14 normal subjects by Ito et al. (2007). The study found that these head positions had significant effects on cVEMP latencies, especially N1 in the upright position, with no effect on normalized amplitude data. It could be that the findings of the BPM and EMGM methods obtained in the present study did not reveal any latency differences because the head position was the same in the two methods and the only observed difference was in cVEMP amplitude data because the amount of produced muscular tension was different in the two methods.

Current study findings also indicate that the lowest SD values obtained for several cVEMP amplitude-related parameters were produced by the EMGM method (see Figure 2.8). Since SD is a measure of variability between sample data points (i.e. within the same subject or among subjects, depending on what we measure), it can be inferred that cVEMP data obtained by EMGM revealed lower inter-subject amplitude variability compared to BPM method. The more stable amplitude data obtained by the EMGM method could be due to the fact that this method involves actual measuring and viewing of EMG activities, so it is a more precise measure of muscle contraction levels as opposed to the BPM method, which involves following a target cuff pressure level on the blood pressure manometer screen. However, since comparing cVEMP amplitude values between subjects is not very useful in clinical settings because of the huge range of amplitude variability reported among subjects, the lower inter-subject amplitude variability demonstrated by EMGM method may be less clinically useful. On the other hand, the more robust cVEMP amplitude demonstrated by the BPM method might be more clinically useful, because a reduced response due to insufficient muscle contraction, produced by EMGM rather than BPM, might be interpreted as a vestibular pathology (i.e. false positive). As stated at the start of this chapter, this is the first study that compares two biofeedback methods used to control SCM muscle contraction variability in cVEMP testing. Thus, these findings have important clinical implications.

The findings that most of the present study participants (91 %) preferred the EMGM method and only few participants (9 %) did so for the BPM method suggest that the EMGM method is a more user-friendly method and is likely to be more acceptable to patients in clinical settings. The higher acceptance rate for the EMGM method could be explained by the fact that this method involves less muscular tension, as demonstrated by the lower cVEMP amplitude levels observed in this study compared with those obtained by the BPM method. Most of the participants, especially those with a past history of hand and/or arm injuries, reported difficulty in performing the BPM method. Participants also reported that the BPM is more difficult to perform because of the involvement of hands and arms in addition to neck flexion and this makes the BPM less comfortable to perform. Participants with frequent complaints of neck and shoulder stiffness due to muscle weakness resulting from lack of exercise also preferred to use the EMGM method to prevent muscular discomfort. Hence, it seems that the less muscular effort and the fewer structures are involved in the method, the more the method will be accepted by users. Thus, based on these findings, the first study hypothesis "i. *There will be no difference in cVEMP response parameters obtained by different biofeedback methods (BPM and EMGM) used to control SCM muscle contraction variability*" was rejected.

Although the effect of using different muscle activation procedures (i.e. HR versus HE), applied in different positions, has not been investigated in the present study because only one procedure was used (HR-S), the application of this procedure has been shown to be advantageous. The HR-S procedure is the only one that can be applied with BPM and EMGM methods since all the other SCM muscle activation procedures are performed in a supine position, in which it would not be practically possible to perform with the biofeedback methods. The findings that the HR-S procedure was able to produce robust cVEMP responses in normal subjects and that it was well tolerated by most users have been demonstrated by several studies (Wang and Young, 2006; Ito et al., 2007; Davenport, 2010). A recent study has reported even higher cVEMP normalized amplitude when the patient was seated compared to when lying supine (Sánchez-Andrade et al., 2014). In contrast, some published data suggest that the HE (supine) procedure revealed the most robust cVEMP amplitudes due to the high associated



muscle contraction involved in this procedure (Wang and Young, 2006; Davenport, 2010; McCaslin et al., 2013; Tseng et al., 2013). However, these investigations highlighted that pain, discomfort and muscle fatigue constitute major drawbacks of the HE (supine) procedure.

In addition to the compatibility of the HR-S procedure with biofeedback methods, the nature of the repeated measures design of this study, which required multiple cVEMP recordings, contraindicated the use of the HE (supine) procedure. If the HE (supine) procedure had been used in this study, it would probably have caused fatigue and affected participants' attention to task and reduced their procedure compliance, which might ultimately have affected the overall results. A similar situation could be encountered in clinic where multiple cVEMP recordings (i.e. to establish cVEMP threshold) are sometimes required. Hence, from the experience of using the HR-S procedure in this study and from the current evidence derived from published literature, it seems that the HR-S procedure would be the most clinically convenient procedure to activate the SCM muscle and hence, would be highly recommended to incorporate in cVEMP protocol.

Whether using an appropriate muscle activation procedure alone, without the use of a biofeedback method, is enough to achieve robust and even amplitude data across sides or not cannot be answered by the findings of the current study, because testing without a biofeedback method was not incorporated in the design. Conducting a similar study with an added testing condition (i.e. control condition) where no biofeedback method is used would help to answer this question. Two studies have examined whether applying the HE (supine) procedure (Isaradisaiikul et al., 2008) and the HR-S procedure alone (McCaslin et al., 2013) produce similar cVEMP amplitude data compared to those obtained with the EMGM method. The results of these two studies showed that cVEMP amplitude levels and inter-aural amplitude asymmetry data were not significantly changed after the application of the EMGM method. Another study used the HR-S procedure, once with a biofeedback method and another time without it, but this time the investigators used the BPM method (Suh et al., 2009). The study found statistically non-significant differences between the two testing conditions except that the lowest

IAR values were demonstrated by the BPM method condition. Hence, the question of how much difference there is in cVEMP amplitude and IAR data with and without applying a biofeedback method is still open for further exploration.

### **2.9.3 The influence of gender on cVEMP data**

The present study did not demonstrate any statistically significant differences between male and female participants in cVEMP normalized amplitude and latency measures, which is in line with a number of previous studies (Ochi and Ohashi, 2003; Basta et al., 2005b; Tourtillott et al., 2010; de Oliveira Barreto et al., 2011). However, the present study did find gender differences in cVEMP non-normalized amplitude data (non-normalized amplitude and pre-stimulus EMG estimate) for both biofeedback methods data. Results revealed that females demonstrated significantly lower amplitude mean values compared to males for both methods (see Table 2.3 and Figure 2.1). Comparison of cVEMP data across the two biofeedback methods, but within the same gender, revealed a method effect. Hence, the BPM method continued to show significantly higher non-normalized amplitude compared to those obtained by the EMGM method for each gender (see section 2.8.4). This outcome agrees well with the findings obtained in section 2.8.2, which suggest that a biofeedback method effect can be observed in cVEMP data without the use of amplitude normalization. Conversely, when amplitude normalization is applied, it is less likely that either a method or a gender effect in cVEMP amplitude will be observed. Interestingly, when cVEMP data of the present study were compared across the two methods but within the same gender (females), cVEMP normalized amplitude data produced by the BPM method continued to be significantly higher ( $p < 0.05$ ) than those obtained by the EMGM method. Hence, amplitude normalization was not able to completely remove all the biofeedback method effect observed in all tested groups.

As explained earlier, in Chapter 1 (section 1.6.4), some studies have noted gender differences in cVEMP latency and amplitude measures, but the findings of these studies are controversial. Although most studies, including the present study found no gender-related latency differences in cVEMP data (Akin et al., 2003; Basta et al., 2005b), some

studies found the opposite. For example, [Brantberg and Fransson et al. \(2001\)](#) found that females had earlier P1 latency and [Lee et al. \(2008b\)](#) found that females had longer latencies compared to males. The finding of significantly longer P1 latency in children and adults with longer necks could provide an explanation of latency differences among subjects ([Farina et al., 2002](#); [Chang et al., 2007](#)). The literature has provided variable results with regards to cVEMP amplitude differences among the two genders. While the majority of studies found no gender-related amplitude differences in cVEMP data, some studies found that females had higher cVEMP amplitudes compared to males ([Lee et al., 2008b](#)). Some authors explained that the thicker neck muscles in males increase the distance between the recording electrode and the contracted muscle, which results in reduced cVEMP amplitude in males ([Chang et al., 2007](#)). Other investigations suggested that females tend to show better compliance and cooperation in testing and this might explain why higher cVEMP amplitudes are seen in females ([Lee et al., 2008b](#)).

Hence, the findings of the present study are in broad agreement with these studies and that structural and anatomical differences between males and females could influence cVEMP results. However, if the explanation of Farina's and Chang's results are applied to this study, then cVEMP data of females should show higher amplitude values, because females tend to have lower muscular density compared to males ([Arts et al., 2010](#)), but this was not the case. The results of the present study showed that cVEMP data for females, with the use of each biofeedback method, consistently showed lower amplitude values compared to males. The gender-related differences observed in BPM and EMGM amplitude data here, were unlikely to be related to differences in muscle thickness between males and females; rather, the most logical explanation for this finding is the difference in muscular effort/strength between the two genders, in that males have stronger muscles than females ([Lee et al., 1994](#); [Ueda et al., 2002](#)). Thus, although both males and females had the same biofeedback methods applied during their cVEMP recordings, because of natural muscular differences between them, the EMG levels produced by stronger and higher density muscles (i.e. males' muscles) will still be different (i.e. higher) than those produced by less dense and relatively weaker muscles (i.e. females' muscles). The relationship between gender and muscle contraction level has been pointed out by [Akin et al. \(2011b\)](#). The investigators of this

study found a gender effect in cVEMP data with the use of the EMGM method in the younger group when responses were elicited at maximum contraction levels. Thus, it could be concluded that because of muscular differences between males and females and the fact that cVEMP amplitude is dependent on muscle contraction, gender should be considered when applying biofeedback methods in cVEMP testing.

The presence of a gender effect in the non-normalized amplitude data in this study and the absence of this effect in normalized amplitude data suggest that the amplitude normalization technique was able to factor out the differences observed in cVEMP amplitude between males and females. Hence, it could be inferred that the findings of this study suggest that the amplitude normalization technique was successful in reducing cVEMP inter-subject amplitude variability. The ability of amplitude normalization to remove the influence of natural differences among subjects was demonstrated by [Chang et al. \(2007\)](#). The study found that subcutaneous tissue was negatively correlated with cVEMP non-normalized amplitude and this relationship was lacking with normalized responses. Similar results were demonstrated by [Van Tilburg et al. \(2014\)](#). The study examined cVEMP responses of 20 normal subjects (9 males and 11 females) and found no effect of amplitude normalization on inter-aural amplitude variability (non-normalized IAR vs. normalized IAR). On the other hand, the study found that normalization caused a significant reduction in cVEMP inter-subject amplitude variability. Unfortunately, the effect of gender on cVEMP non-normalized and normalized amplitude data was not tested in Van Tilburg's study. Furthermore, it should be noted that the researchers in Tilburg's study used coefficient of variation (calculated by dividing the SD by the mean) to evaluate variability between non-normalized and normalized amplitudes (inter-subject amplitude variability) and the present study used SD as a measure of inter-subject amplitude variability.

#### 2.9.4 The optimal data analysis technique in cVEMP testing

The finding that there were statistically non-significant differences in IARs with and without the use of amplitude normalization obtained by the use of two biofeedback methods (see Figure 2.9, section 2.8.3) is in line with the findings of several previous investigations (Bogle et al., 2013; McCaslin et al., 2013; van Tilburg et al., 2014). In contrast, some studies have documented significant differences between non-normalized and normalized IARs in cVEMP testing. For example, Lee et al. (2008a) examined cVEMP IARs in 22 normal subjects using the HR (supine) procedure and BPM method with and without amplitude normalization and showed that the average IARs in the condition where the HR (supine) and BPM were combined, significantly decreased with the use of normalization. Another study compared IARs data obtained by HR (supine) procedure and EMGM method with and without normalization in 97 normal subjects and found that a combination of amplitude normalization with the HR (supine) procedure, without EMGM, revealed the lowest IARs data, but the differences were not statistically significant (McCaslin et al., 2013). In the present study, the upper normal IAR limit for BPM data without normalization was  $\approx 45\%$ . After normalization, it was reduced to  $\approx 42\%$  (Table 2.2, section 2.8.1). Hence, the present study finding of insignificantly reduced normalized IARs is consistent with the findings of McCaslin's study. However, the testing condition that showed this finding in McCaslin's study did not involve the use of a biofeedback method, whereas in the present study, this finding involved the use of the BPM method.

Similar findings were obtained by Welgampola and Colebatch (2001a) who reported an inter-aural asymmetry upper limit of 46% without normalization. When normalization was employed, it was reduced to 35%. McCaslin et al. (2013) reported that without the use of any biofeedback method or amplitude normalization, the upper normal limit for their IAR data was 44%. Again, it was reduced to about 31 to 37% when either a biofeedback method or amplitude normalization was used. In contrast, the upper normal limit for IAR established in the present study with and without amplitude normalization was almost the same for EMGM ( $\approx 42\%$ ). However, for the BPM method, IAR upper normal limit was reduced after amplitude normalization ( $\approx 45\%$  before

normalization and  $\approx 42$  after normalization). Thus, the findings of the current study (only BPM data) and the above discussed studies' findings imply that there is a trend of reduction in IAR data after normalization. This implies that this technique could possibly reduce cVEMP inter-aural amplitude variability. However, none of the obtained differences in the above mentioned studies, including those obtained in the present study, reached statistical significance.

Although the present study found no apparent effect for the use of an amplitude normalization technique on cVEMP inter-aural amplitude variability when measured by IARs, the reduced SD values demonstrated for the normalized responses suggest that amplitude normalization can reduce cVEMP inter-subject amplitude variability (see Figure 2.10, section 2.8.3). Furthermore, because the biofeedback method effect found in the present study (higher amplitude levels produced by BPM method compared to EMGM method) was mainly demonstrated in cVEMP non-normalized responses (see Figure 2.7, Panel A, section 2.8.2) and was not observed in normalized data (for both biofeedback methods), this suggests that amplitude normalization was able to reduce possible amplitude differences arising from muscular tension variations produced by different biofeedback methods. However, the present study showed that amplitude normalization sometimes was unable to remove the biofeedback method effect among female subjects. Hence, this technique is not perfect and it should not be assumed that amplitude normalization is completely effective in reducing cVEMP inter-subject amplitude variability possibly arising from the use of different biofeedback methods.

In brief, because cVEMP amplitude is well-known to be influenced by muscle contraction level, which is obviously affected by muscle strength, amplitude variation between males and females arising from natural differences in muscle strength should be considered while recording and interpreting cVEMP amplitude data. The present study documented gender-related amplitude differences with the use of a visual biofeedback method (BPM or EMGM). Thus, the use of biofeedback methods was not effective in reducing inter-subject amplitude variations produced by muscle strength variations among subjects. However, when an amplitude normalization technique was applied, it not only removed the gender effect but also the biofeedback method effect observed in

non-normalized data. Hence, the amplitude normalization technique produced more stable cVEMP amplitude data, regardless of the participant's gender or the type of biofeedback method used to obtain cVEMP responses.

Hence, based on the findings of the present study and the evidence derived from published data on the kind and amount of effect the amplitude normalization technique has on cVEMP overall amplitude data variability, it seems that this technique is more effective in stabilizing cVEMP inter-subject amplitude variability rather than cVEMP intra-subject (i.e. inter-aural) amplitude variability. Moreover, the existing controversy about the effect of amplitude normalization on cVEMP data in the present literature is probably caused by differences in methodology across investigations, the type of mathematical calculation used to obtain cVEMP normalized response and the possible interacting effect from the use of biofeedback methods. More importantly, the relationship between muscle contraction levels (measured by pre-stimulus EMG estimate) and cVEMP amplitude has been found to be not perfectly linear (Bogle et al., 2013). The authors in Bogle's study explained that in order to appropriately utilize amplitude normalization technique, the amplitude growth relative to pre-stimulus EMG estimate must be monotonic. If not, the results will vary based on the level of muscle contraction. The use of variable degrees of EMG targets across studies could also have added to the variability observed in cVEMP data obtained with and without this technique and consequently caused results' inconsistency.

Thus, based on these findings, the second hypothesis of this study "*the combined use of amplitude normalization technique with a biofeedback method (BPM or EMGM) will stabilize cVEMP inter-aural amplitude variability and produce lower IARs*" was rejected and the third hypothesis "*ii. The combined use of both a biofeedback method (BPM or EMGM) and amplitude normalization technique will stabilize cVEMP inter-subject amplitude variability and produce lower SDs*" was accepted.

## 2.10 Conclusion

Although it is agreed among researchers that controlling SCM muscle contraction variability is critical in cVEMP recording, the experimental findings reported in this chapter suggest that the different biofeedback methods described in the literature might reveal different cVEMP results. Although the EMGM method produced the lowest cVEMP inter-subject amplitude variability and was also preferred by the great majority of this study's participants, the finding that the BPM method produced higher cVEMP amplitude levels is more clinically important. Therefore, the BPM was identified as the optimal biofeedback method to use in cVEMP testing among healthy adults. In addition, application of the BPM method combined with an amplitude normalization technique produced the lowest cVEMP amplitude asymmetries. The findings presented in this chapter suggest that combining the BPM method with an amplitude normalization technique produces more robust cVEMP waveforms and more stabilized amplitude levels by producing lower inter-subject amplitude variability and less effect of this technique has been observed on inter-aural amplitude differences.

Although the majority of published research found no effect of gender on cVEMP data, the findings of this study showed that different biofeedback methods, proposed to control SCM muscle contraction variability, might produce significantly different cVEMP amplitude data between males and females, especially if cVEMP testing has been done without amplitude normalization. This finding is novel as this is the first study revealing gender effects in cVEMP non-normalized amplitude data with the use of a biofeedback method. The present study also is the first one to reveal that the application of amplitude normalization in cVEMP data analysis can reduce possible amplitude differences caused by natural variations in muscular effort and strength between males and females. Similarly, this is the first study to reveal that amplitude normalization can reduce possible amplitude differences arising from variations in muscular tension resulted from the use of different biofeedback methods. Thus, based on these findings, gender-specific cVEMP data is recommended to be used, especially if cVEMP testing is administered using a biofeedback method without amplitude normalization. The possibility of encountering gender differences or biofeedback method differences in



cVEMP amplitude data is less likely to occur if amplitude normalization is applied, but should not be excluded at this stage. The cVEMPs methodological findings obtained in this chapter will inform the cVEMP protocol used for the next study described in Chapter 3. Chapter 3 describes a study designed to examine the main thesis research question *"Does noise exposure affect vestibular function?"*

### **Chapter 3**

## **Noise-induced audio-vestibular dysfunctions in Saudi National Guard personnel**

### 3.1 Introduction

Following identification of an optimal cVEMP methodology in Chapter 2, this chapter describes a study aimed at identifying the effects of noise exposure on the vestibular system, particularly saccular function. The chapter starts by providing a brief overview of audio-saccular dysfunction among individuals affected by noise exposure. The review summarizes current knowledge of the effect of noise exposure on hearing, cochlear and saccular function using pure tone audiometry, otoacoustic emissions (OAEs) and cervical vestibular evoked myogenic potential (cVEMP). This is followed by reporting the findings of the second study of this thesis.

### 3.2 Audio-saccular dysfunction in noise-exposed individuals

It is well established that prolonged exposure to high noise intensity levels is associated with damage of hair cells in the inner ear and the development of permanent hearing threshold shift known as noise-induced hearing loss (NIHL). NIHL has been extensively studied. However, because noise exposure is a widespread hazard in modern life, investigators are still continuing to study NIHL. As explained earlier in Chapter 1 (section 1.7.3), pure tone audiometry (PTA) is the current gold standard to diagnose NIHL. Another important diagnostic tool, the otoacoustic emission (OAE), has been identified as a sensitive tool to monitor and/or detect outer hair cell (OHC) damage resulting from noise exposure. Therefore, there is a general consensus in the literature that the use of both behavioural (i.e. PTA) and physiological (i.e. OAE) assessment tools is important in the clinical diagnosis of NIHL. Several investigations suggest that OAE, particularly distortion product otoacoustic emission (DPOAE), is capable to detect earlier changes in cochlear function due to noise exposure compared to behavioural audiometric thresholds. This was demonstrated by the findings of reduced or absent OAE amplitudes in the presence of normal pure tone audiometric thresholds (Stephenson and Stephenson, 2000; Kim, 2006; Yankaskas, 2013). When some OHCs tuned to a specific frequency die due to excessive noise exposure, they may not change audiometric hearing thresholds unless there are sufficient dead OHCs in

that frequency region, then a permanent hearing reduction will be reflected in the audiogram. This explains why DPOAE can often detect damage to OHCs before it appears in the audiogram. Thus, DPOAE could be a potential test to assess risks for cochlear changes as a result of noise exposure and could be employed as a screening test for NIHL (Marshall et al., 2001; Seixas et al., 2004).

As other health consequences of noise exposure, like balance disturbances, are being identified in the literature, this has increased the need to conduct more studies to investigate the relationship between NIHL and these pathologies. As explained in Chapter 1 (section 1.7.4), the evidence of saccular damage due to noise exposure is gradually increasing and given that cVEMP is currently the only available clinical tool to evaluate saccular function, the application of this technique in clinical diagnosis of patients suspected of saccular dysfunction has increased over the last couple of years. Moreover, the use of cVEMP has recently been advocated to detect possible noise-induced saccular dysfunction in individuals suffering from NIHL. Although abnormal cVEMPs resulting from excessive noise exposure in animal models have been demonstrated by several investigations (see Chapter 1, section 1.7.2), only a few studies have been conducted in humans (Wang et al., 2006; Wang and Young, 2007; Wu and Young, 2009; Kumar et al., 2010; Akin et al., 2012; Tseng and Young, 2013). These studies found that cVEMP characteristics for NIHL and acoustic trauma patients were different (i.e. absent or abnormal) from those obtained in adults with normal audio-saccular function and no history of noise exposure. Nonetheless, the reported cVEMP characteristics in individuals affected by NIHL in these studies were controversial. For example, while Kumar et al. (2010) demonstrated a prolongation of P1 and N1 latencies among NIHL patients, several other investigators reported no changes to P1 and N1 latencies in these cases (Wang and Young, 2007; Wu and Young, 2009; Akin et al., 2012; Tseng and Young, 2013). The same is true for amplitude. Only a few studies showed that the investigated NIHL patients had smaller cVEMP amplitudes compared to controls (Kumar et al., 2010; Akin et al., 2012; Tseng and Young, 2013), the rest of them found that amplitude measurements for cVEMP obtained from NIHL were similar to controls. The cVEMP absence rates reported among NIHL cases by these studies were

variable as well (between 33 to 75 %). Hence, there is some documentation of cVEMP abnormalities among NIHL cases but the available data is incomplete. Moreover, the above studies are confounded by the use of small sample sizes ( $\leq 20$  subjects), different cVEMP methodologies and diverse subjects' characteristics, such as different age groups and different noise exposure histories. The fact that cVEMP is a relatively new clinical procedure and most cVEMP studies were conducted on controls as part of investigating the procedure protocol contributes also to lack of definition of cVEMP characteristics in many vestibular disorders including noise-induced saccular dysfunction.

Because the above studies have documented cVEMP abnormalities in cases of NIHL, a relationship between noise-induced cochlear changes and noise-induced saccular changes has been assumed. However, this is just an assumption because the mechanism of noise-induced saccular damage and its relationship with NIHL are not yet established. It is currently assumed that both cochlear and vestibular systems might receive equal amounts of effects from noise exposure (Damiano and Rabbitt, 1996; Rabbitt et al., 1996). This assumption came from the fact that both structures are in close anatomic proximity, they have a common embryological origin, they share the membranous labyrinth, they have similar hair cell ultra-structures and they also share a common arterial blood supply via the same end artery. The close proximity of the stapes footplate to macular structures also makes the vestibular structures close to the entry point for sound energy. This all supports the proposition that noise levels, which can cause damage to the cochlea, could also affect the vestibular system. Although an association between hearing loss and saccular damage has been demonstrated in individuals aged 70 years or older (Zuniga et al., 2012) and also in patients with high frequency sensorineural hearing loss (Sazgar et al., 2006), the association between noise-induced cochlear damage and noise-induced saccular damage has not been determined yet.

Although there is a significant gap in our understanding of the relationship between cochlear damage and vestibular damage in general, both at the peripheral and the central levels, there is a growing evidence in the literature of central vestibular-auditory interaction

(Todd et al., 2014a; Todd et al., 2014b). The evidence from Todd and colleagues' research comes in from electroencephalography (EEG), cVEMP and late auditory potentials data collected in humans. The results showed that vestibular receptors may contribute to late auditory potentials which are cortical in origin. The findings of these studies are supported by vestibular neuroimaging studies (Barker et al., 2012; Lopez et al., 2012). The evidence that acoustic activation of the vestibular system may play a role in normal hearing was further supported by the findings that vestibular inputs may improve temporal and spatial aspects of hearing (Probst and Wist, 1990; Emami and Daneshi, 2012; Brimijoin and Akeroyd, 2012) and may contribute as well to speech perception and metical aspects of musical perception (Phillips-Silver and Trainor, 2008; Emami et al., 2012).

Thus, the evidence of auditory and vestibular interaction at the cortical level is gradually growing in the literature and it supports the general presumed association, discussed earlier, between hearing loss and vestibular dysfunction. However, there are several issues at a peripheral level that are still unclear. For example, it is still unknown if noise-induced saccular damage occurs first, after or at the same time as noise-induced cochlear damage. Hence, the possibility of saccular dysfunction without or before noise-induced cochlear damage becomes evident in the pure tone audiogram has not been looked at yet. To the best of the author's knowledge, there are no published cVEMP data for individuals with a history of noise exposure, who are at risk of developing cochlear damage, but still have normal hearing. If cochlear damage in noise-exposed individuals with normal hearing evident by PTA has been identified earlier via OAEs, then saccular damage could have become evident in noise-exposed individuals with normal hearing but with documented OHCs dysfunctions evident by OAEs. In other words, individuals with a self-reported history of noise exposure but with normal audiometric hearing thresholds and abnormal OHCs function could possibly have abnormal saccular function when assessed by cVEMPs. The only study the author is aware of that has reported vestibular dysfunction in noise-exposed individuals with normal hearing was the one carried out by Raghunath et al. (2012). However, this study documented only subjective vestibular complaints from 20 normal hearing factory workers presenting with long-term history of occupational noise exposure

and no cVEMP data were obtained in this study.

Given that it is usually recommended to incorporate a test battery approach in clinical diagnosis to ensure consistency between tests results, a number of studies, though limited in number, have evaluated the relationship between cVEMP responses and other common audio-vestibular clinical procedures (Wang and Young, 2007; Kumar et al., 2010; Akin et al., 2012; Zuniga et al., 2012). These studies found that abnormal cVEMP occurred more frequently in noise-exposed ears with poorer NIHL in the high frequency region. The established association between high frequency hearing loss and cVEMP findings could be explained by the tonotopic organization in the cochlea (i.e. high frequencies stimulate the basal end of the cochlea while low frequencies stimulate the apical end), which is maintained throughout the auditory system (Clark, 2008). Hence, there is emerging evidence of a relationship between cVEMP findings and pure tone audiometric thresholds, particularly at high frequencies but the present evidence so far is insufficient and more data is needed to support this evidence. Thus, by collecting both PTA and cVEMP findings from noise-exposed individuals, the present study aimed to clarify the relationship between those two important clinical tools. If there is a potential association between cVEMP responses and pure tone audiometric thresholds then it would be sensible to test this relationship also with OAE. The fact that both cVEMP and DPOAE are physiological measures and the established high sensitivity of DPOAE to detect early changes in the cochlea as a result of noise exposure support the need to investigate such possible relationship.

Hence, in view of the demonstrated research gaps in the audio-saccular dysfunction presented in noise-exposed population and because of the uncertainty in the relationship between hearing loss, OHC dysfunction and saccular dysfunction due to noise exposure, the study presented in this chapter aimed to expand existing studies by evaluating audio-saccular function among noise-exposed individuals with and without NIHL as well as with and without OHC dysfunction using the optimized cVEMP protocol, previously established in Chapter 2. To gain more understanding of the relationship between cochlear and saccular

dysfunctions resulting from noise exposure, the study also aimed to look at possible associations among three commonly used diagnostic tools (cVEMP, PTA and DPOAE).

To summarize, despite the presence of several investigations supporting that excessive noise can affect vestibular function, the available literature is limited and inconclusive. If excessive noise exposure impairs vestibular function and if the saccule is the most likely affected site, then cVEMP may be an appropriate measure to evaluate this effect. However, the present literature lacks a clear description of how exactly noise alters cVEMP responses. Some studies have described cVEMP characteristics in NIHL cases, but the use of small sample sizes and varied cVEMP methodologies have led to inconsistent findings among these studies. Although the mechanism of noise-induced saccular damage is not yet fully understood, Animals' pathophysiological studies suggested a resemblance between the damage observed in the cochlea and vestibular structures due to similarities in hair cell ultrastructure between the cochlea and the vestibular system. The available literature has only investigated saccular involvement in NIHL or acoustic trauma patients. To the author's best knowledge, cVEMP characteristics in individuals who are at high risk of developing NIHL but still have normal audiometric thresholds with or without OHC dysfunction evidenced by OAEs have not been investigated yet. In addition, there have been some attempts to combine different vestibular function tests with conventional diagnostic tests, such as PTA and OAEs to understand the audio-vestibular changes in noise-exposed individuals. However, collection of cVEMP data along with PTA and DPOAE from such a population has not been reported previously. Thus, given the demonstrated research gaps in this area of research, the study described in this chapter attempted to explore in more depth saccular damage using cVEMP among noise-exposed individuals with and without NIHL as well as with and without OHC dysfunction.



### **3.3 Aim of the work described in this chapter**

The literature has suggested the usefulness of using PTA, OAEs and the relatively new cVEMP technique to detect audio-saccular damage due to noise exposure in both animal and human studies (see Chapter 1, section 1.7.2). Hence, the research reported in this chapter utilizes these three procedures to investigate noise-induced audio-saccular damage among noise-exposed individuals. The experimental work presented in this chapter has three aims; 1) to determine the effects of noise exposure on cVEMP among workers with a self-reported history of occupational noise exposure and confirmed cochlear damage (NIHL group) 2) to determine the effects of noise exposure on cVEMP among workers who have a similar self-reported history of occupational noise exposure but intact auditory structures (noise-exposed normal hearing "NH" group). The findings obtained from those two noise-exposed groups were compared with the findings of healthy individuals with normal audio-saccular function and no history of noise exposure (control group) 3) due to the inconsistencies shown in the literature for the relationship between the three diagnostic procedures (PTA, DPOAE, cVEMP), the present study aims also to investigate the relationship between PTA versus DPOAE, cVEMP versus PTA and cVEMP versus DPOAE. The data collected in this study will help in understanding the relative sensitivity of the cochlea and the saccule to excessive noise exposure.

The nature of differences expected to occur in cVEMP response parameters among the three investigated groups (controls, noise-exposed NIHL group and noise-exposed NH group) were inferred from previous investigations discussed earlier in the introduction of this chapter. It has been hypothesized in this study that because of the close proximity and the anatomical and physiological similarities between the saccule and cochlear structures, excessive noise exposure is likely to cause saccular damage and cVEMP is sensitive to detect such damage. Additionally, if the saccule is prone to damage from excessive noise exposure, then it would be expected to find cochlear damage too, and DPOAE and PTA are sensitive tools to detect such damage. However, if the saccule is more sensitive to excessive noise exposure compared to the cochlea, then it would be expected to see saccular damage

shown by abnormal cVEMP and normal cochlear function demonstrated by DPOAE and PTA. The opposite is also true, meaning that if the cochlea is more sensitive to excessive noise exposure, then it would be expected to see cochlear damage shown by DPOAE and PTA and normal saccular function demonstrated by normal cVEMP. Thus, the present study examined three hypotheses:

- i) If noise exposure affects saccular function, then cVEMP findings of *noise-exposed individuals with NIHL (NIHL group)* would demonstrate:
  - a) A higher abnormal/absent cVEMP rate compared to those obtained from individuals with normal audio-vestibular function without a history of noise exposure (controls).
  - b) A longer P1 latency compared to those obtained from controls.
  - c) A longer N1 latency compared to those obtained from controls.
  - d) A reduced P1-N1 peak to peak amplitude compared to those obtained from controls.
- ii) If long-term noise exposure can cause early vestibular dysfunction and cVEMP is sensitive to detect such damage, even if noise-exposed individuals still have normal hearing evident by routine clinical testing, then, *noise-exposed individuals with normal hearing (NH group)* would demonstrate:
  - a) A higher abnormal/absent cVEMP rate compared to those obtained from controls.
  - b) A longer P1 latency compared to those obtained from controls.
  - c) A longer N1 latency compared to those obtained from controls.
  - d) A reduced P1-N1 peak to peak amplitude compared to those obtained from controls.
- iii) Because the literature has provided evidence for noise-induced saccular damage mainly in individuals with *NIHL (NIHL group)*, it was hypothesized that noise-exposed individuals with documented NIHL are more likely to develop noise-induced saccular damage compared to *noise-exposed individuals with normal hearing (NH group)*. Hence, the *NIHL group* would demonstrate:
  - a) A higher abnormal/absent cVEMP rate compared to those obtained from the noise-exposed NH group.
  - b) A longer P1 latency compared to those obtained from the noise-exposed NH group.
  - c) A longer N1 latency compared to those obtained from the noise-exposed NH group.

- d) A reduced P1-N1 peak to peak amplitude compared to those obtained from the noise-exposed NH group.

### **3.4 Methods**

#### **3.4.1 Participants**

One hundred and nine male working personnel ranging in age from 22 to 60 years (mean age =  $38.42 \pm 9.01$ ) with a self-reported history of occupational noise exposure were recruited for this study. Participants were hospital technicians working at the Utility and Maintenance Department in King Abdulaziz Medical City (National Guard hospital) and soldiers working at two NG military sectors. Recruitment and data collection took place in the audiology unit in the ENT clinic at NG Hospital in Riyadh City, Saudi Arabia. Several recruitment meetings were conducted with heads and senior staff of military services in National Guard hospital to identify the personnel working in potentially noisy worksites. The purpose of the study and participants' inclusion criteria including age ( $\leq 60$  years), type of job (involved high levels of noise exposure) and employment duration (at least one year in current noisy worksite) were explained during the meetings. Prior to data collection, follow-up phone calls with units' supervisors were carried out on a weekly basis to ensure appropriate referrals for the target population.

Findings obtained from the noise-exposed group were contrasted with a control group, which was the same group enrolled in the previously described study in Chapter 2. The control group consisted of 90 normal hearing volunteers (50 females and 40 males) with no history of occupational or leisure noise exposure. Ethical approval was granted by two committees: the School of Healthcare Research Ethics Committee (SHREC/RP/225) at the University of Leeds and the Institutional Review Board and Research Committee at King Abdullah International Medical Research Centre (KAIMRC- Ref no. RC 12/017) in Riyadh City, Saudi Arabia. Prior to testing, information sheets were provided to all participants, which

explained the overall aim of the study, what they were required to do, possible risks, discomforts and benefits from participation, confidentiality of data, how to get more information about the study and the participants' research rights. In addition, written informed consent was obtained from all participants. Because the study involved Arabic and non-Arabic speaking participants, the consent forms and the information sheets were made available in two languages (Arabic and English). Prior to testing, demographic data regarding type of current job, department the subject belongs to, previous jobs and duration spent in each job held were collected to ensure the presence of sufficient noise exposure history. In addition, self-reported medical and occupational history was obtained from all participants by the main investigator to ensure that none of the enrolled participants had any of the following exclusion criteria:

- i. History of outer ear, middle ear or inner ear disease
- ii. History of head trauma to rule out cochlear and/or vestibular trauma
- iii. History of previous ear surgery
- iv. History of congenital or familial hearing deafness
- v. History of musculoskeletal diseases or neck problems
- vi. Taking prescription medication at the time during conducting measurements (e.g. vestibular suppressant medications).

Participants older than 60 years were not included in the study to avoid the overlapping of age related hearing loss (presbycusis) with NIHL and also because age-related changes after the age of 60 have been documented in cVEMP (Janky and Shepard, 2009; Maes et al., 2010). Because participants reported different durations and levels of noise exposure, their hearing status was expected to be varied and therefore the study included participants who either had normal hearing or NIHL in one or both ears. Normal hearing sensitivity was defined as normal pure tone air conduction thresholds  $\leq 25$  dB hearing level (dB HL) at 0.25, 0.5, 1, 2, 3, 4, 6 and 8 kHz and less than 10 dB audiometric difference between air conduction and bone conduction thresholds. The participants who presented with hearing

loss identified later as non-typical audiometric configuration of NIHL were excluded from the study.

The diagnostic criteria of a typical NIHL audiogram were based on the guidelines of the American College of Occupational and Environmental Medicine (ACOEM, 2003), which are as follows:

- i. The hearing loss is of sensorineural type, which is known to affect the hair cells in the inner ear
- ii. Usually, both ears are affected, "bilateral hearing loss"
- iii. No significant hearing loss asymmetries between ears unless the person reported only a unilateral noise exposure, which is commonly seen in cases of rifle or gun shooting
- iv. Greatest hearing loss around 4 kHz "audiometric notch"
- v. Pure tone average (PTA) of high frequencies (3, 4, 6 and 8 kHz) is greater than PTA of low frequencies (0.25, 0.5, 1 and 2 kHz).

The audiometric notch also known as "noise notch" or "high frequency notch" is commonly seen at 4 kHz, but can be seen also at 3 or 6 kHz, with recovery at 8 kHz. The notch was defined by a hearing threshold at 3, 4 or 6 kHz, which is at least 10 dB greater than at 1 or 2 kHz and at 6 or 8 kHz (Coles et al., 2000). As explained in Chapter 1 (section 1.7.2), although the documentation of this notch in the presence of a history of noise exposure has been accepted as a clinical sign of NIHL, it is not always seen because it tends to deepen and widen as the noise exposure continues. For this reason, the audiometric notch is a clinical feature of NIHL but not a major diagnostic factor for this type of pathology (McBride and Williams, 2001a; McBride and Williams, 2001b; Osei-Lah and Yeoh, 2010). Thus, not all participants identified in this study with typical NIHL had the classical audiometric notch. In addition, if a noise-exposed participant had been identified with a typical NIHL only in one ear and the other ear had a high frequency sensorineural hearing loss but it does not match all the criteria items specified above (ACOEM criteria), the participant was still included in the study and this ear was still classified under the NIHL group. Hence, all the participants included in the present study, had been identified with at least one ear with a typical NIHL.

### 3.4.2 Pure tone audiometry (PTA)

All participants underwent hearing threshold testing using a calibrated GSI 61 clinical audiometer (Grason-Stadler Instruments, Viasys Healthcare Corp., USA). Air and bone conduction thresholds were measured at octave and half-octave frequencies between 250 to 8000 using the American Speech-Language-Hearing Association clinical recommended procedures for manual pure tone audiometry (ASHA, 1997; ASHA, 2005). Pulsed pure tone stimuli were delivered to participants' ears using standard headphones (TDH-39, Medical Electronics Devices and Instrumentation 'MEDI', Benicia, CA, USA). Pulsed pure tones were used as opposed to steady tones because they are easier to distinguish for normal hearing individuals as well as for patients with sensorineural hearing loss and tinnitus (Mineau and Schlauch, 1997; Burk and Wiley, 2004). Pure tone audiometric testing was carried out in a sound-treated room meeting the American National Standards Institute (ANSI, 2004). Audiometry was performed 48 hours after subjects' last episode of noise exposure to rule out the presence of any temporary shift of hearing thresholds as a result of noise exposure (NIOSH, 1998). For some participants, especially those who worked on shift, it was only possible to test them after 12 hours removal from noise. Thus, if their audiograms showed a hearing loss then they were scheduled for re-testing to exclude the presence of any temporary threshold shifts. Prior to audiometric testing, all participants had normal otoscopic findings and bilateral normal middle ear function measured by tympanometry (Grason-Stadler 'GSI' TympStar, Viasys Healthcare Corp., USA). Normal middle ear function was defined by normal middle ear pressure and compliance; type A tympanogram; middle ear pressure within  $\pm 50$  daPa and compliance between 0.3 to 1.5 ml 'equivalent volume' (ASHA, 1990; Wiley et al., 1996; ASHA, 1997).

### 3.4.3 Distortion product otoacoustic emissions (DPOAEs)

DPOAEs were recorded using the Echoport ILO288 system (ILO V6 clinical OAE software, Otodynamic, London, UK) using clinical recommended procedures for DPOAE measurements (Dhar and Hall, 2011). Recordings were obtained with an adult probe after calibrating with a 1-cc calibration cavity. Prior to each recording, probe fit verification was automatically performed by the system to ensure there was no leakage between the probe loudspeaker and the microphone, to verify signal characteristics within the ear canal and to obtain a reasonably flat spectral frequency response between 0.5 to 6 kHz. DPOAEs were recorded using the Distortion Product (DP) gram method (see Chapter 1, section 1.7.3). The stimuli levels were held constant at  $L_1 = 65$  dB SPL and  $L_2 = 55$  dB SPL and the  $f_2/f_1$  ratio was held at 1.22. DPOAE amplitude level and signal to noise ratio (SNR) occurring at  $2f_1-f_2$  were measured in half octave band frequencies of 1, 2, 3, 4 and 6 kHz. The noise rejection level was set at 6 mPa (49.5 dB SPL). DPOAE amplitudes and noise floors were monitored by the investigator and the test was terminated manually when all DP amplitudes were seen on the DP graph for all tested frequencies. Because DPOAE measurements were performed in a standard quiet clinical room, a super-aural full size headphone (R 80, Koss Corp., WI, USA) was placed on participants' ears to reduce the effect of any possible ambient room noise. Because DPOAE measurement systems provide a measure of both the DPOAE level and the surrounding noise level, the presence of a particular DPOAE is usually determined by comparing the DPOAE amplitude measured within its frequency region with the noise levels in the surrounding frequency region and using some difference criterion. For example, DPOAE might be considered present if the DPOAE amplitude level is 3 dB or more above the level of the surrounding noise floor or if its amplitude exceeds two SD above the mean noise level. Published DPOAE data from normal adult populations are widely available (Cazals et al., 1980; Gorga et al., 1993). Therefore, DPOAE data were collected only from the noise-exposed group and no DPOAE data were collected from the control group.

The following criteria were used to characterize DPOAE outcomes (Dhar and Hall, 2011):

- i. *Present normal DPOAE*; DPOAEs were detectable and replicable for all tested frequencies and their levels fell within an appropriate normal region ( $> 0$  dB SPL) in the presence of a sufficiently low noise floor at all tested frequency ( $\text{SNR} \geq 3$  dB)
- ii. *Present abnormal DPOAE*; DPOAE levels were reduced (0 to -10 dB SPL) at one or more of the tested frequencies and/or DPOAE levels occurred within the noise floor ( $\text{SNR} < 3$  dB)
- iii. *Absent DPOAE*; DPOAEs were neither detectable nor replicable at one or more of the tested frequencies ( $< 0$  to -10 dB SPL) and/or DPOAE levels occurred within the noise floor ( $\text{SNR} < 3$  dB).

#### **3.4.4 Cervical vestibular evoked myogenic potentials (cVEMPs)**

The optimal cVEMP protocol established in the previous chapter (Chapter 2) was adopted here in this study incorporating heading rotation-sitting (HR-S) as a muscle activation procedure, blood pressure manometer (BPM) as biofeedback method and normalized amplitude as the data analysis technique. For a complete description of cVEMP protocol employed in this study, see Chapter 2 (section 2.7.2). cVEMP response rate, which is the number of present cVEMP responses as a proportion of the total number of ears tested, was calculated for all participants. cVEMP abnormality rate is the number of present but abnormal cVEMP responses as a proportion of the total number of ears tested. The mean levels of the following cVEMP response parameters were measured; P1 absolute latency, N1 absolute latency and P1-N1 peak to peak amplitude. A definition of cVEMP response parameters and an illustrative figure of a typical cVEMP response obtained from a person with normal saccular function were provided in Chapter 1 (section 1.6.3). Although cVEMP threshold was found to be a useful measure to diagnose certain vestibular pathologies like superior SCD (Brantberg et al., 1999; Zuniga et al., 2013), it was not included here because it is beyond the scope of this research and for several other reasons previously outlined in Chapter 1 (section 1.6.3). Two measures were used to examine participants' cVEMPs



responses; cVEMP response rate (present/normal vs. absent/abnormal) and comparison of cVEMP response parameter values (P1 absolute latency, N1 absolute latency and P1-N1 peak to peak amplitude) with normative data obtained from controls. The following criteria were used to characterize cVEMP responses:

- i. *Present/normal cVEMP*: the biphasic P1-N1 waveform occurred at latencies and amplitudes corresponding to the normative values reported in Chapter 2. The normal ranges for cVEMP response parameters (obtained using the optimal protocol established in Chapter 2) were used (P1 absolute latency (11.86 – 19.78 ms), N1 absolute latency (20.11 – 29.33  $\mu$ V), normalized amplitude (0.12 – 2.46 ratio). The normal ranges were calculated using 95 % prediction interval which equals the mean  $\pm$  1.96 multiplied by SD.
- ii. *Present/abnormal cVEMP*: the biphasic P1-N1 waveform was reliably recorded and reproducible but one or more of the response parameters values fall outside the expected normal ranges specified above.
- iii. *Absent cVEMP*: the biphasic P1-N1 waveform could not be clearly identified and reproducibility was poor or questionable in at least two runs.

All test procedures (PTA, DPOAE and cVEMP) were conducted on the same day within a single recording session lasting approximately one hour per participant.

### **3.4.5 Data analysis**

Data collected from 85 participants (170 ears) were analyzed using IBM SPSS 21.0 software (SPSS Software, SPSS Inc., Chicago, IL, USA). Initial descriptive statistics, histograms and normality measures (Shapiro-Wilk) performed on data showed that the data were not normally distributed. Thus, non-parametric tests (Wilcoxon Signed Ranked Test and Mann-Whitney *U* Test) were used to analyze data and an alpha level of  $p < 0.05$  was used to determine significance. Since mean values are more commonly reported in published literature, they are reported in this study to facilitate comparison. However, median values are reported as well because they more accurately represent non-normally distributed

data. Because the regions of the basilar membrane responsible for high frequencies (i.e. the basal turn of the cochlea) are more sensitive to noise exposure (Savolainen and Lehtomäki, 1996; Karatas, 2008), PTA thresholds and DPOAE response parameters (DP absolute amplitudes, SNR and DP amplitude average) were reported only at 2, 4 and 6 kHz. Participants' PTA data were divided into two main groups according to participants' hearing status a) noise-exposed normal hearing (NH) group and b) noise-exposed NIHL group. The normal PTA and cVEMP responses obtained from the normal hearing participants with no history of noise exposure (N = 90) established in the previous study in Chapter 2 served as control group data for this study. It should be noted here that because a gender effect was demonstrated in non-normalized amplitude data in the normative data obtained in Chapter 2 (see section 2.8.4), only cVEMP normalized amplitude data were analyzed in this study. The data collection procedures (PTA, DPOAE and cVEMP) used were identical for the two noise-exposed groups. The differences between the two noise exposed groups' (NIHL group and noise-exposed NH group) findings and also the differences between each noise-exposed group's findings and the control group's findings were highlighted.

In addition, the overall noise-exposed group data (PTA, DPOAE and cVEMP) were further examined to seek evidence for any possible relationship between the three sets of measures (two test variables at a time). Since most of the data obtained in this study were not normally distributed, Spearman's Correlation Coefficient ( $r_s$ ) was used to test the relationship between PTA, DPOAE and cVEMP. The following criteria was used to determine the size of correlation: very strong correlation ( $0.9 < r_s < 1.0$ ), strong correlation ( $0.7 < r_s \leq 0.9$ ), moderate correlation ( $0.5 < r_s \leq 0.7$ ), weak correlation ( $0.3 < r_s \leq 0.5$ ) and no to very weak correlation ( $r_s \leq 0.3$ ) (Satake, 2015). Scatter plots were used to illustrate the direction and the strength of the established relationships between the tested variables (PTA thresholds, P1 latency, N1 latency, P1-N1 normalized amplitude, DP amplitudes).

## 3.5 Results

Out of the 109 recruited participants in this study, 24 were excluded; 12 participants were not able to complete all investigations due to time constraints and 12 participants had non-typical NIHL pure tone audiograms. Thus, the remaining data of 85 participants (170 ears) went under analysis. Participants were all adult male workers aged between 22 and 60 years (mean =  $38.42 \pm 9.01$ ). Twenty seven of them were hospital technicians and 58 were soldiers. All participants reported a minimum of one year occupational noise exposure and their years of work history ranged from one to 35 years (mean =  $15.53 \pm 8.17$ ). The occupational environments of the participants included power plant in 15, water treatment in 11, artillery in 41 and weapons/explosions in 17.

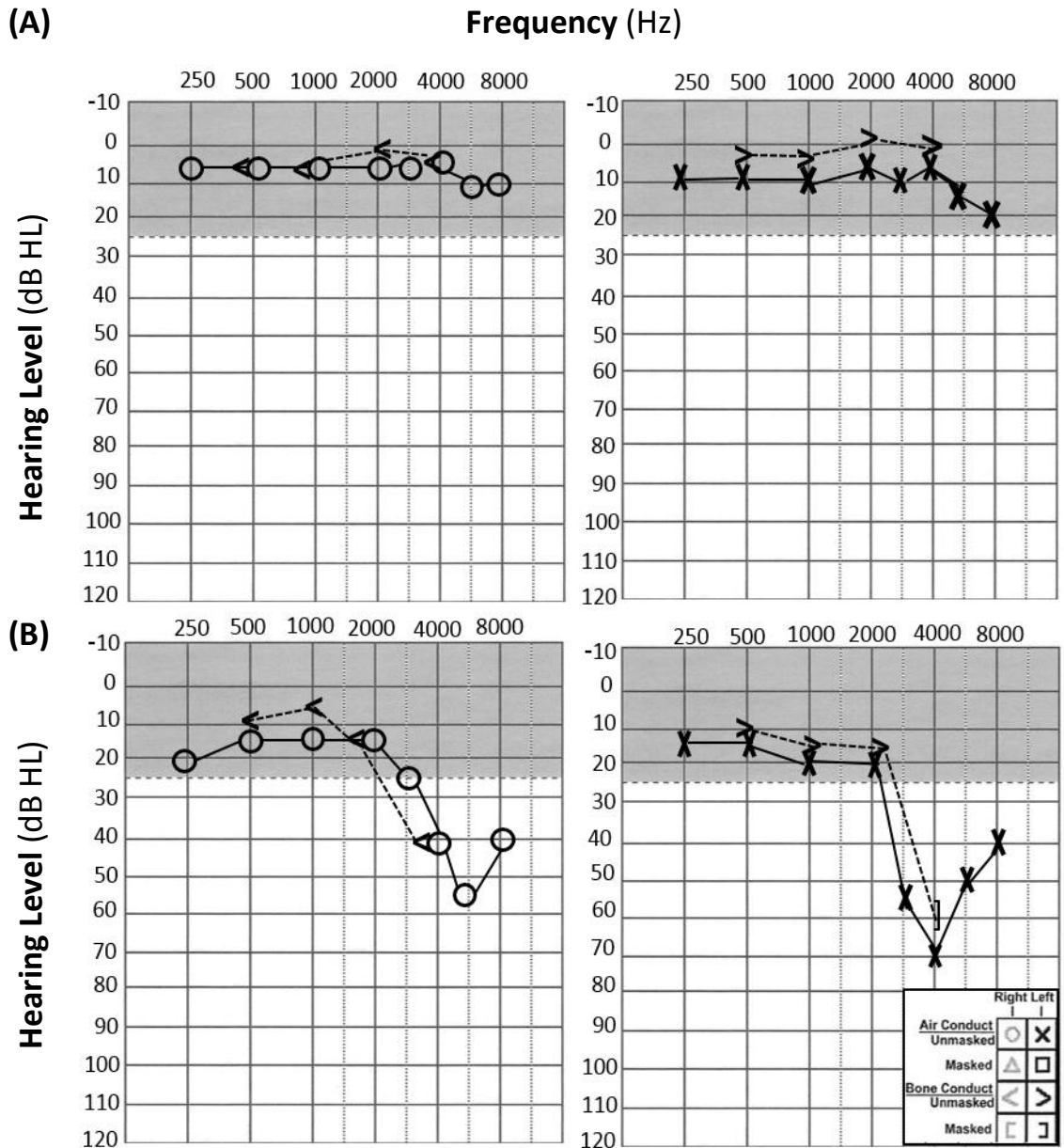
### 3.5.1 Pure tone audiometry (PTA) data

All participants had unremarkable otoscopic examination and normal middle ear function on the days of testing. Table 3.1 shows the classification of study participants (N = 85 participants = 170 ears) according to their hearing status. Figure 3.1 shows examples of normal and abnormal pure tone audiograms obtained from two participants. As explained earlier in section 3.4.1, although all participants' audiograms satisfied the criteria of a typical NIHL, not all participants had the audiometric notch (at 4, 3 or 6 kHz), because it is commonly seen at early stages of noise damage and then it tends to flatten and disappear with long-term exposure (McBride and Williams, 2001a; McBride and Williams, 2001b). Hence, among the 78 ears with NIHL, 17 (21.8 %) had mild to moderate sensorineural hearing loss demonstrated only at one high frequency (i.e. audiometric notch at 3, 4 or 6 kHz). Fifty ears (64.1 %) had mild to moderate degree of NIHL and 11 ears (14.1 %) had moderate, severe or profound NIHL. Mean, median and SD for pure audiometric thresholds obtained at 2, 4 and 6 kHz as well as the PTA average of these three frequencies for the three groups (controls, noise-exposed NH group and NIHL group) are given in Table 3.2. Wilcoxon Signed Rank test showed that there were statistically non-significant differences between PTA data of the right and left ears within each group ( $p > 0.05$ ). Hence, subsequent

analysis was performed for both ears combined. Mann-Whitney *U* test showed that pure tone thresholds calculated at 2, 4 and 6 kHz as well as the average PTA calculated at these three frequencies were significantly different among all groups (Figure 3.2). Results showed also that the NIHL group had the worst PTA thresholds and the worst PTA average compared to the control and noise-exposed NH groups. Moreover, the worst hearing thresholds were observed at 6 kHz across all groups.

**Table 3.1 Classification of study participants (N = 170 ears) according to hearing status.** Age range (mean  $\pm$  standard deviation 'SD'), number of ears (N) and percentages are provided for each group.

<b>Groups</b>	<b>Age range (mean <math>\pm</math> SD )</b>	<b>N (%)</b>
Noise-exposed - normal hearing (NH)	22 – 60 (34.30 $\pm$ 7.86)	92 (54.1)
Noise-induced hearing loss (NIHL)	25 – 60 (43.28 $\pm$ 7.82)	78 (45.9)
Both groups (NH and NIHL)	22- 60 (38.42 $\pm$ 9.01)	170 (100)

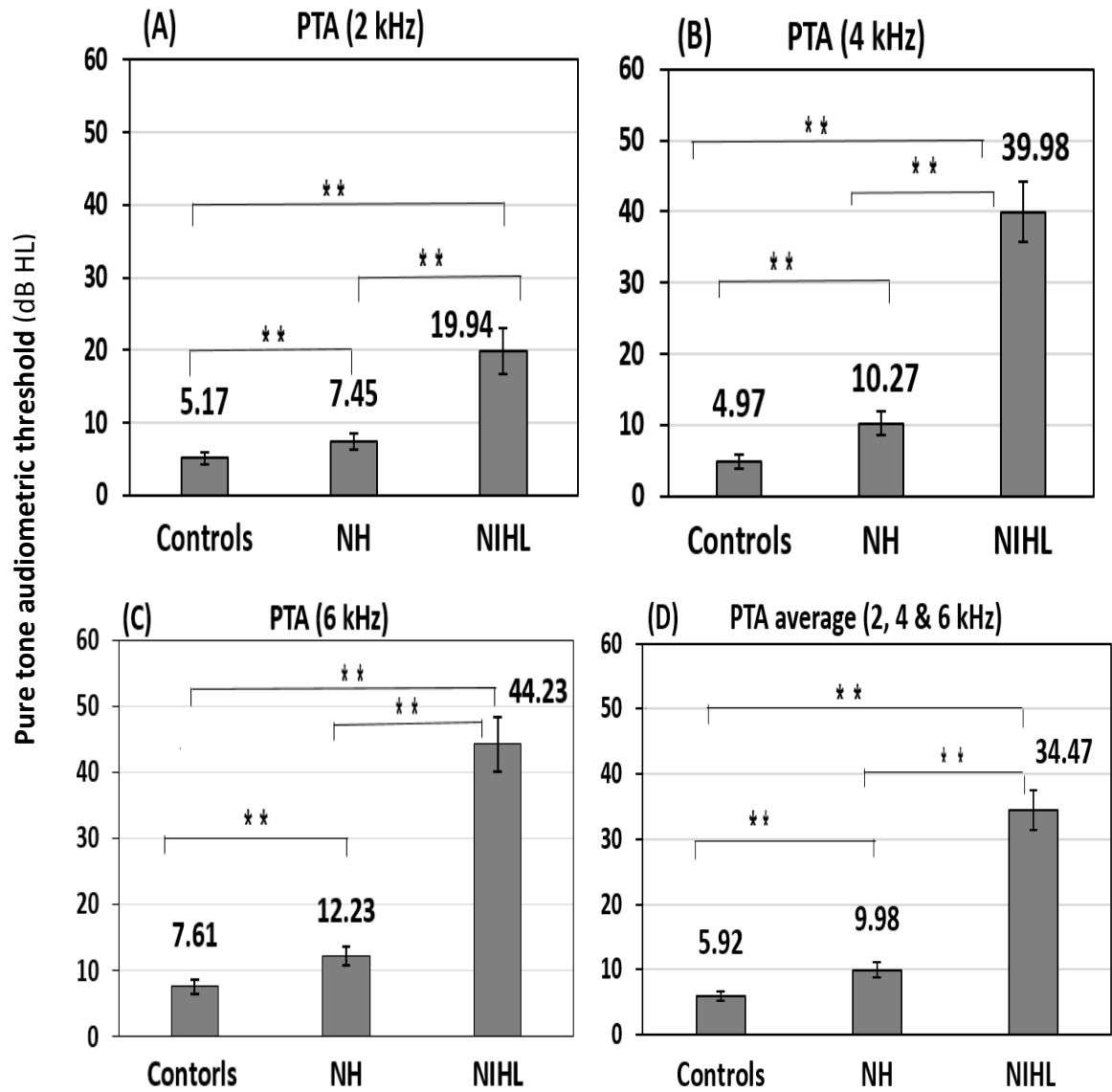


**Figure 3.1** An example of normal and abnormal pure tone audiograms obtained from two noise-exposed participants. Panel A (top) shows bilateral normal pure tone audiograms obtained from one of the noise-exposed normal hearing (NH) group; 47 years old male hospital technician with a history of 18 years of industrial noise exposure. Panel B (bottom) shows bilateral abnormal pure tone audiograms obtained from one of the noise-induced hearing loss (NIHL) group; 46 years old male soldier with a history of 16 years of military noise exposure.

**Table 3.2 Mean, median and standard deviation (SD) for pure tone audiometric (PTA) thresholds obtained at 2, 4 and 6 kHz and the PTA average of these three frequencies for three groups; controls, noise exposed-normal hearing (NH) group and noise-induced hearing loss (NIHL) group.** Values are calculated in decibels hearing levels (dB HL) and are presented for each ear separately.

Group (N)		Ear (N)	Pure tone audiometric thresholds (dB HL)												
			2 kHz			4 kHz			6 kHz			PTA average (2, 4 & 6 kHz)			
			Mean	Median	SD	Mean	Median	SD	Mean	Median	SD	Mean	Median	SD	
<b>Controls</b> (180)		RE (90)	5.44	5.00	5.28	4.56	5.00	7.09	7.44	5.00	7.50	5.81	5.00	5.04	
		LE (90)	4.89	5.00	5.95	5.39	5.00	7.78	7.78	5.00	7.27	6.02	5.00	5.11	
<b>Noise-exposed groups</b> (170)		<b>NH</b> (92)	RE (49)	7.76	5.00	5.21	10.51	10.00	7.99	12.35	10.00	6.70	10.21	10.00	5.04
			LE (43)	7.09	5.00	6.29	10.00	10.00	8.02	12.09	15.00	7.89	9.73	10.00	5.91
		<b>NIHL</b> (78)	RE (36)	19.86	15.00	15.24	41.25	40.00	18.34	48.47	45.00	20.35	36.53	33.33	14.32
			LE (42)	20.83	20.00	14.76	38.47	35.00	19.63	44.76	45.00	20.39	34.21	31.67	15.03

N = number of ears. RE: right ear. LE: left ear. SD: standard deviation.



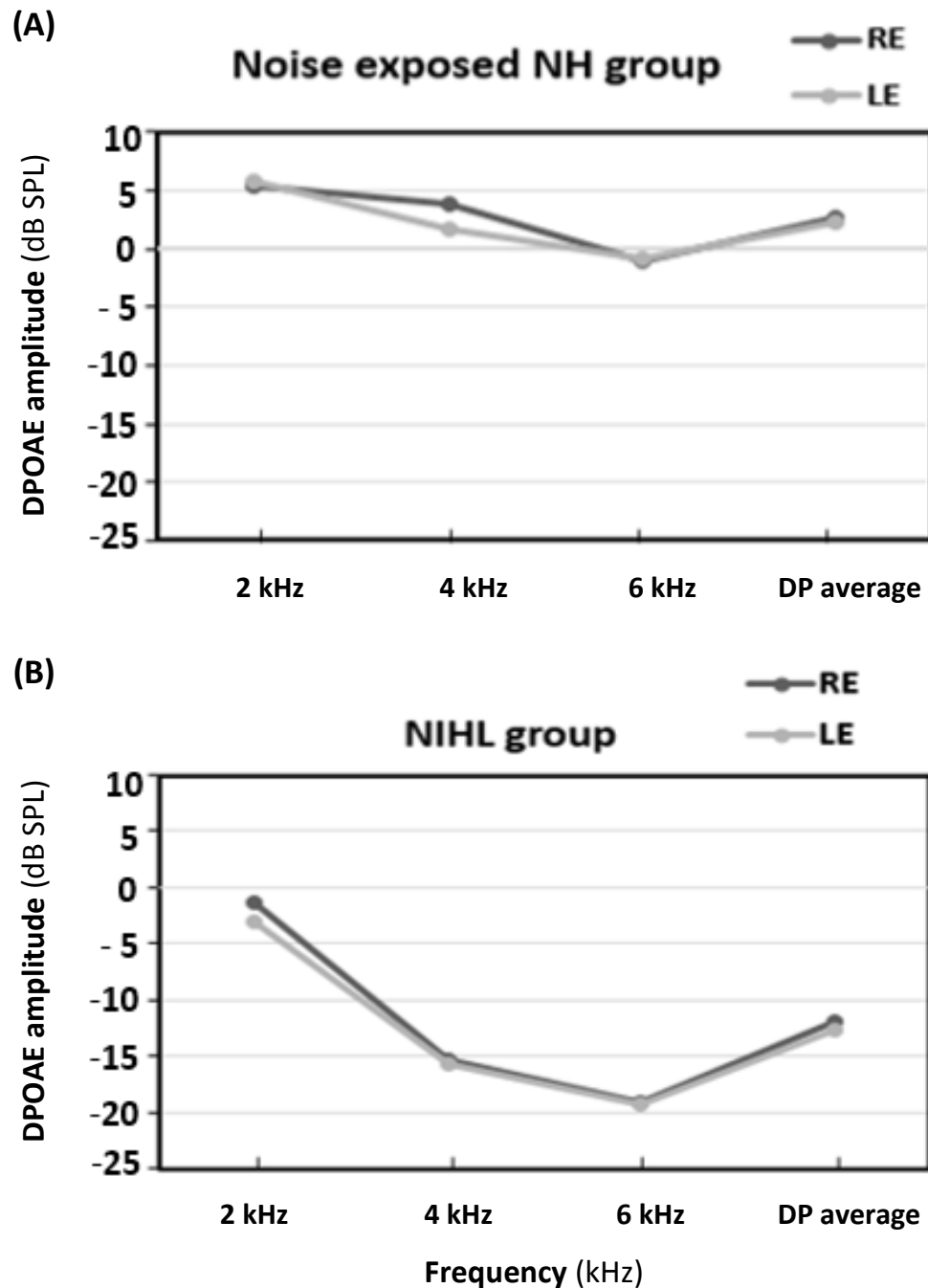
**Figure 3.2.** Bar graphs showing statistically significant differences between controls (N = 180 ears), noise-exposed normal hearing (NH) group (N = 92 ears) and noise-induced hearing loss (NIHL) group (N = 78 ears) in pure tone audiometric (PTA) thresholds. Panel A shows data for 2 kHz, Panel B shows data for 4 kHz. Panel C shows data for 6 kHz and Panel D shows data for PTA average calculated at these three frequencies. Differences between groups were tested by Mann-Whitney *U* test. Data labels indicate mean values calculated from both ears combined. A 95 % confidence interval was used to calculate error bars. Significance level: \*  $p < 0.05$ , \*\*  $p < 0.01$ , \*\*\*  $p < 0.001$ .

### 3.5.2 DPOAE data

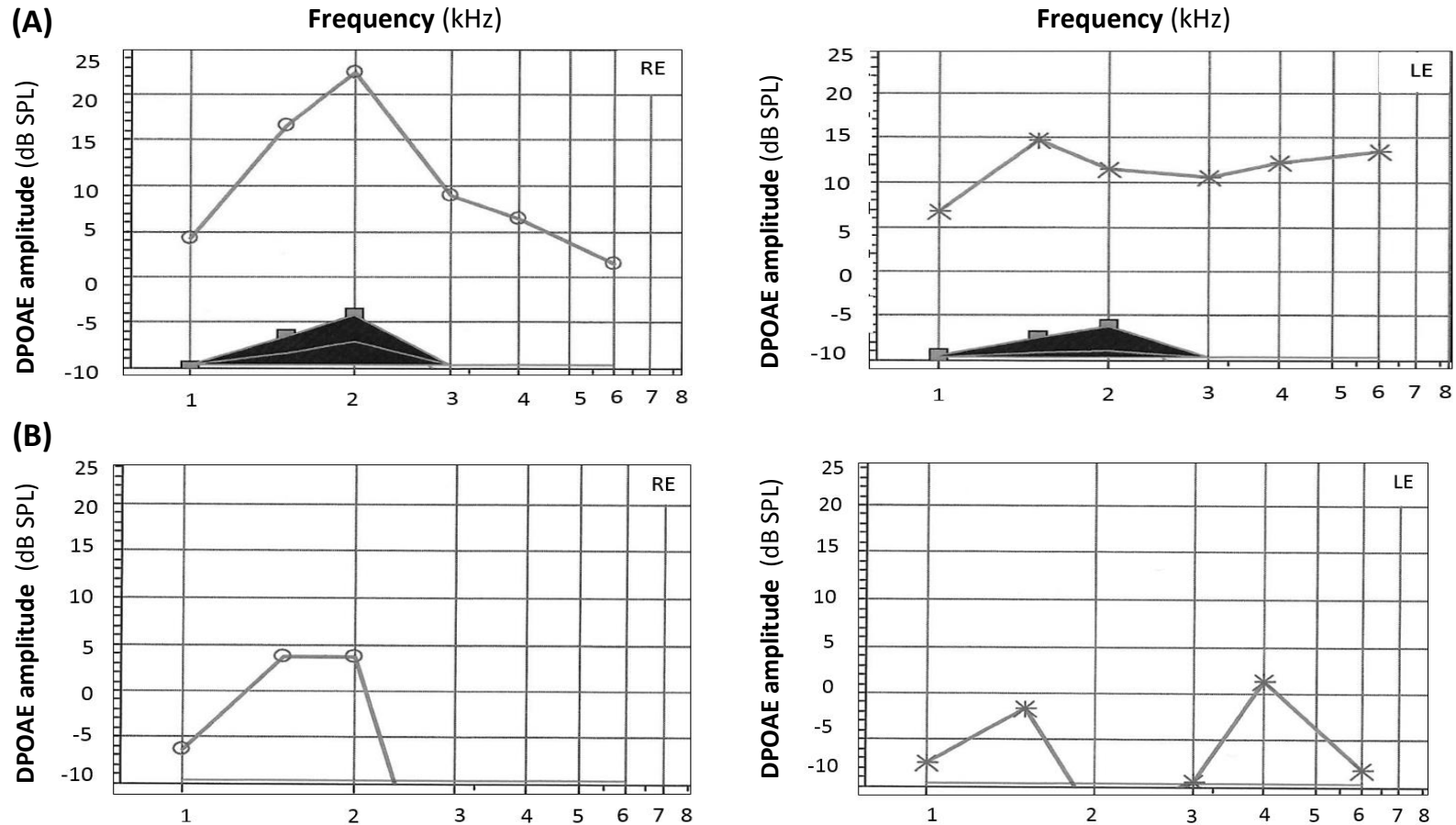
Total DPOAE data were calculated for 170 ears. Data for 7 ears were incomplete. Thus, the remaining data for analysis were for 163 ears. Among the 90 noise-exposed NH group, 44 ears (48.9 %) had normal DPOAE responses across all tested frequencies (2, 4, 6 kHz) and 48 ears (53.3 %) had abnormal or absent DPOAE responses at least at one of the three analyzed frequencies. Among the 73 NIHL group, 5 ears (6.8 %) had normal DPOAE responses across all tested frequencies and 70 ears (95.9 %) had abnormal or absent DPOAE responses at least at one of the three analyzed frequencies. Thus, the overall DPOAE abnormality rate identified in the overall noise-exposed participants was 72.4 % (118/163).

Figure 3.3 shows DPOAE amplitude levels for the right and left ears for each group (NIHL group and noise-exposed NH group) calculated at 2, 4, 6 kHz and the average of those three frequencies. The frequency that was most commonly absent in DPOAEs among the noise-exposed group was 6 kHz (73 ears, 44.8 %) followed by 4 kHz (51 ears, 31.3 %) then 2 kHz (24 ears, 14.7 %). DPOAE mean amplitude levels at 6 kHz were the lowest across both noise-exposed groups with the NIHL group demonstrating the lowest DPOAE amplitude level. Similarly, SNR values were the lowest at 6 kHz in both groups. Examples of normal and abnormal DPOAE responses obtained from two study participants are provided in Figure 3.4.





**Figure 3.3** Average DPOAE amplitude levels for 2, 4 and 6 kHz as well as the mean of those three frequencies are shown for two noise-exposed groups (noise-exposed normal hearing (NH) group and noise-induced hearing loss (NIHL) group). Panel A (top) shows data for noise-exposed NH group (N = 90 ears). Panel B (bottom) shows data for NIHL group (N = 73 ears). DPOAE amplitude values are calculated in dB SPL and are reported for each ear (RE: right ear, LE: left ear).



**Figure 3.4** Examples of normal (Panel A/top) and abnormal (Panel B/bottom) DPOAE responses for the right ear (RE) and left ear (LE) obtained from two noise-exposed participants. The data shown in Panel A are for a 42 years old male hospital technician with a history of 20 years of industrial noise exposure and bilateral normal hearing sensitivity (NH group). The data shown in Panel B are for a 54 years old male soldier with a history of 28 years of military noise exposure and bilateral mild high frequency hearing loss (NIHL group).

### 3.5.3 cVEMP data

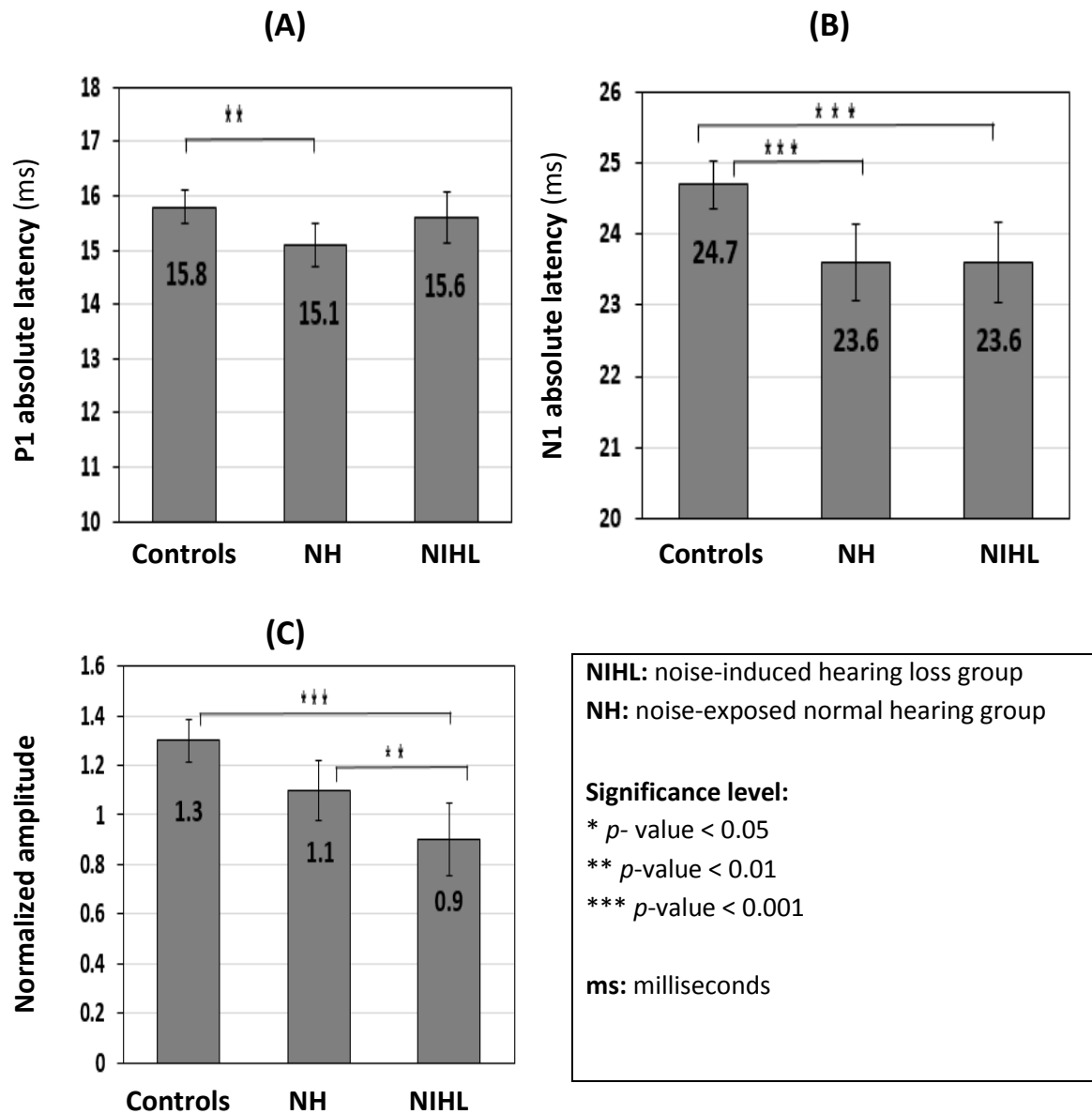
cVEMP response rate for controls and the overall noise-exposed groups (NH and NIHL) is given in Table 3.3. When cVEMP response rate was compared across the three groups by means of a Pearson's Chi-Squared test, results showed statistically significant differences between controls and noise-exposed groups (controls vs. noise-exposed NH group:  $X^2 = 10.219, p < 0.05$ ; controls vs. NIHL group:  $X^2 = 19.538, p < 0.001$ ). However, statistically non-significant differences were observed in cVEMP response rates between the two noise-exposed groups ( $X^2 = 3.074, p > 0.05$ ). In addition, it was noted that among the 10 ears with absent cVEMP responses in the noise-exposed groups, 4 ears (40 %) had normal hearing and 6 (60%) had abnormal hearing with hearing loss occurring only at high frequency (3 to 8 kHz). Initial data analysis showed that cVEMP data obtained from the noise-exposed groups were not normally distributed. Thus, Wilcoxon's Signed Rank Test was used to rule out any ear effect on cVEMP data (N: left ear = 80; right ear = 80). Results showed statistically non-significant differences between cVEMP right and left ears data ( $p > 0.05$ ). Therefore, cVEMP results obtained from the right and left ears were combined for subsequent analysis.

Figure 3.5 shows the differences demonstrated in cVEMP response parameters (P1 and N1 latencies "Panel A and B" and normalized amplitude "Panel C") among the three groups (controls, noise-exposed NH group and NIHL group) by Mann-Whitney  $U$  test. Results showed statistically significant differences between the control and noise-exposed NH groups in both P1 absolute latency ( $Z = -3.214, p < 0.01$ ) and N1 absolute latency ( $Z = -3.888, p < 0.001$ ). Results also showed statistically significant differences between the control and NIHL groups in both N1 absolute latency ( $Z = -3.683, p < 0.001$ ) and normalized amplitude ( $Z = -4.616, p < 0.001$ ). Comparison of the noise-exposed NH group with the NIHL group revealed statistically significant differences between the two groups only in normalized amplitude ( $Z = -2.653, p < 0.01$ ).

**Table 3.3 Differences in cVEMP response rate, calculated in number of ears (N) and percentages, between controls and noise-exposed groups; noise-exposed normal hearing (NH) group and noise-induced hearing loss (NIHL) group.** The reported values are for both ears combined. The differences were tested by Pearson Chi-squared test and *p*-values were reported.

cVEMP response rate		Controls N =180 (%)	Noise-exposed groups N = 170 (%)		Pearson Chi-squared and <i>p</i> -values		
			NH group N = 92 (%)	NIHL group N = 78 (%)	Controls vs. NH group	Controls vs. NIHL group	NH group vs. NIHL group
Present	Normal	180 (100)	81 (88)	61 (78.2)	$\chi^2 = 10.219$  $p < 0.05$	$\chi^2 = 19.538$  $p < 0.001$	$\chi^2 = 3.074$  $p > 0.05$
	Abnormal*	0 (0)	7 (7.6)	11 (14.1)			
Absent	Unilateral	0 (0)	1 (1.1)	1 (1.3)			
	Bilateral	0 (0)	3 (3.3)	5 (6.4)			

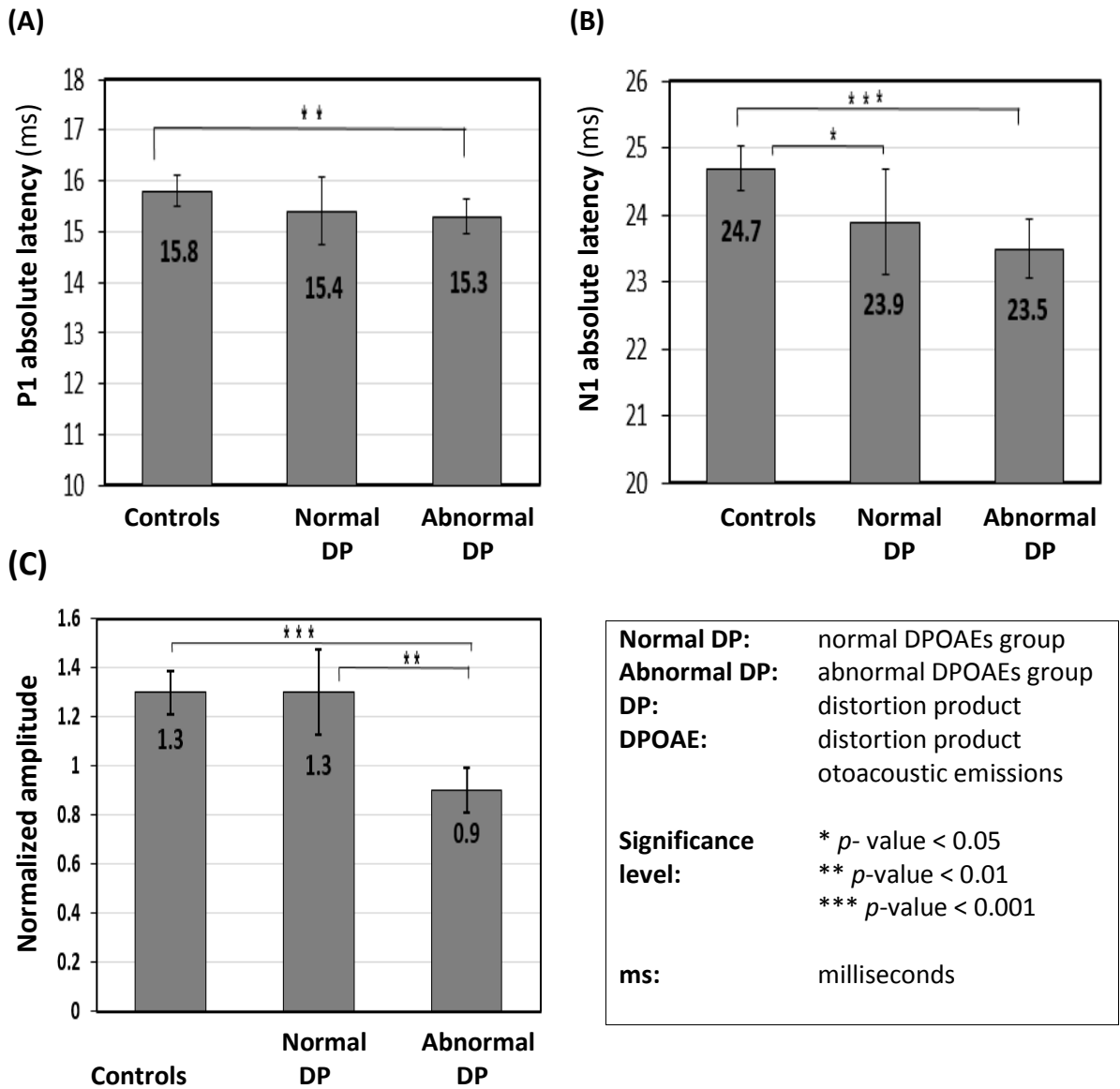
N: number of ears.\* Abnormal cVEMPs implies early P1 or N1 latency, prolonged P1 or N1 latency and/or reduced P1-N1 amplitude.



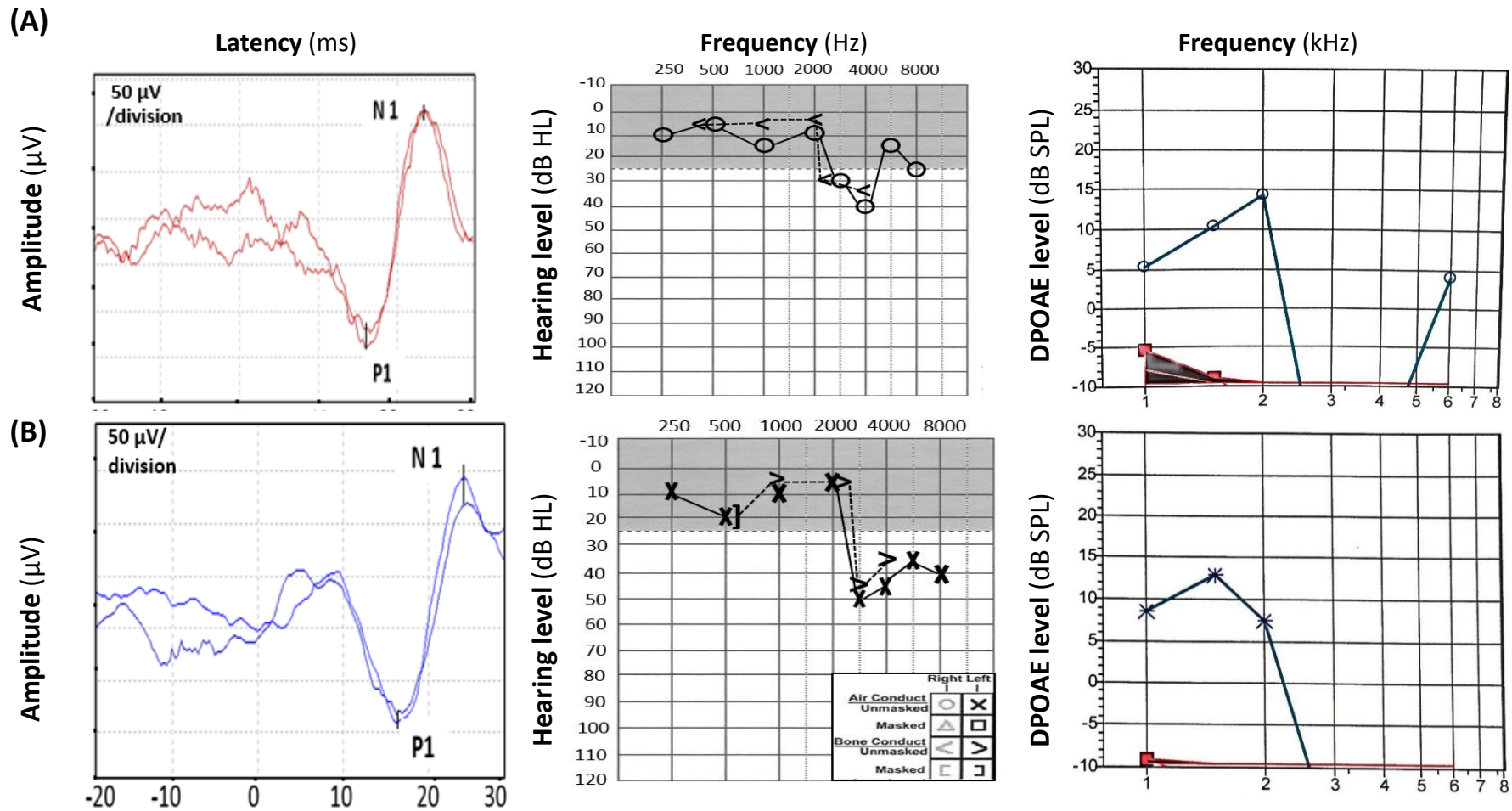
**Figure 3.5 Comparison of cVEMP response parameters in noise-exposed groups; noise-exposed NH group (N = 88 ears) and NIHL group (N = 72 ears) versus controls (N = 180 ears).** Panel A shows P1 absolute latency data. Panel B shows N1 absolute latency data and Panel C shows normalized amplitude data. Statistically significant differences between the three groups (controls, noise-exposed NH group and NIHL group) were demonstrated by Mann-Whitney  $U$  test in almost all cVEMP response parameters, particularly N1 absolute latency and normalized amplitude. The reported mean values are for both ears combined. The discussion of these findings is provided later in sections 3.6.2 and 3.6.3. Data labels indicate mean values and error bars were calculated using a 95 % confidence interval.

Figure 3.6 shows cVEMP data (P1 and N1 latencies “Panel A and B” and normalized amplitude “Panel C”) obtained from the noise-exposed groups (N = 170 ears), which were further classified according to DPOAE status. The aim of this classification was to examine if cVEMP data would be different according to DPOAE results. The first group was the normal DP group; ears with present and normal DP findings (N = 46 ears, age range = 23 to 60, mean age = 34.94, SD = 9.17). The second group was the abnormal DP group; ears with absent or abnormal DPOAE responses (N = 114, age range = 22 to 59, mean age = 39.80, SD = 8.61). Differences in cVEMP response parameters between the two DP groups were examined by Mann-Whitney *U* test. Results showed highly statistically significant differences between the control and abnormal DP groups in all cVEMP response parameters (P1 latency:  $Z = -2.637$ ,  $p < 0.01$ ; N1 latency:  $Z = -4.685$ ,  $p < 0.001$ ; normalized amplitude:  $Z = -4.901$ ,  $p < 0.001$ ). Statistically significant differences were noted as well between controls and normal DP groups only in N1 latency ( $Z = -2.315$ ,  $p < 0.05$ ) and between normal DP and abnormal DP groups only in normalized amplitude ( $Z = -3.107$ ,  $p < 0.01$ ).

Among the 10 absent cVEMP ears in the noise-exposed groups, 8 ears (80 %) had absent or abnormal DPOAE at one or more of the following frequencies (2, 4 or 6 kHz) and 2 ears (20 %) had present normal DPOAE at all frequencies. As indicated above in Table 3.3, of the 10 ears with absent cVEMPs, 4 were from the noise-exposed NH group. In those 4 absent cVEMPs ears, one ear (25 %) had normal/present DPOAEs and 3 ears (75 %) had absent/abnormal DPOAEs. The remaining 6 absent cVEMP ears were from the NIHL group. Among those 6 ears, 5 ears (83.3 %) had absent/abnormal DPOAEs at least at one frequency and only one ear (16.7 %) had present/normal DPOAEs at all frequencies. Figures 3.7 and 3.8 show examples of normal and abnormal cVEMP responses obtained from two noise-exposed participants along with their pure tone audiograms and DPOAE findings.

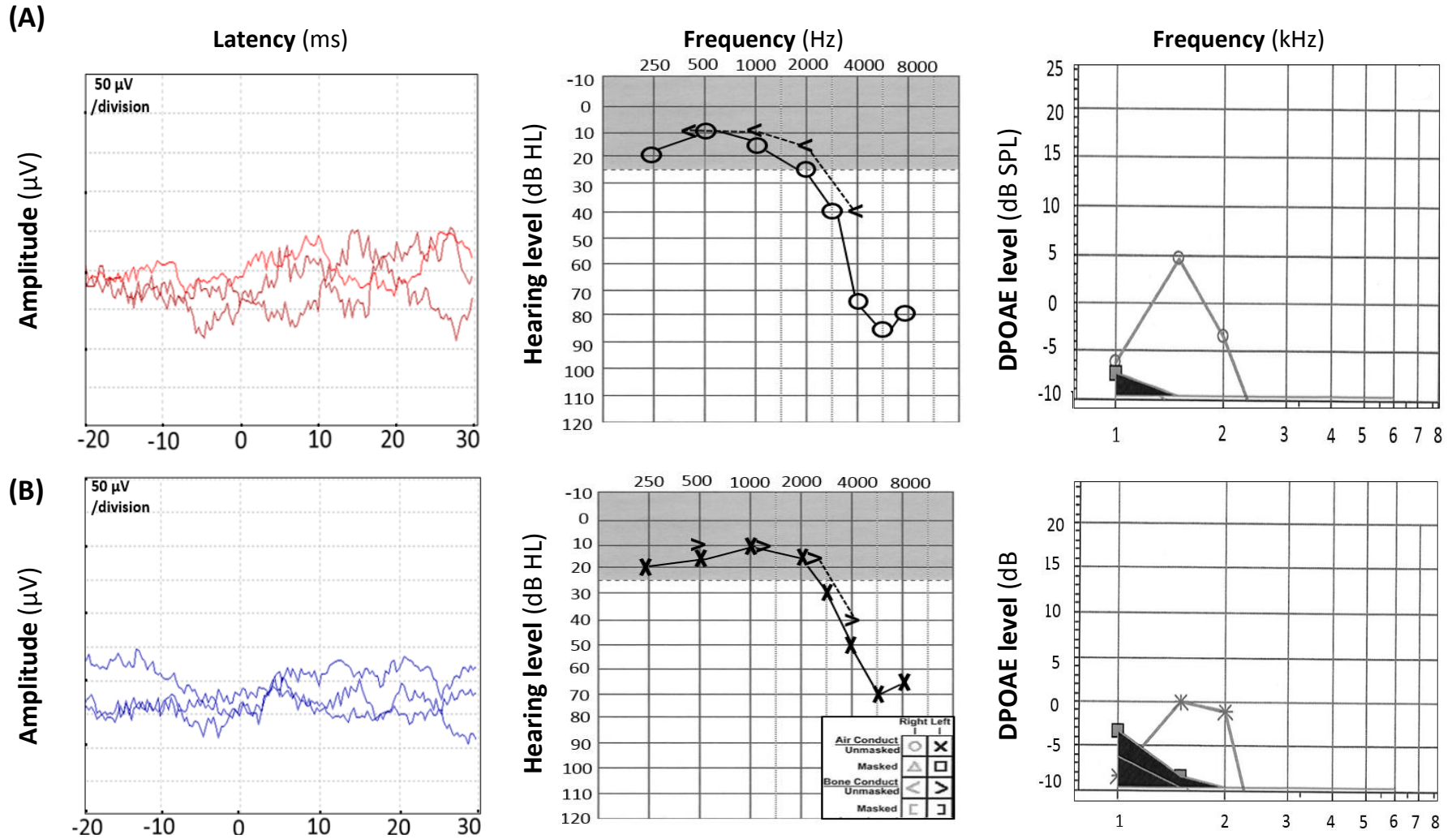


**Figure 3.6 Comparison of cVEMP response parameters in noise-exposed groups; normal DP group (N = 46) and abnormal DP group (N = 114 ears) versus controls (N = 180 ears).** Panel A shows P1 absolute latency data. Panel B shows N1 absolute latency data and Panel C shows normalized amplitude data. Differences between groups were tested by Mann-Whitney  $U$  test. The reported mean values are for both ears combined. Data labels indicate mean values and error bars were calculated using 95 % confidence interval.



**Figure 3.7** Example of bilateral normal cVEMP response waveforms from a representative noise-exposed participant along with PTA and DPOAE results. Panel A (red/top) shows right ear results. Panel B (blue/bottom) shows left ear results. The participant is a 49 years old male soldier with a history of 20 years of military noise exposure. Audiograms indicate bilateral high frequency NIHL with a clear noise notch at 3000 & 4000 Hz in both ears. DPOAE findings indicate bilateral present/normal DPOAEs up to 2 kHz and bilateral absent DPOAE in the high frequencies (except at 6 kHz, DPOAE is present and normal in the right ear).

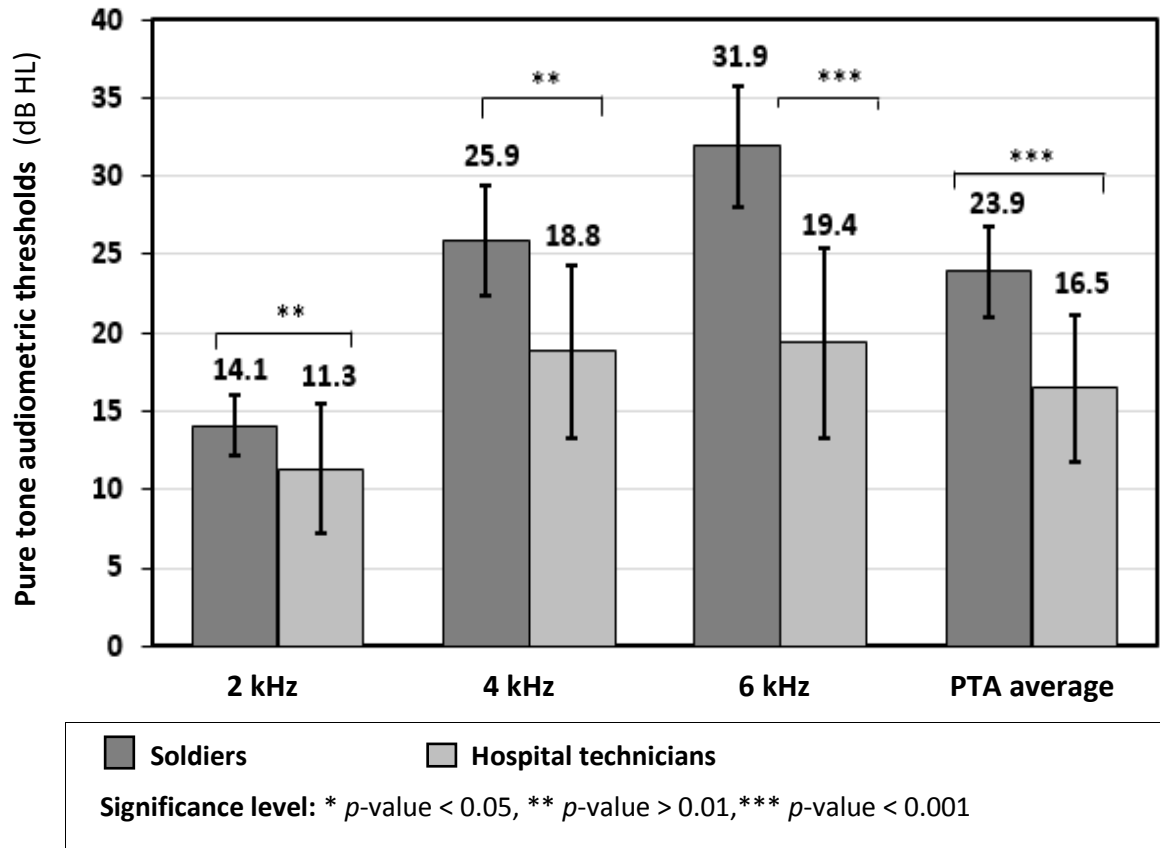




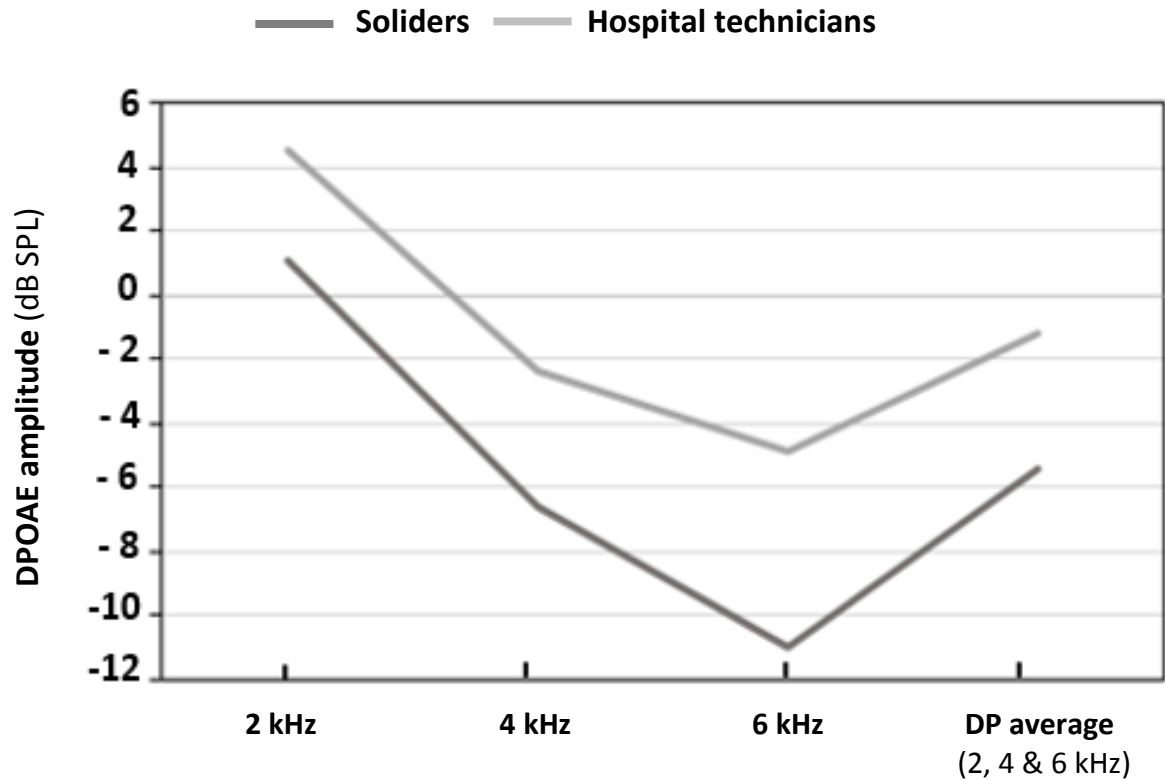
**Figure 3.8** Example of bilateral absent cVEMP response waveforms from a representative noise-exposed participant along with PTA and DPOAE results. Panel A (red/ top) shows right ear results. Panel B (blue/bottom) shows left ear results. The participant is a 43 year old male with a history of 14 years of military noise exposure. Audiograms and DPOAE findings indicate bilateral high frequency NIHL and abnormally reduced/absent DPOAE responses.

### 3.5.4 Differences between hospital technicians and soldiers

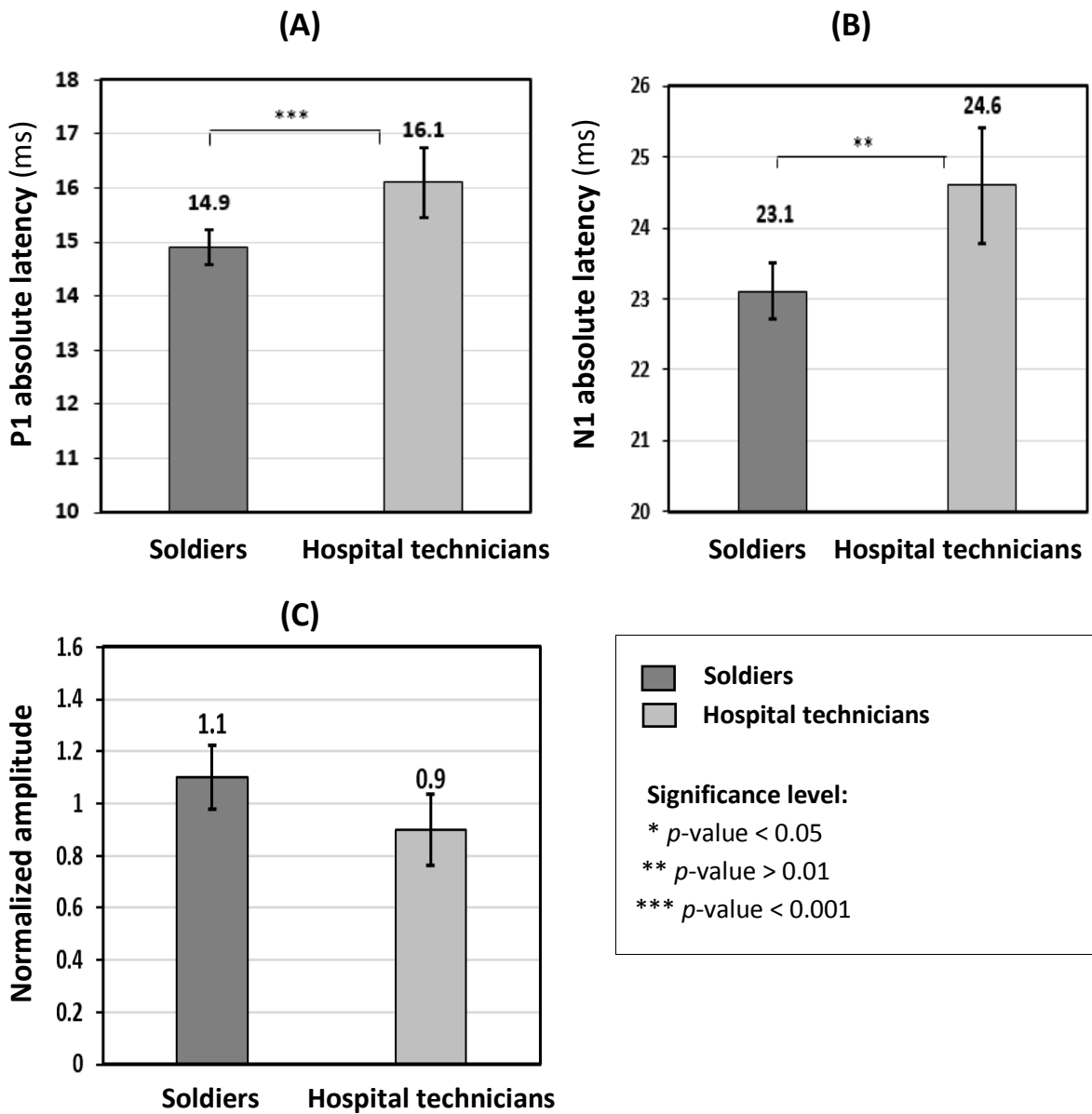
Because the participants within the noise-exposed groups came from different occupational backgrounds (military and industrial), Mann-Whitney  $U$  test was employed to examine possible differences between soldiers and hospital technicians in PTA, DPOAE and cVEMP findings. Results showed that hospital technicians had statistically significant better PTA thresholds (2 kHz:  $Z = -3.004$ ,  $p < 0.01$ ; 4 kHz:  $Z = -2.779$ ,  $p < 0.01$ ; 6 kHz:  $Z = -4.493$ ,  $p < 0.001$ ; PTA average (2, 4 and 6 kHz):  $Z = -3.955$ ,  $p < 0.001$ ), higher DPOAE amplitudes (4 kHz:  $Z = -2.082$ ,  $p < 0.05$ ; 6 kHz:  $Z = -2.524$ ,  $p < 0.05$ ; DP average:  $Z = -2.472$ ,  $p < 0.05$ ), longer P1 and N1 latencies (P1 absolute latency:  $Z = -3.650$ ,  $p < 0.001$ ; N1 absolute latency:  $Z = -2.990$ ,  $p < 0.01$ ) compared to soldiers. However, normalized amplitude data were similar for both occupational groups ( $Z = -0.302$ ,  $p > 0.05$ ). Figures 3.9, 3.10 and 3.11 show the difference between the two occupational groups in PTA thresholds, DPOAE amplitude levels and cVEMP response parameters respectively. Table 3.4 summarizes as well the overall findings of both occupational groups. A further discussion about these findings will be provided later in section 3.6.4.



**Figure 3.9** Bar graphs showing differences in pure tone audiometric (PTA) thresholds between two noise-exposed occupational groups; soldiers (N = 116 ears) versus hospital technicians (N = 54 ears). Differences in PTA were tested at 2, 4, 6 kHz and the average of those three frequencies (PTA average) using Mann Whitney  $U$  test. These findings indicate that hospital technicians demonstrated better PTA thresholds across all tested frequencies compared to soldiers. A discussion of this finding is provided later in section 3.6.4. Data labels indicate mean values and error bars were calculated using a 95 % confidence interval.



**Figure 3.10** A graph showing differences in DPOAE amplitude levels between the two noise-exposed occupational groups; soldiers (N = 115 ears) and hospital technicians (N = 52 ears). The differences in DPOAE amplitude levels were tested at 2, 4, 6 kHz and the average of those three frequencies (DP average) using Mann Whitney *U* test. These findings indicate that hospital technicians demonstrated higher DPOAE amplitude levels across all tested frequencies compared to soldiers. A discussion of this finding will be provided later in section 3.6.4.



**Figure 3.11** Bar graphs showing differences in cVEMP response parameters between two noise-exposed occupational groups; soldiers (N = 108 ears) versus hospital technicians (N = 52 ears) demonstrated by Mann Whitney *U* test. Panel A shows P1 absolute latency data. Panel B shows N1 absolute latency data and Panel C shows normalized amplitude data. These findings indicate that hospital technicians demonstrated longer P1/N1 latencies and similar normalized amplitude data compared to soldiers. A discussion of this finding will be provided later in section 3.6.4. Data labels indicate mean values and error bars were calculated using a 95 % confidence interval.

**Table 3.4 Summary of overall findings for the two noise-exposed occupational groups (85 participants = 170 ears); hospital technicians and soldiers.**

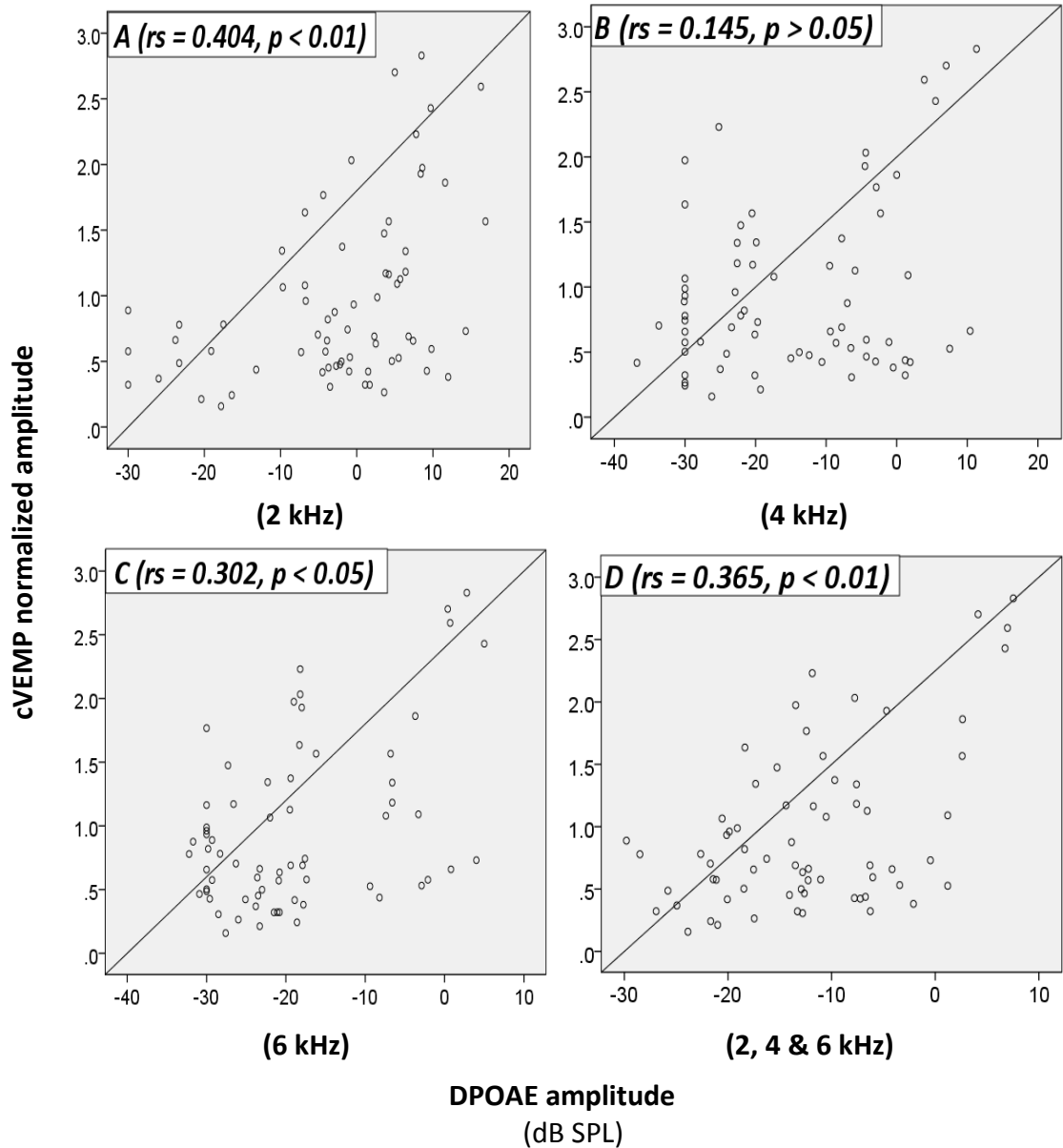
Job title (N)	Age (mean $\pm$ SD)	Employment length (Yr.)* (mean $\pm$ SD)	PTA outcome N (%)		DPOAEs outcome N (%)		cVEMP outcome N (%)		
			NH	NIHL	Present	Absent/ abnormal	Present/ normal	Abnormal**	Absent
<b>Hospital technicians</b> (N = 54)	38.70 $\pm$ 10.47	12.30 $\pm$ 8.12	39 (72.2)	15 (27.8)	23 (42.6)	29 (53.7)	45 (83.3)	7 (12.9)	2 (3.7)
<b>Soldiers</b> (N = 116)	38.29 $\pm$ 8.30	17.03 $\pm$ 7.78	53 (45.7)	63 (54.3)	26 (22.4)	89 (76.7)	97 (83.6)	11 (9.5)	8 (6.9)

N = number of ears. \*All noise-exposed participants (hospital technicians and soldiers) had a minimum of one year and a maximum of 30 years of occupational noise exposure.\*\* Abnormal cVEMPs implies early P1 or N1 latency, prolonged P1 or N1 latency and/or reduced P1-N1 amplitude.

### 3.5.5 Relationship between cVEMP, PTA and DPOAE

The relationship between the three administered test procedures (DPOAE, PTA and cVEMP) was examined to determine if there is any correlation between these three measures. Finding such evidence will facilitate clarification of the relationship between, noise-induced OHC damage, NIHL and noise-induced saccular damage. Bivariate associations between PTA thresholds and DPOAE amplitude levels, cVEMP response parameters (P1 latency, N1 latency and P1-N1 normalized amplitude) and PTA thresholds or DPOAE amplitude levels were examined in the two noise-exposed groups (NH and NIHL) using Spearman's Correlation Coefficient. In the noise-exposed NH group, results showed a statistically significant but weak correlation between PTA thresholds and DPOAE amplitude levels ( $r_s = -0.408$ ,  $r_s = -0.383$ ,  $r_s = -0.347$ ,  $r_s = -0.493$ ,  $p < 0.001$  for all except  $p < 0.01$  at 6 kHz) at 2 kHz, 4 kHz, 6 kHz and the DP average at 2, 4 and 6 kHz respectively. In the NIHL group, results continued to show similar weak correlation between PTA thresholds and DPOAE amplitude levels ( $r_s = -0.475$ ,  $r_s = -0.484$ ,  $r_s = -0.478$ ,  $p < 0.001$  for all) respectively for 2 kHz, 4 kHz and 6 kHz.

Spearman's correlation coefficient testing showed a statistically non-significant very weak correlation between cVEMP response parameters (P1/N1 latencies and normalized amplitude) and PTA thresholds or DPOAE amplitude levels at all tested frequencies for both groups (noise-exposed NH group and NIHL group). However, in the NIHL group, a slight increase in correlational values between cVEMP normalized amplitude and DPOAE amplitudes was noted at 2 kHz ( $r_s = 0.404$ ,  $p < 0.01$ , Figure 3.12, Panel A), 6 kHz ( $r_s = 0.302$ ,  $p < 0.05$ , Figure 3.12, Panel C) and DPOAE amplitude average of 2, 4 and 6 kHz ( $r_s = 0.365$ ,  $p < 0.01$ , Figure 3.12, Panel D), except at 4 kHz, correlational values continued to be very weak ( $r_s = 0.145$ ,  $p > 0.05$ , Figure 3.12, Panel B). A further detailed discussion about these findings is provided later in section 3.6.5.



**Figure 3.12** Scatter plots showing statistically significant weak positive correlation between cVEMPs normalized amplitude and DPOAE amplitude levels demonstrated in the NIHL group (78 ears) by Spearman's Correlation Coefficient test at  $p < 0.05$  significance level. Panel A shows data for 2 kHz. Panel B shows data for 4 kHz. Panel C shows data for 6 kHz and Panel D shows data for DPOAE amplitude average at 2, 4 & 6 kHz. A slight increase in correlational values was noted between cVEMP normalized amplitude and DPOAE amplitude level at 2 kHz (Panel A), 6 kHz (Panel C) and DPOAE average of 2, 4 & 6 kHz (Panel D).



### 3.6 Discussion

This study examined the effect of noise exposure on the audio-saccular function of adult workers with and without hearing loss. It was hypothesized that if noise exposure affects saccular function then cVEMP findings of the noise-exposed individuals would exhibit different cVEMP characteristics (higher abnormal/absent response rate, longer P1/N1 absolute latencies and a reduced P1-N1 peak to peak amplitude levels) compared to those obtained from healthy individuals without history of noise exposure (controls). It was hypothesized also that noise-induced saccular dysfunction could occur before hearing loss is evident in the audiogram and/or OHC dysfunction is evident in OAEs and that the cVEMP technique is able to detect such early changes. Hence, similar changes were hypothesized to occur in the noise-exposed normal hearing (NH) group compared to those obtained from controls. Furthermore, since noise-induced saccular dysfunction has been documented mainly in cases of NIHL, it was hypothesized that the NIHL group would demonstrate different cVEMP characteristics (higher abnormal/absent response rate, longer P1 and N1 absolute latencies and a reduced P1-N1 peak to peak amplitude levels) compared to the noise-exposed NH group.

To examine these hypotheses, the audio-saccular function of 85 workers (27 hospital technicians and 58 soldiers) presenting with self-reported history of occupational noise exposure and with and without NIHL was assessed using routine PTA, DPOAE and cVEMP. PTA and cVEMP findings were contrasted with those obtained from 90 individuals with normal audio-saccular function previously established in Chapter 2 (control group). Because the study involved noise-exposed participants with and without hearing loss, this allowed the investigation of the relationships between NIHL, OHC dysfunction resulting from noise exposure and noise-induced saccular dysfunction. PTA and DPOAE findings obtained from some of the participants in this study suggest existence of OHC dysfunction and NIHL in these individuals. Saccular dysfunction demonstrated by cVEMP abnormality was also evident in these groups. The present study also documented saccular abnormalities in participants who were at risk of developing NIHL (i.e. were regularly exposed to high intensity sound levels) but had not yet developed audiometric hearing loss. The present study suggests that combining both

OAEs and cVEMP could increase the likelihood of detecting noise-induced saccular dysfunction in these groups. The next sub-sections discuss each of these findings in more details.

### **3.6.1 PTA and DPOAE findings in noise-exposed groups**

Abnormal PTA thresholds were found in about 46 % of noise-exposed participants. The rest of participants (54 %) had bilateral normal hearing sensitivity. The variability in hearing results among the investigated participants is probably because they came from different backgrounds (i.e. industrial and military). Moreover, the time course of their noise exposure was variable as it ranged from at least one year to a maximum of 30 years depending on their employment duration. The noise exposure data were self-reported and it is possible that some participants felt they had been exposed to high noise intensity levels although it may not have been sufficiently high to damage hearing. Another contributing factor to the variability observed in participants' hearing results was the use of hearing protection, which might have played a role in preserving hearing in the participants who demonstrated normal hearing sensitivity. The self-reported noise exposure data collected in the next study, described in Chapter 4 illustrate the effects of using hearing protection on participants' PTA results. To gain further clarity regarding participants' exposure to high noise intensity levels, detailed self-reported data were collected in Chapter 4.

The finding of poorer 6 kHz threshold bilaterally in noise-exposed individuals with NIHL is consistent with the findings reported by [Wu and Young \(2009\)](#) and [Seixas et al. \(2010\)](#). In a more recent study, [Tseng and Young \(2013\)](#) showed that the worst hearing thresholds mean in 30 NIHL patients were at 4 kHz. Although there is a variation in the reported frequency with greatest hearing loss among NIHL individuals, published studies agree that the greatest hearing loss fall somewhere between 3 and 6 kHz. The finding of absent/abnormal DPOAE responses in about three quarters (72.4 %) of the noise-exposed ears in this study is consistent with OHC dysfunction in this group. Conversely, abnormal PTAs were only evident in fewer than half of the noise-exposed ears (46 %). The observed DPOAE abnormality in the great majority (96 %) of ears with NIHL is

consistent with the well-known documented effects of noise on both humans' and animals' DPOAE (Eleftheriou, 2002; Bauer et al., 2006; Wang et al., 2006; Tak et al., 2009). Furthermore, the finding of abnormal DPOAE in more than half (53.3 %) of the noise-exposed NH ears supports that OAEs are more sensitive to detect earlier cochlear changes before they become evident in pure tone audiograms (Desai et al., 1999; Seixas et al., 2005; Atcharyasathian et al., 2008; Baradarnfar et al., 2012). The results of this study along with published data support the recommendation that absence of or reduced OAEs in the presence of normal pure tone audiometric thresholds may reflect noise exposure. Therefore, OAEs can be used to monitor changes in hair cell function as a result of noise exposure and can be used also as an indicator of early noise-induced cochlear changes. Similar to PTA findings, the worst DPOAE amplitude levels and SNRs were observed at 6 kHz in all noise-exposed groups (see Figure 3.3). Hence, both PTA and DPOAE findings of this study support cochlear sensitivity to noise exposure at high frequencies, which has been well reported previously in the literature (Clark and Bohne, 1999; Karatas, 2008).

### **3.6.2 cVEMP findings in noise-induced hearing loss (NIHL) group**

The present study results showed absent/abnormal cVEMPs in approximately 17 % of the overall noise exposed individuals. However, when considering only the noise-exposed individuals with NIHL, this rate increased to about 22 %. This finding suggests that saccular dysfunction is evident in individuals affected by NIHL, which has been reported previously in the literature (Wang and Young, 2007; Wu and Young, 2009; Kumar et al., 2010; Akin et al., 2012; Tseng and Young, 2013). However, these studies reported a wide range of abnormal cVEMP rates (33 to 75 %) among individuals with NIHL. The highest cVEMP abnormality rate was reported by Wu and Young (2009), which was 75 %. In this study, the investigators looked at the longitudinal effect of chronic gunshot noise exposure among 20 police officers who performed regular shooting practice over 10 years. The study revealed statistically significant differences of mean hearing thresholds only at 4 and 6 kHz frequencies on the officers' left ears compared to controls. Although the study did not involve any semicircular canal testing, the authors attributed the lack of vestibular symptoms to intact semicircular canals. The

closest abnormal cVEMP rate to the present study (22 %) was the one reported by Akin et al. (2012), which was 33 %.

A possible contributing factor to the higher abnormal cVEMP rate reported by these published studies is the use of cVEMP methodology that might have resulted in abnormal or absent cVEMP. Among the most common problems encountered in cVEMP recording are the use of low stimulation level and insufficient muscle contraction level as a result of application of less than optimal SCM muscle activation procedure, which might have caused the higher abnormal or absent cVEMP rate in these studies. Conversely, the current study utilized an optimal cVEMP recording technique based on the available evidence from published studies as well as the findings of methodological data collected from a large number of normal subjects established in the previous chapter (Chapter 2). Furthermore, the present study and the other published studies have utilized different norms to interpret cVEMP response parameters in individuals with NIHL. The use of different cVEMP protocols to establish cVEMP norms (i.e. stimulus type, stimulus frequency, mode of stimulation, stimulation rate, etc.) would likely have resulted in variability across these norms. The variations among the investigated noise-exposed groups across these studies, including the current study (i.e. inclusion and exclusion criteria, noise intensity level and duration or length of noise exposure, age, degree of NIHL) should also be taken into consideration. Hence, the first study hypothesis: *“i (a): the noise-exposed individuals with NIHL would demonstrate a higher abnormal/absent cVEMP rate compared to those obtained from controls”* was accepted.

When cVEMP response parameters (P1 latency, N1 Latency and P1-N1 normalized amplitude) of the NIHL group were compared with other groups (controls and noise-exposed NH group, see Figure 3.5), results showed highly statistically significant differences in N1 latency in that it occurred earlier in the NIHL group compared to controls. The NIHL group showed significantly reduced normalized amplitudes compared to controls ( $p < 0.001$ ). Equally, the NIHL and the noise-exposed NH group had statistically significant differences only in normalized amplitude ( $p < 0.01$ ). Hence, based on these findings, the following study hypotheses: *“i (b & c): if noise exposure affects saccular function, then cVEMP findings of noise-exposed individuals with NIHL would*

*demonstrate a longer P1 and N1 absolute latencies compared to those obtained from controls” and “iii (b & c): the noise-exposed individuals with NIHL would demonstrate a longer P1 and N1 absolute latencies compared to those obtained from noise-exposed NH group” were rejected. However, the following hypotheses “i (d): the noise-exposed individuals with NIHL would demonstrate a reduced P1-N1 peak to peak amplitude compared to those obtained from controls” and “iii (d) the noise-exposed individuals with NIHL would demonstrate a reduced P1-N1 amplitude compared to those obtained from noise-exposed NH group” were accepted.*

To differentiate between individuals with and without saccular pathology, published studies have focused primarily on cVEMP response rate (i.e. waveform presence vs. absence) and have given less attention to cVEMP response parameter characteristics by comparing them to control groups. Hence, detailed information on the effect of noise on specific cVEMP response parameters is limited. However, the current study used both diagnostic criteria (i.e. cVEMP response rate as well as latency and amplitude measures) to distinguish between individuals with and without noise-induced saccular damage. cVEMP abnormalities in NIHL cases were described in the literature as either absent responses, delayed latencies or reduced amplitudes. The results of the present study are consistent with most of the studies available in the literature, in that individuals with NIHL had reduced cVEMP amplitudes. However, the present study observed earlier latencies (only N1) in individuals with NIHL as opposed to delayed latencies as reported by some investigators (Itoh et al., 2001; Pollak et al., 2006; Tseng and Young, 2010). These investigations suggested that the delayed cVEMP latencies seen in individuals with NIHL might be indicative of central vestibular lesions caused by reduced conduction time along the vestibule-spinal pathways. Although the effects of noise exposure and NIHL on cortical structures are less understood compared to peripheral structures, there is a growing evidence in the literature for changes in central auditory system function (i.e. attenuated or abnormal central auditory processing) among patients suffering from sensorineural hearing loss, including those diagnosed with NIHL (Oates et al., 2002; Wang et al., 2011; Fetoni et al., 2013). In contrast, some studies found that noise-exposed individuals with NIHL showed no evidence of abnormal central vestibular function (Akin et al., 2012). Thus, the effect of noise exposure on

central vestibular pathways is not yet understood. Although it is hard to explain why N1 latency was early in individuals with NIHL compared to controls in this study, there are several possible explanations of this finding. [Cassandro et al. \(2003\)](#) documented a statistically significant increase in cVEMP amplitude among 40 healthy young adults after being exposed to 128 dB(C) disco music for 3 hours. The investigators of the study suggested that this could be due to irritative action of the sound stimulus upon the macular receptors and this could be one of the possible explanations of the earlier N1 latencies observed in the NIHL participants of the current study. Some studies found that N1 latency has higher test-retest reliability compared to P1 latency ([Isaradisaikul et al., 2008](#); [Nguyen et al., 2010](#)) and this might explain also why the N1 latency measure rather than the P1 latency measure identifies statistically significant differences between NIHL and controls as indicated in the present study. Another explanation is the possible effect of cVEMP amplitude levels on latency measures. Some studies showed a relationship between cVEMP latencies and high EMG levels in that high EMG levels, which usually results in large cVEMP amplitudes, could lead to a reduction in cVEMP latency ([Davenport, 2010](#)). Therefore, it could be that the early N1 noted in the current study is not due to noise effects on the saccule but rather to the larger amplitude values resulting from the recording process (i.e. the application of an optimal cVEMP recording protocol). The great majority of studies that investigated noise-exposed individuals did not use an optimal cVEMP recording protocol and as a consequence, the NIHL groups investigated by these studies had lower amplitudes compared to the NIHL participants of this study.

Further, some studies reported statistically significant differences in P1/N1 latencies with the use of different SCM muscle activation procedures ([Ito et al., 2007](#)). The authors of Ito's study reported that N1 latency was significantly longer when cVEMP responses were obtained at upright position compared to those obtained at the supine position. The authors of this investigation explained this difference by the alterations in the excitability of the saccule due to gravitational effects in the supine position compared to the upright position. Other studies found that cVEMP response obtained with the HE (supine) procedure produced significantly shorter P1/N1 latencies compared to those obtained by the HR (supine) procedure ([Wang and Young, 2006](#); [Davenport, 2010](#)).

Another group of researchers reported significantly reduced P1/N1 latencies with the use of bilateral stimulation compared to monaural stimulation (Wang and Young, 2006; Eleftheriadou et al., 2008). The authors in Eleftheriadou's study suggested that this difference might be due to the alterations at the level of motor neuron. In brief, procedural differences in recording cVEMP, such as differences in the type of muscle activation procedure or mode of stimulation (monaural stimulus stimulation versus bilateral acoustic stimulation) as well as the inclusion of a biofeedback method that produces large cVEMP amplitudes like the BPM method, are the most sensible explanation for the observed latency differences between the current study and the other existing studies. In addition to methodological differences, the fact that the exact values of cVEMP response parameters, especially N1 latency and P1-N1 amplitude, for both the NIHL participants and the control groups usually are not mentioned by most published investigations makes it difficult to conduct an accurate comparison across studies.

### **3.6.3 cVEMP findings in noise-exposed normal hearing (NH) group**

One of the interesting and novel findings of this study is the cVEMP abnormality observed in noise-exposed individuals who had not yet developed a hearing loss due to noise exposure. The evidence of this came from the significantly different cVEMP response rate found between controls and the noise-exposed NH group. Hence, the present study hypothesis *"ii (a) the noise-exposed individuals with normal hearing (NH group) would demonstrate a higher abnormal/absent cVEMP rate compared to those obtained from controls"* was accepted. Although the abnormal cVEMP rate observed in the noise-exposed NH group (12 %) was less than the one observed in the NIHL group (22 %), statistically non-significant differences were observed between the two rates. Hence, the present study hypothesis *"iii (a) the noise-exposed individuals with NIHL would demonstrate a higher abnormal/absent cVEMP rate compared to those obtained from noise-exposed NH group"* was rejected. This finding suggests the possibility of saccular dysfunction in noise-exposed individuals without a hearing loss, which has not been reported previously.

Furthermore, this finding suggests that saccular dysfunction due to noise exposure could occur without or prior to cochlear damage. Given the reported history of the noise-exposed NH group, the identified saccular dysfunction in these individuals is probably caused by noise exposure and not due to any other factor. To the best of the author's knowledge, investigating noise-induced saccular dysfunction in noise-exposed individuals without hearing loss using cVEMP has not been done previously. The only published study that has investigated vestibular disturbances in noise-exposed individuals with normal hearing was the one carried out by [Raghunath et al. \(2012\)](#). Although this study revealed vestibular symptoms in 20 factory workers with normal hearing, the saccular function of the noise-exposed participants was not examined in this study. It is important to highlight here that the high number of present/normal cVEMP responses in the noise-exposed participants of this study (78 % in NIHL group and 88 % in noise-exposed NH group) could be due to several factors. The heterogeneity of the investigated noise-exposed workers of this study (differences in age, noise exposure characteristics like level and length of noise exposure and how much noise protection they had in their noisy environments) might have played an important role in cVEMP outcomes. Other factors like individuals' susceptibility to noise-induced vestibular damage ([Henderson et al., 1993](#)) and sensitivity of cVEMP as a saccular function measure to detect saccular changes due to excessive noise exposure are also possible contributing factors to the low observed abnormal cVEMP findings in this group. The present author is not aware of any study that has looked at the sensitivity of cVEMP test to detect noise-induced saccular dysfunction and hence, this could be an area that merits further investigation.

When cVEMP response parameters of the noise-exposed NH group were compared with those obtained from other groups (controls and NIHL group), statistically significant differences were observed between this group and controls only in P1/N1 latency measures (P1:  $p < 0.01$ ; N1:  $p < 0.001$ , see Figure 3.5) in that they occurred earlier in the noise-exposed NH group compared to controls. Hence, the present study hypotheses: "*ii (b & c) the noise-exposed individuals with normal hearing (NH group) would demonstrate a longer P1 and N1 absolute latencies compared to those obtained from controls*" were rejected. The observed statistically significant differences between



controls and the noise-exposed NH group only in latency measures (both P1 and N1), could possibly suggest that cVEMP latency measures are more sensitive to detect early noise-induced saccular changes, when there is a significant noise exposure but cochlear changes are still not evident in the audiogram, compared to amplitude measures. The well-known stability of cVEMP latency measures and the highly variable nature of cVEMP amplitude measures also supports this suggestion. The present study showed statistically non-significant difference in amplitude measure between the noise-exposed NH group and controls. Thus, the present study hypothesis *“ii (d) the noise-exposed individuals with normal hearing (NH group) would demonstrate a reduced P1-N1 peak to peak amplitude compared to those obtained from controls”* was rejected. In addition, statistically significant differences were noted between noise-exposed NH group and NIHL group only in P1-N1 normalized amplitude ( $p < 0.01$ ) in that it was reduced among the NIHL group compared to the noise-exposed NH group. The significantly reduced amplitude levels in the NIHL group in relation to controls and noise-exposed NH group suggest that cVEMP amplitude levels might not be altered by noise exposure unless cochlear damage has already occurred and hearing loss is evident in the audiogram.

#### **3.6.4 Differences between noise-exposed occupational groups**

Current study findings show statistically significant differences between the two occupational groups (soldiers and hospital technicians) in all test procedures (see Figures 3.9, 3.10 and 3.11). For example, abnormal OHC function evident by DPOAE was demonstrated in the majority (77 %) of soldiers but evident only in approximately half (54 %) of hospital technicians. Hearing loss was evident in approximately half of soldiers (54 %) compared with only 28 % in hospital technicians. Despite the variations in PTA and DPOAE results between the two occupational groups, the rate of cVEMPs abnormality (P1-N1 waveform was reliably recorded and reproducible but one or more of the response parameters values fall outside the expected normal ranges observed in controls) was almost the same for both groups (soldiers = 10 %, hospital technicians = 13 %). However, cVEMP absence rate was higher in soldiers (8 %) compared to hospital technicians (4 %). The variations observed in cochlear and saccular function between soldiers and hospital technicians may be explained by the fact that the two groups came

from different occupational backgrounds. Although the two occupational groups had similar age mean values and similar employment duration, differences in noise exposure characteristics between the two professions (job task, time course of noise exposure, the use of hearing protection) are likely to play a role in the observed differences.

Another factor, which might also contribute to the observed differences between the soldiers and the technicians is the differences in the acoustic characteristics of the noise they were exposed to. It is well known that military noise is different from industrial noise. The noise type commonly encountered in military services has a sudden and impulsive nature commonly produced by weapon systems and explosions (Durch et al., 2005; Collee et al., 2011; Yankaskas, 2013) while continuous and intermittent types of noise are more commonly seen in industrial settings as a result of engines and industrial-type activities (Neuberger et al., 1992; Clark and Bohne, 1999; Atmaca et al., 2005). Some animal studies showed that long-term or continuous noise exposure has a more detrimental effect on the cochlea compared to short-term or intermittent noise types (Ward, 1991; Pourbakht and Yamasoba, 2003). Similar findings have been reported on cVEMP findings of guinea pigs (Hsu et al., 2008; Akdogan et al., 2009). There are other important factors playing a role on the extent of noise damage, such as the frequency and length of exposure, which were obviously different between the two groups due to differences in working hours and employment length. Thus, the established differences in DPOAE and PTA findings among the two groups were not surprising.

Although direct physical noise measurements were not conducted in this study due to the great challenges in obtaining such data from a large study sample, the obtained rates of NIHL and abnormal DPOAE findings from both occupational groups suggest that those workers were being exposed to occupational noise at high intensity levels, which were significant enough to affect their OHC function and hearing. The demonstrated abnormality in cVEMP findings suggests that the saccular function of both groups was affected as well. The higher cochlear and saccular abnormalities observed among soldiers suggest that this group might have greater exposure to noise compared to hospital technicians. According to the Occupational Safety and Health Administration (OSHA) in USA, personnel working in military and industrial occupations are at extreme

risk of developing NIHL because they are often exposed to noise intensity levels exceeding 120 dB (OSHA, 2002; OSHA, 2005). However, several studies have shown that the noise intensity levels produced by heavy weapons and explosions commonly used in military service could produce significant noise intensity levels exceeding 140-150 dB SPL (Ylikoski et al., 1995; Flamme et al., 2009; Meinke et al., 2013) and that is why the military profession has been ranked among the top occupations for developing NIHL. To the best of the author's knowledge, the information on differences of cochlear or saccular function as a result of noise exposure between military and technical personnel is scanty. Obtaining more information about the noise exposure characteristics of those two occupational groups would help to explain the observed differences in their audio-saccular test results, which is done in the next study described in Chapter 4.

### **3.6.5 Relationship between cVEMP, PTA and DPOAE**

The finding that PTA thresholds and DPOAE amplitudes had statistically significant moderate correlation observed in both groups (NIHL and noise-exposed-NH) is consistent with the findings of several published reports (Reshef et al., 1993; Attias et al., 1995; Attias et al., 1998). Although some studies suggested a relationship between hearing loss severity and abnormal cVEMP findings in cases of NIHL (Wang and Young, 2007; Kumar et al., 2010; Akin et al., 2012), the current study findings found no correlation between PTA thresholds and cVEMP response parameters (see section 3.5.5). Although the present study findings found very weak correlation between cVEMP response parameters and DPOAE amplitude levels and between cVEMP response parameters and PTA thresholds, a slight increase in correlational values was noted between cVEMP normalized amplitude and DPOAE amplitude levels at most tested frequencies only in the NIHL group (see Figure 3.12, Panels A, C and D). The better identified relationship between cVEMP and DPOAE findings may suggest that cVEMP data are more related to DPOAE data compared to PTA data.

When cVEMP data for the noise-exposed groups were classified according to DPOAE results and then compared to cVEMP control data (Figure 3.6), the same trend was observed as when cVEMP data for the noise-exposed groups were classified according

to PTA results (Figure 3.5). In other words, cVEMP response parameters for the investigated groups (controls vs. noise-exposed groups) consistently showed statistically significant differences whether cVEMP data were classified according to PTA or DPOAE results. The only exception to this was in P1 latency data. P1 latency data for the noise-exposed NH group were significantly different from those obtained from controls. However, statistically significant differences were noted in P1 latency between controls and the abnormal DP group. When looking also at the rates figure of cVEMP and DPOAE absence/abnormality obtained in this study (see section 3.5.3), a similar trend was observed. The majority of ears with absent cVEMPs (80 %) had absent/abnormal DPOAE findings. However, DPOAE absence/abnormality rate was reduced to 47 % in ears with present but abnormal cVEMPs. Hence, these findings are in line with the correlation test results reported in this study in that cVEMP data seems to be more related to DPOAE outcomes compared to PTA outcomes. The findings of this study suggest that noise-exposed individuals with normal hearing (NH group), but reduced OHC function evident by DPOAE, are more likely to show saccular dysfunction identified by cVEMP. Conversely, noise-exposed individuals with normal DPOAE are less likely to show saccular dysfunction because if they have been exposed to noise but to a level that has not changed their OHC function, then, most likely their saccular function will be intact. In that case, OAE and cVEMP procedures might be more sensitive to detect cochlear and saccular changes resulting from noise exposure compared to PTA.

Although published data indicate the existence of a relationship between NIHL and noise-induced saccular damage, the findings of the current study suggest that saccular dysfunction as a result of noise exposure could be more related to OHC dysfunction. The fact that both responses (cVEMP and DPOAE) require functional sensory hair cells and the close proximity of cVEMP anatomical origin (saccular hair cells) to OAE's origin (OHC in the cochlea) explains the better consistency established between cVEMP and DPOAE findings in this study compared to the weak relationship seen between cVEMP and PTA findings. Hence, these findings suggest that combining both OAE and VEMP procedures to diagnose noise-exposed individuals may increase the likelihood of detecting noise-induced saccular dysfunction. It is important to mention here that the present study is the first study to employ both cVEMP and DPOAE to investigate audio-saccular

dysfunction in noise-exposed population with and without NIHL.

### **3.7 Conclusion**

The experimental findings reported in this chapter add to the body of evidence regarding vestibular consequences of noise exposure in cases of NIHL. Saccular abnormalities evident by abnormal cVEMP were more evident in noise-exposed individuals with reduced/absent OHC function as well as greater degrees of hearing loss in the high frequencies. The study described in this chapter also showed that saccular dysfunction could occur before cochlear dysfunction or hearing loss is evident in routine diagnostic testing. Therefore, saccular dysfunction in noise-exposed individuals should be considered regardless of whether noise-induced OHC dysfunction or NIHL is present or not. However, absent cVEMP seems to be related to OHC dysfunction. To further investigate the effects of noise exposure on these individuals, self-reported audio-vestibular data were collected from the same workers in the next study, described in Chapter 4. This conclusion will be further discussed in relation to the overarching question of this thesis, along with the previous and subsequent studies described in Chapters 2 and 4, in Chapter 5.

## **Chapter 4**

### **Audio-vestibular symptoms and noise exposure data reported by noise-exposed individuals**

## 4.1 Introduction

Since cVEMPs are thought to be of saccular origin, the abnormal cVEMP findings found in noise-exposed participants in Chapter 3 suggest noise-induced saccular dysfunction in individuals with and without NIHL. Thus, in this chapter, the data obtained from participants in Chapter 3 were taken one step further to investigate the presence of vestibular symptoms, particularly those thought to be of saccular origin. This was done by studying their self-reported audio-saccular symptoms obtained using a questionnaire. Additional noise exposure data were collected from participants to help understand the self-reported symptoms associated with the identified audio-saccular damage. This data also helped to understand the variability observed in the results obtained from both studies described in this chapter and Chapter 3 (self-reported audio-vestibular symptoms and pure tone audiometry (PTA), Distortion product otoacoustic emissions (DPOAE), cVEMPs respectively). The present chapter starts with a brief overview of published research on self-reported data used to describe the frequency and nature of vestibular symptoms among noise-exposed individuals. This is followed by presentation and discussion of the findings in this third study.

## 4.2 Self-reported vestibular symptoms in noise-exposed individuals with noise-induced hearing loss (NIHL)

Reporting on the incidence of vestibular symptoms or “dizziness” in general has posed a challenge for investigators due to variability of descriptions, variability of clinical presentation, diagnostic techniques, settings and methods of obtaining such data (Cherchi, 2012). However, several studies showed that the incidence of vestibular symptoms in the general population averaged across lifespan is about 20 to 30 % (Hannaford et al., 2005; Karatas, 2008; Mendel et al., 2010) with this number estimated to be higher in females and the elderly (Sloane et al., 2001; Jönsson et al., 2004). Fewer data are available regarding the incidence of vestibular symptoms arising from specific vestibular disorders, such as noise-induced vestibular damage. As explained in Chapter 3, vestibular damage arising from noise

exposure has not been widely studied. Vestibular damage due to noise exposure, particularly saccular damage evident by abnormal cVEMP findings, has been demonstrated by a limited number of studies including the study described in Chapter 3 (Wang et al., 2006; Wang and Young, 2007; Wu and Young, 2009; Kumar et al., 2010; Akin et al., 2012; Tseng and Young, 2013). If noise-induced cochlear damage results in auditory symptoms, such as a reduction in hearing demonstrated by PTA and reduced or absent outer hair cell (OHC) function demonstrated by otoacoustic emissions (OAEs), then saccular dysfunction indicated by cVEMP abnormalities may lead to saccular symptoms. Although several studies have described vestibular symptoms and their relationship with known vestibular lesions, only a limited number of studies have provided evidence for vestibular symptoms arising from noise exposure (Shupak et al., 1993; Golz et al., 2001; Cassandro et al., 2003; Atmaca et al., 2005; Scherer et al., 2007; Akin et al., 2012; Raghunath et al., 2012).

Early investigations explored noise-induced otolith lesions by examining the relationship between symmetrical/asymmetrical NIHL and noise-induced vestibular symptoms. For example, Golz et al. (2001) reported the presence of vestibular symptoms in 258 male military personnel with a history of significant occupational noise exposure and NIHL. Approximately half of Golz's study participants had symmetrical NIHL and the other half had asymmetrical NIHL. Although the study found that the rate of the reported vestibular symptoms, which were vertigo and dizziness, was higher in the asymmetrical NIHL group (21 %) compared to the symmetrical NIHL group (11 %), there were statistically non-significant differences between the two groups. Vertigo indicates a spinning or rotary sensation and is commonly reported by individuals with semicircular canal lesions so their participants might have had canal lesions, most likely not related to noise damage. Moreover, describing symptoms as "dizziness" does not add any useful information because this is a broad term commonly used to cover a wide range of vestibular sensations.

A subsequent study investigated 40 young subjects aged between 18 and 26 years with no history of audio-vestibular disorders before and after exposure to 128 dB(C) disco music for three hours (Cassandro et al., 2003). The study included PTA, videonystagmography and



cVEMP before and after the noise exposure. Analysis of data revealed no apparent abnormality except a statistically significant increase in cVEMP amplitude post-exposure data, particularly those obtained at supra-threshold stimulus intensity levels. The authors suggested that a direct and irritative action of the sound stimulus upon the macular receptors may be responsible for the observed increase of cVEMP amplitude in post-noise exposure data. The study also reported a direct correlation between the higher observed increase in cVEMP amplitude and intensity of symptoms reported. In the same study, another group of 214 university students were surveyed to study the relationship between audio-vestibular symptoms and habitual disco visiting. Results showed that while 42 reported hearing loss, at least one vestibular symptom (i.e. vertigo, instability, oscillopsia) was reported by 41 participants. The authors concluded that the reported audio-vestibular symptoms due to excessive recreational noise exposure are much more frequent than commonly believed.

In a more relevant study, [Akin et al. \(2012\)](#) investigated 43 rifle shooters diagnosed with asymmetrical NIHL using cVEMPs and a questionnaire. The questionnaire focused on the presence or absence of dizziness and on categorizing the reported symptoms as vertigo, imbalance or lightheadedness. Vestibular symptoms were reported in almost 50 % of the investigated sample. Dizziness complaints were more evident in the noise-exposed participants with abnormal cVEMPs compared to those with normal cVEMP. The authors suggested a relationship between noise-induced saccular damage evident by cVEMP, vestibular symptoms due to noise exposure, poorer hearing and greater inter-aural high frequency pure tone threshold differences (i.e. greater NIHL asymmetries). However, because the study involved only cases of asymmetrical NIHL and cases of symmetrical NIHL were not included in the study, the evidence supporting a relationship between asymmetrical cochlear damage and the presence of saccular damage and symptoms cannot be concluded. As explained earlier, in Chapter 1 (section 1.4), based on what has been established so far regarding vestibular pathology and vestibular compensation studies, it is currently hypothesized that vestibular symptoms are more likely to occur in cases of asymmetrical vestibular damage. So in the case of noise exposure, if noise-induced cochlear

damage has already taken place and the hearing loss is unilateral or bilateral but asymmetrical, then a similar configuration could be expected to occur in the vestibular system and symptoms would arise from corresponding neural asymmetries. In contrast, symptoms might not be observed because of the absence of neural asymmetries in individuals with bilaterally equal or symmetrical cochlear damage, then bilateral symmetrical vestibular loss could be expected. It should be noted that most of the knowledge derived about vestibular compensation has come from studies done on semicircular canal lesions and little has been done on the compensation process for otolith lesions. However, it seems reasonable to suggest that the vestibular compensation process for otolith lesions will behave similarly to that of canal lesions (Barin, 2016).

Since all the published evidence points to the saccule as the structure in the vestibular system most likely to be affected as a result of noise exposure, then the reported symptoms are expected to reflect saccular dysfunction. Nevertheless, none of the previously discussed studies have related noise-induced vestibular symptoms to saccular damage. Additionally, the reported incidence of vestibular symptoms in noise-exposed individuals with or without NIHL was highly variable (16 to 60 %). Another limitation of the aforementioned studies is that they tend to give more attention to diagnostic test results and less attention to self-reported data. As a consequence, self-reported noise-induced vestibular symptoms have been collected using small scale questionnaire tools, which are usually not enough to reveal the nature and characteristics of these symptoms. From the above, it is clear that few studies are available concerning noise-induced vestibular symptoms. Most published data in this area have indicated only the absence/presence of vestibular symptoms in noise-exposed individuals and not clearly specified or described the symptoms in any great detail. The studies which relate noise-induced vestibular symptoms to the established evidence of saccular origin of noise-induced vestibular damage are still lacking. Hence, the currently available literature lacks a clear description of vestibular symptoms, more specifically saccular symptoms, resulting from noise exposure.

### 4.3 Self-reported vestibular symptoms in noise-exposed individuals with normal hearing (NH)

As noted earlier in the first section of this chapter, the majority of documented self-reported vestibular symptoms related to noise exposure has come from NIHL cases. However, it was shown in Chapter 3 that saccular dysfunction due to noise exposure was evident not only in noise-exposed individuals with NIHL, but also in normally hearing individuals with a similar history of noise exposure. The latter may therefore be at risk of developing NIHL even though they have normal hearing. Since saccular damage in noise-exposed individuals with normal hearing (NH group) was evident in Chapter 3, then it would be logical to investigate if this damage would also manifest itself behaviourally in this group. The only study the present author is aware of in this area was the one carried out by [Raghunath et al. \(2012\)](#). In this study, 20 factory workers presenting with long-term occupational noise exposure without NIHL were examined using PTA, transient evoked otoacoustic emissions (TEOAEs) and a vestibular symptoms questionnaire. The study used a survey that contained questions adopted from several published dizziness questionnaires. Results showed that 35 % of the investigated workers had vestibular symptoms, which was significantly higher than the rate reported in their control group. Although the noise-exposed participants of this study had normal hearing, their TEOAE amplitudes were reduced compared to the control group. Since OHCs play a major role in the active process of the cochlea and they are thought to be the primary generators of OAEs and the most susceptible structures to noise damage, the reduced TEOAEs in the presence of normal audiometric thresholds observed in Raghunath's study is consistent with loss of OHCs prior to an increase in hearing thresholds, which have been reported previously ([Miller and Marshall, 2007](#)).

Although Raghunath's study suggested that vestibular symptoms, possibly related to noise exposure, might arise before NIHL is evident in the audiogram, the study had several limitations. First, the study used a small sample, which makes its findings difficult to generalize to the population. Second, because no vestibular function testing was carried

out in this study, the observed vestibular symptoms cannot be specifically related to noise-induced vestibular dysfunction. Third, the expressed symptoms in this study could be related to other vestibular lesions than saccular damage because the questions used to ascertain the symptoms were adopted from dizziness questionnaires, designed to evaluate general dizziness symptoms, which could be caused by numerous health problems, and not specifically related to saccular damage due to noise exposure. Therefore, the accuracy of the questionnaire outcomes used in this study to evaluate symptoms arising from noise-induced saccular damage is questionable. Since noise-induced saccular damage among noise-exposed individuals with and without NIHL was investigated in the previous chapter - Chapter 3, similarly, in this chapter, noise-induced vestibular symptoms was investigated in both groups.

#### **4.4 The difference between vestibular symptoms reported due to otolith dysfunction versus semicircular canal dysfunction**

Another important issue that has not been given much attention in the literature is that if symptoms are most likely caused by saccular damage, then there is a need to differentiate between noise-induced saccular symptoms and symptoms resulting from lesions to other structures (i.e. semicircular canal lesion or utricular lesions). There is a general consensus in the literature that the nature and characteristics of behavioural manifestations of vestibular dysfunction usually depend on the structure being affected. Because semicircular canals are responsible for detecting angular motion or motions in lateral plane, the typical symptom of canal lesions, most commonly unilateral horizontal canal lesions, is a rotary/spinning sensation or vertigo. Bilateral peripheral vestibular lesions, which are less common than unilateral, usually result in different kinds of symptoms, such as vague unsteadiness, oscillopsia and loss of visual acuity, which may be associated with head movements. On the other hand, because the otolith structures (utricle and saccule) are responsible for linear and gravitational accelerations and decelerations due to translational head movements and head tilts they are thought to contribute significantly to postural stability and spatial orientation and lesions in these structures result in symptoms like

swaying, tilting, unsteadiness, disequilibrium, rocking and falling. The usefulness of using rotary and linear symptoms to differentiate between semicircular canal lesions versus otolithic lesions was demonstrated by [Farrell and Rine \(2014\)](#).

Hence, it is clear from the literature discussed above that self-reported data have the potential to be used as a tool to differentiate noise-induced vestibular symptoms arising from otolith dysfunction, such as noise-induced saccular dysfunction from other symptoms caused by other lesions like semicircular canal lesions. However, very limited data is available in this area. Thus, the study described in this chapter aimed to examine self-reported data obtained from individuals affected by noise exposure, NIHL and noise-induced saccular damage evident by abnormal cVEMP to see if they can be distinguished from the commonly reported symptoms seen in patients with semicircular canal lesions. The study described in this chapter also aimed to investigate the frequency and nature of self-reported vestibular symptoms among noise-exposed workers presenting with self-reported history of occupational noise exposure with and without NIHL. Some of the sample investigated in the present study had already demonstrated saccular dysfunction evident by abnormal cVEMP (reported in Chapter 3). The symptoms were evaluated using a questionnaire developed based on what is known so far in the literature about otolith damage, particularly saccular dysfunction caused by noise exposure. Since the present thesis utilized both objective and subjective assessment tools to evaluate the effect of noise on human audio-vestibular function, at the end of the study described in this chapter, the diagnostic test measures reported in Chapter 3 (PTA, DPOAE and cVEMP) were contrasted with the self-reported audio-vestibular symptoms identified in this Chapter. The next section provides a brief overview of the available research which have attempted to integrate diagnostic test results with self-reported data to evaluate audio-vestibular dysfunction in noise-exposed individuals.

#### 4.5 The use of self-reported data to estimate noise exposure levels

This section provides a brief overview of information regarding the estimation of lifetime cumulative noise exposure using self-reported data (i.e. a noise exposure questionnaire) and also summarizes the literature, which has applied this method with noise-exposed samples. As previously mentioned in Chapter 1 (section 1.7.1), in order to determine if the noise level an individual is exposed to is enough to damage the audio-vestibular system, it is vital to assess the level of noise by direct physical noise measurements, which are commonly obtained by recording sound pressure levels at the noise source. Alternatively, one could estimate the noise levels using self-reported noise exposure history data in a form of a questionnaire or a noise survey. One of the most common measures used to estimate noise exposure levels is *Noise Immission Level (NIL)*. NIL can be defined as a cumulative measure of A-weighted noise exposure, used to assess accumulated risk to hearing and to predict hearing levels in individuals exposed to noise (Lutman et al., 2008). The notion of NIL was first introduced in the early 70s by Robinson (1971). Obtaining NIL is based on collecting details regarding the noise the individual experienced, such as an estimate of the typical noise level, the duration of exposure (years, weeks, days and hours) and proportion of normal full-time working where the noise was present in case of occupational noise and the usage of hearing protection devices (HPDs). The NIL should be determined separately for each noisy task or activity and also for each noise type (social, occupational or military noise).

There are a number of ways in which noise levels expressed in dB(A) can be estimated. For example, in rare cases, individuals are aware of the noise level they are exposed to, because sound pressure levels have been measured previously in their worksite. For occupational noises, one could use the noise exposure examples table, which acts as guide to equivalent continuous A-weighted noise levels from common noisy processes and industrial machines. It is possible also to use personal or local governmental documents that have been collected previously to estimate noise levels in similar locations. However, for the majority of cases, a speech communication table is used (Smith et al., 2000; Lutman et al., 2008). Speech

communication tables provide an estimate of typical noise level ranges based on the expected difficulty in communication at various distances as a function of noise level. In speech communication tables, vocal efforts required to hold a conversation are linked to an approximate sound pressure level in dB(A) (see Appendix F "Guide to Noise Levels - Speech communication difficulty versus estimated noise levels"). Additional information is usually sought from subjects pertaining to subjective symptoms like reports of hearing difficulty, tinnitus and which side is affected. All these data are compiled separately for each noisy task/activity and for each noise type and then entered in a mathematical formula (see Equation 4.1 in section 4.9.3), which gives *Units of Lifetime Cumulative Noise Exposure (U Value)*. The total number of units is calculated for each task or noise type (*Total U value*), then this number is used to derive the *Noise Immission Rating (NIR)*. The NIR values are equivalent to continuous noise exposures at 8 hours/day, 5 days/week and 48 weeks/year at a specific sound pressure level expressed in dB(A) throughout a full 50 year working lifetime (Lutman et al., 2008).

Several investigations have collected self-reported noise exposure data in order to estimate noise exposure levels using the NIL method. For example, Lutman and Spencer (1991) estimated the levels of exposure to occupational, social and gunfire noises for a large sample of subjects (N = 2162) using structured interviews. The study used noise exposure history information to calculate the cumulative NILs and found that subjects were exposed to occupational noise energy equivalent of up to 90 to 100 dB(A) for 50 years workday exposure and this had only modest effect on their hearing threshold levels. Jokitulopp et al. (1997) studied 405 Finnish teenagers aged between 12 to 17 years old to estimate their weekly noise exposure levels due to leisure activities like sports, disco/concert attending and listening to music through personal stereos, using a questionnaire. The study revealed that 51 % of their sample had a weekly noise exposure of equivalent to at least 85 dB(A) for a 37-hour working week, which suggested that a high proportion of teenagers were exposed to noise levels detrimental to hearing sensitivity. Similar findings were demonstrated by Smith et al. (2000). The study looked at the prevalence and significance of three types of noise exposure (social noise from nightclubs and the use of personal cassette players,

occupational noise and gunfire noise) in 356 Nottingham residents, aged between 18 to 25 years old. Noise levels were estimated by interviewing subjects to obtain noise history information. To verify the estimates made for noise levels, sound pressure levels were recorded within three local nightclubs and from personal cassette players. The study found that the estimated sound pressure level for nightclubs using the NIL method was 101 dB(A), which correlated well with the sound pressure level measurements, which were around 85 to 105 dB(A).

[Jokitulppo et al. \(2006b\)](#) estimated the personal weekly noise exposure levels and the total cumulative noise exposure levels of 1054 Finnish conscripts for two types of noise (military and leisure) using a questionnaire. The study showed that 27 % of the conscripts had a weekly noise exposure over 85 dB(A), which suggested that those individuals were exposed to high noise levels enough to make them at risk of developing NIHL. The study showed that the estimated noise dose of the investigated sample correlated well with the incidence of hearing symptoms. Similar findings were demonstrated by [Jokitulppo et al. \(2008\)](#). The estimation of lifetime noise exposure for 416 Finnish conscripts in this study using a questionnaire showed that 89 % of the conscripts had a weekly exposure to military noise of over 85 dB(A). The study found that during the conscripts' military service, 21 % of them were exposed to leisure noise equivalent to noise levels of over 85 dB(A).

[Lutman et al. \(2008\)](#) studied 154 noise-exposed employees aged 18 to 25 years, recruited from 19 companies. The study performed annual audiometric and otoacoustic emission measures over a period of three years. The workers' lifetime cumulative noise exposure for three types of noises (occupational, social and gunshot and explosive noises) was estimated using a questionnaire and compared to data obtained from noise dosimetry. Results of noise measurements showed an average of approximately 88 to 89 dB(A) and estimated noise levels were greater for social noise compared to occupational or gunfire noise. Although the authors mentioned that because the estimation method was totally subjective so it was potentially prone to inaccuracy and bias, comparison of the noise dosimetry data with estimates of noise exposure lacked an overall bias because the differences found



between direct noise measurements and estimated noise levels were within 3 dB in 43 % of cases and within 6 dB in 84 % of cases. Hence, it is apparent from the above research that the method of estimating noise exposure levels using subjective measures like questionnaires is a useful approach to quantify noise levels, which is vital to identify individuals who are at potential risk of noise damage. Hence, in the present study, lifetime cumulative noise exposure was expressed as a noise immission level (NIL) estimated from the self-reported audio-vestibular symptoms of workers described in Chapter 3.

#### **4.6 Combining self-reported data with audio-vestibular test results to evaluate noise-exposed individuals**

Because of the high variability revealed by investigations of noise-induced vestibular symptoms, several studies have questioned the accuracy of such data to identify noise-induced vestibular damage. For example, it has been suggested that the variability in self-reported data might be greatly influenced by the fact that some individuals have difficulty articulating their symptoms or simply cannot recall or describe them accurately. Moreover, the validity of self-reported data has often been criticized for effects of researcher's bias in data collection or analysis. Nonetheless, in many instances, combining self-reported data and audio-vestibular test results helps to understand the variability observed in diagnostic test measures. Integrating both self-reported data and audio-vestibular test measures to evaluate noise effects may improve our understanding of the underlying problem, and ultimately facilitate the diagnostic process of noise-exposed individuals. For this reason, a number of investigators have examined the utility of patients' self-reported data, such as auditory symptoms and tinnitus after noise exposure by comparing them with results obtained from diagnostic test procedures, such as PTA (Williams et al., 2004; Muhr and Rosenhall, 2010). These studies showed that such self-reported auditory data correlated well with measured audiograms. Hence, evidence of a good relationship between self-reported hearing status and auditory symptoms with diagnostic test results like PTA is emerging.

Other investigations looked at the relationship between self-reported vestibular symptoms in general and audio-vestibular test outcomes (Spitzer, 1990). The study evaluated 51 military personnel diagnosed with high frequency hearing loss using electronystagmography (ENG), which can record involuntary eye movements (e.g. nystagmus) caused by several vestibular system disorders. The study found that self-reported questionnaires were poor predictors of ENG results. Possible causes of the weak correlation established in this study might be the wide inclusion criteria for the participants. The author indicated that the only inclusion criterion was dizziness reporting and the only persons excluded from the study were those who could not read or answer the questionnaire. In Spitzer's study, several sources of variability among subjects were not taken into account, such as the location of the vestibular pathology (i.e. whether it was in the semicircular canals or the otolith organs and the severity of lesion) and also the possibility of the presence of vestibular compensation in some subjects. In addition, the participants of this study were all military personnel with high frequency sloping sensorineural hearing loss, but the possible cause of this audio-vestibular pathology was not discussed (i.e. NIHL, presbycusis or both). All these are contributing factors that would have affected the type and nature of the dizziness complaints reported in this study.

Golz et al. (2001) examined the effects of noise on the vestibular system of 258 military personnel diagnosed with symmetrical and asymmetrical NIHL using PTA, ENG and caloric testing. Vestibular symptoms were investigated in this study by asking the participants if they had any vestibular complaints or not. The study revealed a strong correlation between the reported vestibular symptoms and vestibular test results only in the asymmetrical NIHL group. Again, this study employed vestibular measures which evaluate semicircular canals and the established correlation between the test measures and vestibular symptoms rate (i.e. presence/absence) might indicate that those participants had lesions related to the semicircular canals rather than lesions related to noise-induced saccular damage. The other alternative explanation is the possibility that those individuals might have had lesions in both organs, the semicircular canals and also the saccule, but the latter cannot be confirmed since no VEMP testing was carried out in this study. When researchers started to narrow

their participants' inclusion criteria by examining self-reported symptoms in certain groups, such as those affected by noise exposure and use more appropriate diagnostic tools targeting the most likely site of lesion, an evidence of a relationship between self-reported data and diagnostic test results started to emerge. For example, [Seo et al. \(2008\)](#) examined the relationship between vestibular symptoms and cVEMP findings of 18 patients with undiagnosed dizziness. The study found a relationship between abnormal cVEMP results and a momentary falling sensation and thus, suggested that this kind of symptom might be related to saccular dysfunction. However, the findings of this study cannot be generalized to all pathologies affecting saccular function including those related to noise exposure because the investigated group in this study had vestibular complaints of unknown origins.

The evidence of a relationship between cVEMP findings and self-reported data was further supported by [Akin et al. \(2011b\)](#). The study investigated 31 military personnel with a history of blast exposures and found that 84 % of participants with self-reported symptoms had abnormal cVEMP and/or abnormal subjective visual vertical test results, which is a clinical test of utricular function. [Akin et al. \(2012\)](#) subsequently investigated 43 rifle shooters diagnosed with asymmetrical NIHL using cVEMPs and a questionnaire. The study revealed a relationship between cVEMPs abnormality and vestibular symptoms reported in about 50 % of the investigated sample. In brief, the studies noted above support the evidence of a possible relationship between self-reported vestibular symptoms and objective vestibular test results. However, because cVEMP is a relatively new clinical procedure, there are only a few studies in the literature that have attempted to link cVEMP findings with self-reported audio-saccular symptoms possibly arising from noise-induced audio-saccular damage. Hence, the relationship between saccular damage evident by abnormal cVEMPs and self-reported saccular symptoms is not yet clearly understood. For this reason, the present study aimed to explore noise-induced saccular symptoms in more depth. At the same time, it aimed also to clarify the relationship between cVEMP outcomes and self-reported symptoms.

## 4.7 Summary

Saccular dysfunction in noise-exposed adults with NIHL has been documented by some studies (Wang et al., 2006; Wang and Young, 2007; Wu and Young, 2009; Kumar et al., 2010; Akin et al., 2012; Tseng and Young, 2013) including the second study described in Chapter 3 of this thesis. However, the published research to date has tended to focus on diagnostic procedures to evaluate the integrity of the audio-vestibular system rather than self-reported audio-vestibular symptoms. Even less has been done concerning the nature and characteristics of symptoms possibly resulting from noise-induced vestibular damage. The few published studies which reported noise-induced vestibular symptoms (Shupak et al., 1993; Golz et al., 2001; Cassandro et al., 2003; Scherer et al., 2007; Akin et al., 2012; Raghunath et al., 2012) have not discussed these symptoms in any great detail. Rather, much of the available data up to now has focused on the presence or absence of symptoms, with only a brief description of noise-induced vestibular symptoms. The few studies that have described self-reported vestibular symptoms in noise-exposed individuals did not relate observed symptoms to saccular damage. This is because no cVEMP testing was carried out, or the questionnaires used were too general to provide a specific description of noise-induced saccular symptoms.

In addition, little attention has been paid to the existence of vestibular symptoms in normally hearing noise-exposed individuals who are at risk of developing NIHL. Thus, behavioural manifestations of noise-induced saccular damage both in noise-exposed individuals with and without NIHL remain unclear. Saccular dysfunction defined by abnormal cVEMPs was documented in noise-exposed individuals with and without NIHL in Chapter 3. In this Chapter, Chapter 4, the same cohort was investigated to determine whether they experienced symptoms that could be related to noise-induced saccular damage as a result of an estimated cumulative lifetime noise exposure and co-incidentally help in identifying different symptoms that could be distinguished from other pathologies, such as those occurring in the semicircular canals. Conducting an estimation of lifetime cumulative noise exposure of those individuals is expected to inform the discussion of the

overall findings obtained in this thesis. This data might identify the level of noise which may lead to vestibular damage and further may lead to manifestation of noise-induced vestibular symptoms.

#### **4.8 Aim of the work described in this chapter**

The experimental work presented in this Chapter has three aims: 1) to determine the frequency and nature of vestibular symptoms among noise-exposed individuals in two groups: a) individuals with self-reported history of occupational noise exposure and a confirmed noise-induced cochlear damage (NIHL group) and b) individuals with similar self-reported history of occupational noise exposure but with normal hearing (noise-exposed-normal hearing "NH" group), 2) to determine if there is a relationship between self-reported audio-vestibular symptoms data and the diagnostic test results obtained in Chapter 3 (PTA, DPOAE and cVEMP) and 3) to estimate the lifetime cumulative noise exposure of both noise-exposed occupational groups (hospital technicians and soldiers) and assess if there is any association between this data and the self-reported data (the questionnaire data) and the diagnostic test findings (PTA, DPOAEs and cVEMP) obtained from the same individuals in Chapter 3. Thus, the study described in this chapter examined seven hypotheses:

- i. If vestibular dysfunction is related to noise exposure, then *the noise-exposed NIHL group* will report vestibular symptoms which reflect saccular dysfunction as a result of noise exposure.
- ii. If vestibular dysfunction is related to noise exposure and this occurs before hearing loss is detected by PTA, then *the noise-exposed group with normal hearing (NH group)* will report vestibular symptoms which reflect saccular dysfunction as a result of noise exposure.
- iii. If noise-induced audio-vestibular dysfunction can express itself as audio-vestibular manifestations, then an association would be expected between the self-reported audio-vestibular symptoms reported in Chapter 4 and their (a) PTA findings (b) DPOAE findings (c) cVEMP findings, reported in Chapter 3.

- iv. If the self-reported audio-vestibular symptoms are related to noise exposure, then an association would be expected between the self-reported audio-vestibular symptoms data and participants' estimated lifetime cumulative noise exposure data.
- v. If the identified audio-vestibular dysfunction is related to noise exposure, then a relationship would be expected between the hospital technicians' estimated lifetime cumulative noise exposure data and their (a) PTA thresholds (b) DPOAE amplitudes (c) cVEMP response parameters, reported in Chapter 3.
- vi. If the identified audio-vestibular dysfunction is related to noise exposure, then a relationship would be expected between the soldiers' estimated lifetime cumulative noise exposure data (rifles/machine guns) and their (a) PTA thresholds (b) DPOAE amplitudes (c) cVEMP response parameters, reported in Chapter 3.
- vii. If the identified audio-vestibular dysfunction is related to noise exposure, then a relationship would be expected between the soldiers' estimated lifetime cumulative noise exposure data (light artillery/explosives) and their (a) PTA thresholds (b) DPOAE amplitudes (c) cVEMP response parameters, reported in Chapter 3.

## **4.9 Methods**

### **4.9.1 Participants**

The one hundred and nine workers enrolled in the study described in Chapter 3 were recruited for this study. The participants worked at two potentially noisy working environments (military and utility and maintenance services of the Saudi National Guard Hospital). The recruitment process and the criteria used to define the two groups (NIHL group, a noise-exposed NH group) were described in section 3.4.1. Data were collected at the end of the testing session described in Chapter 3. Information sheets were provided at the beginning of the session and written informed consent was obtained. The study involved Arabic and non-Arabic speaking participants, so the consent forms and the information sheets were made available in Arabic and English. Because of the subjective

nature of the study reported here and to ensure that participants were providing an accurate description of their noise exposure, it was explained that all answers would remain anonymous (i.e. not be revealed to their employer) and would not affect their current employment and/or benefit status. Ethics approval has been granted by two committees: the School of Healthcare Research Ethics Committee (SHREC/RP/225) at University of Leeds and the Institutional Review Board and Research Committee at King Abdullah International Medical Research Centre (KAIMRC- Ref no. RC 12/017) in Riyadh City, Saudi Arabia.

#### 4.9.2 Questionnaire

Two previously published questionnaires; *Self-use History Questionnaires for Dizzy Patients* developed by Busis (1973) (Appendix A) and *The Noise at Work Questionnaires* developed by Purdy and Williams (2002) (Appendix B) were adapted for use in this study. These questionnaires were selected based on their relevance to noise-induced vestibular symptoms and how much noise exposure history data they contained. Furthermore, those two questionnaires have been used by several investigations. For example, Purdy and Williams (2002) examined the psychometric properties of the Noise at Work Questionnaire and found that this measure had a good overall internal reliability. The Noise at Work Questionnaire was also used as part of a training session designed to raise the awareness of noise as a worksite hazard to 69 noise-exposed workers (Williams et al., 2007). Spitzer et al. (1990) used the Noise at Work Questionnaire as well to examine the relationship between self-reported data and audio-vestibular test results (PTA and ENG).

The areas assessed in the questionnaire and the questions being asked to participants for each area with the response choices for each question are listed in Table 4.1. The majority of the questionnaire items were closed-ended questions and few questions were open-ended. The closed-ended questions were scalable questions (i.e. the participant chose an answer from a set of available answers) and to ensure that the participant understood the question before giving the answer, the investigator orally obtained the participant's answer

and recorded it in the questionnaire. For the open-ended questions, a semi-structured interview format was used to record participants' answers. Because not all participants were Arabic speaking, the questionnaire was made available in two languages (Arabic and English, Appendices C and D). Translation of the questionnaire items to Arabic was made by a group of undergraduate speech-language pathology and audiology students in their final year. The students were fluent in both languages and were blinded to the purpose of the study. The translation was subsequently reviewed and edited by the author. The questionnaire contained 23 items distributed over three sub-sections; A) noise exposure history, B) auditory symptoms history and C) vestibular symptoms history. Additional demographic and general medical history information, such as age, job title, length of current and past employment, presence or incidence of head trauma, neuro-muscular diseases, neurologic diseases, vestibular diseases, medication intake and the presence of any other major health conditions were also collected.

In Section A: *Noise Exposure History*, self-reported noise exposure data were collected to define the noise exposure characteristics of the noise-exposed sample. This section involved eight questions aimed to characterize participants' noise exposure history. These questions were related to each individual's perception of noise intensity levels experienced, building an estimate of work-related noise exposure intensity levels and durations, presence of leisure noise activities, types of noise exposure sources and use of hearing protection devices (HPD). Since the use of HPDs would reduce noise effects, additional details on HPDs were collected. In Section B: *Auditory History*, participants were asked five questions. These questions aimed to assess: hearing monitoring, expectation of hearing loss, the level of workers' and employers' awareness of risks of noise damaging hearing and the presence of noise-associated symptoms, such as tinnitus. It was important to include questions about tinnitus in the questionnaire because the published literature suggests that tinnitus is a frequent symptom reported in NIHL (Stephenson and Stephenson, 2000; Mazurek et al., 2010) and could be an early indicator of noise-induced damage (Griest and Bishop, 1998; Mrena et al., 2004).



The final section, Section C: *Vestibular History*, comprised 10 questions related to the presence of vestibular symptoms and their characteristics, associated symptoms and triggers. The questions of this section were adapted from the *Self-use History Questionnaires for Dizzy Patients* (Busis, 1973) and were administered only to participants who reported the presence of vestibular symptoms. The term "dizziness" was used throughout the questionnaire because it is the term commonly used by patients in clinical settings to describe vestibular disturbances. However, participants were provided with a simple definition for the terms used in the questionnaire to help them choose the most appropriate term that described their symptoms. For example, "light-headedness" was defined as a vague symptom, giddiness or feeling disconnected from environment whereas "unsteadiness" was defined as disequilibrium, which is an impaired balance or gait without abnormal head sensation or illusions of movement or faintness. "Vertigo" was defined as a sensation of spinning in the room or the sense that the room/things are spinning around you (Post and Dickerson, 2010; Lee, 2012). It should be noted that explanations and clarifications were sought from participants for some question answers, depending on the answers provided. The collected self-reported vestibular data were inspected to determine if noise-induced saccular dysfunction would result in symptoms which can be distinguished from the other common vestibular symptoms caused by other lesions like semicircular canal lesions.

**Table 4.1 Summary of the areas assessed in the questionnaire developed in this study.** The Table shows questions included in each area and the response options provided for participants for each question.

Areas of assessment		Questions		Response options
Major	Specific			
<b>A. Noise exposure history</b>	Workers' noise perspectives	1	Do you consider the noise level where you are working now to be high?	Never = 1, strongly agree = 2, agree = 3, undecided = 4, disagree = 5, strongly disagree = 6
	Estimation of noise exposure	2	Do you have to shout to be heard at work because of noise?	
		3	What is the approximate number of hours you spend in this noisy worksite?	8 hours/day = 1, < 8 hours/day = 2, > 8 hours/day = 3, I don't know = 4
		4	How often do you use the following; small arms, portable listening devices, home tools, musical instruments. If others, please specify.	Never = 1, a few times = 2, several times = 3, quite often = 4, very often = 5
		5	What are the most frequent noise sources encountered in your worksite?	Open ended
	Hearing protection devices (HPDs)	6	Are hearing protection devices (HPDs) provided at your workplace? If yes, what is the type of the HPDs you use to protect your hearing?	Yes, No, sometimes, recently/inconsistently Open-ended
		7	Do you use HPD at your worksite? If yes, how often do you use your HPD?	Yes/No - Never =1, a few times = 2, several times = 3, quite often= 4, very often= 5
		8	If you do not use HPDs, please explain why.	Open-ended
<b>B. Auditory History</b>	Hearing monitoring	9	Has your hearing being examined previously?	Yes/No
	Expectation of hearing loss	10	Do you expect to have a hearing loss in today's exam?	
	Awareness of noise risks to hearing	11	Which one of the following do you think is the cause of your hearing loss?	Hereditary = 1, ear infection= 2, exposure to noise = 3, I do not know = 4, others = 5

<b>Table 4.1 continued</b>				
		12	Have you received any treatment/rehabilitation for your hearing loss? If yes, please specify.	Yes/No – open ended
	Associated symptoms	13	Do you have ringing in your ear (tinnitus)? If yes, please describe it.	
<b>C. Vestibular History</b>	Symptoms description	14	Did you experience dizziness over the last 6 or 12 months? If yes, have you experienced any of the following? A feeling of being light-headed 'swimmy' or giddy, a sensation of 'spinning' in the room or the room/things are spinning around you (vertigo), feeling unsteady or about to lose balance (disequilibrium), unable to walk properly without support, veering or staggering to one side, unsteadiness so severe that you actually fall	Yes/No  Never = 1, a few times = 2, several times = 3, quite often = 4, very often = 5
	Associated symptoms	15	Was your dizziness ever associated with any of the following symptoms? Pressure or fullness in your ears, nausea or vomiting, visual disturbances, headache or pressure in your head, feeling faint or about to block out	
	Characteristics	16	Is your dizziness constant or does it come in attacks?	Yes/No
		17	Does change of position make you dizzy?	
		18	Do you have trouble walking in the dark?	
		19	When you are dizzy, can you stand up unsupported?	
	Triggers		Are you aware of anything that will:	Yes/No Open ended
		20	Stop your dizziness or make it better?	
		21	Make your dizziness worse? If yes, please say what it is.	
		22	Were you exposed to any irritating fumes, paint, or others at the onset of dizziness? If yes, please specify.	
	23	If you have tinnitus, does it change with dizziness, if so, how?		

#### 4.9.3 Estimation of noise exposure levels using noise immission levels (NILs)

The purpose of this assessment was to estimate the lifetime cumulative noise exposure of the noise-exposed group up to the time they participated in this study. This was done by using the self-reported noise levels and durations experienced over the lifetime of an individual. The procedure used to conduct this assessment was based on calculating noise immission levels (NILs) (Smith et al., 2000; Lutman et al., 2008). Usually, the estimation is carried out for all noise types the individual is exposed to during his/her life, meaning that it covers occupational and non-occupational noise exposure. However, because the majority of information collection in this study was related to occupational noise exposure and little information was collected in respect to other noise types like social or leisure-time noise, estimation of noise exposure was only carried out for occupational noise.

Calculation of NIL values was based on the same methodology described in these published studies (Smith et al., 2000; Lutman et al., 2008). Because of differences in investigated groups and conditions of data collection between the current study and these studies, it was necessary to adapt the method slightly to ensure suitability. However, the reader should assume that the method described here is similar to the one described by these studies, unless otherwise stated. Although the method used to estimate noise exposure for all types of noise is similar, the actual calculation for occupational noise levels is different from the calculation used for military noise levels. This is because occupational noise, particularly noise in industrial settings, is often continuous and of a steady-state nature. However, military settings often involve impulse noise generated by weapons, such as gun fire and explosives. To avoid confusion over terms, from now on, the noise the hospital technicians were exposed to will be referred to as “Occupational Noise” while the noise the soldiers were exposed to will be referred to as “Military Noise”.

### ***Estimation of occupational noise exposure in hospital technicians***

Occupational noise exposure was estimated in 27 hospital technicians. Because the noise exposure estimation was done retrospectively, some of the information was obtained from the answers to the original questionnaire developed in the present study (Table 4.1) and some were obtained separately from participants. In principle, the estimation should be obtained for each of the jobs (current, past) and for each individual task/activity, where noise levels are estimated to be greater than 80 dB(A) and then the information obtained from each task were summed and converted into a single NIR. However, because most of the collected noise exposure history data for the hospital technicians were related to their current job, the estimation was done only for their current job. In addition, those technicians were exposed mainly to one job task, which involved excessive noise exposure, so the estimation was done for that task. The procedure for estimating lifetime cumulative noise exposure for occupational noise involved three parts. Part (1) involved calculation of *Units of Lifetime Cumulative Noise exposure (U Value)*, a mathematical formula, based on the equal energy principle (see Equation 4.1).

$$U = 10^{(L-A-90)/10} \times Y \times W \times D \times H / 2080 \quad \text{(Equation 4.1)}$$

U = units of lifetime cumulative noise exposure

L = estimated noise level in dB(A)

A = hearing protection attenuation in dB

Y = years of exposure

W = weeks per year of exposure

D = days per week of exposure

H = hours per day of exposure

The formula combines several variables related to the participant's personal noise exposure history. To calculate *Units of Lifetime Cumulative Noise exposure (U values)*, the following information was obtained: the estimated noise level in the participant's worksite (L), duration of noise exposure, which is the typical number of years (Y), weeks (W), days (D) hours (H) spent in noise. Details of HPD type and its usage were also obtained. The number

of years of exposure (Y) was determined by the employment length for each participant. If the participant reported a previous job, with similar noise exposure history, such as a past experience of working in a similar work field with a similar working schedule and an approximately similar noise level, then the total number of years for the exposure of the current and the previous jobs were added together. The total number of weeks per year (W), days per week (D) and hours per day (H) were obtained from participants based on the typical working time schedule, where the participant was usually in noise.

Part (2) involved determining the method used for noise level estimation. Each method was given a code: 1 = actual knowledge, 2 = personal/documentary, 3 = examples table, 4 = speech communication table. A brief description of these methods was provided previously in section 4.5. Table 4.2 shows the speech communication table used to estimate noise levels in each participant's worksite. The speech communication table provides a guide to typical noise levels based on the reported vocal effort the workers tend to use to communicate with each other (normal voice, raised voice, very loud voice, shouting, impossible) in the following conditions: (a) both are 1.2 or 0.5 metres apart and facing each other, (b) neither was wearing hearing protection, (c) neither had a hearing impairment, (d) normal gesturing and lip reading were used (Smith et al., 2000). The answers to Q2 "*Do you have to shout to be heard at work because of noise?*" were used to determine the approximate vocal effort the participant tended to use in noise. For example, if the participant reported frequent shouting, then either 99 dB(A) or 105 dB(A) was selected as the estimated noise level according to the reported communication distance by the participant. If the participant reported a frequent use of hand signing because shouting was often found ineffective, then "impossible" was chosen as the vocal effort required and 110 dB(A) was selected as the estimated noise level in this case.

**Table 4.2 Estimation of noise levels by the speech communication table.** The table links the vocal effort required to hold a conversation above the noise at a particular distance to an estimated sound pressure level in dB(A). The table is adopted from Smith et al. (2000) - Table 2 and Lutman et al. (2008) - Table 4 (page 23).

For one worker to communicate with another in a working environment that they are both used to (assuming that neither has any deafness and they often are assisted to some extent by gestures and lip reading) approximate communication-limiting noise levels are follows:			
Vocal effort required	Communication distance		
	1.2 m	0.6 m	Close to listener's ear
Normal voice	< 81 dB(A)		
Raised voice	87 dB(A)		
Loud voice	90 dB(A)		
Very loud voice	93 dB(A)		
Shouting	99 dB(A)	105 dB(A)	
Impossible			> 110 dB(A)
<b>Note:</b>			
(a) Persons who do not normally work in noise, but then enter a noisy place and try to communicate verbally (with an unlimited choice of words or context) will have speech interference levels some 20 dB lower than the above			
(b) It is important to distinguish between a raised voice and very loud voice; 6 dB difference.			

Part (3) involved obtaining the auditory after-effects experienced by the participant, such as subjective reports of hearing loss, tinnitus, dizziness, site where symptoms exists (right ear, left ear or both) and the duration of symptoms (permanent, temporary). The following coding scheme was used when the participant expected to have a hearing loss or reported hearing difficulty: dullness of hearing = 1, tinnitus = 2, dullness of hearing and tinnitus = 3,

permanent = 1, temporary = 2, left = 1, right = 2, both/central = 3. Subjective reports of hearing loss and tinnitus were obtained from the answers to Q10 *“Do you expect to have a hearing loss in today's exam?”* and Q13 *“Do you have ringing in your ear (tinnitus)? If yes, please describe it”*. Information on the duration of symptoms and whether the symptoms were permanent or temporary was obtained from the open-ended answers of the questionnaire.

Because a hearing protection device (HPD) will attenuate sound reaching the inner ear, information regarding the type and the frequency of using HPDs was obtained. The amount of attenuation reduces the risk of noise damage to the ear by a corresponding amount. Hence, the hearing protection attenuation in dB was used in the estimation formula (Equation 4.1). Table 4.3 shows the correction values for use of HPDs, based on published mean attenuation values in dB. The information needed to obtain HPD attenuation values (A values) was obtained from the answers to Q6 *“Are hearing protection devices provided at your worksite? If yes, what is the type of the HPDs you use to protect your hearing?”* and Q7 *“How often do you use your HPDs?”*. In addition, the participants were asked to specify the proportion of time (in %) HPD was worn. If the participant reported usual use of HPD, which implies only very occasional non-use in noise ( $\geq 90\%$ ), then the full attenuation factor for hearing protection in dB was entered. If the HPD was used for only part of the time ( $< 90\%$ ), then the work of the participant was divided into two separate tasks or sub-jobs: one with HPD and one without HPD. The full attenuation value was entered when participants reported using their HPD all of the time or virtually all of the time ( $\geq 90\%$ ); otherwise, attenuation value was entered as 0 dB. The hours in each sub-job were calculated according to the time without or with the HPD and the attenuation value in dB was adjusted according to the type of HPD assumed, then the *Units* for the two sub-jobs were then added together to reveal one *Unit of Lifetime Cumulative Noise Exposure Value (U value)*. More details on how to choose the appropriate correction values for variable HPD use can be found in [Lutman et al. \(2008\)](#).



**Table 4.3 Correction for hearing protection devices (HPDs) based on published mean attenuation values in dB.** The attenuation values in this table are used to derive A values in Equation 4.1. The table is adopted from Lutman et al. (2008), Table 5 (page 24).

Hearing protection device (HPD)		Attenuation value (dB)
<b>Ear muffs</b>		24
<b>Ear plugs</b>	Ear plugs	21
	Solid plastic ear plugs	15
	Glass-down (“Anti-noise”)	15
	Bilsom wool (2Bilsom Propp)	1
	Cotton wool (Vaseline or wax impregnated)	6
	Mallock Armstrong	6
	Cotton wool (dry)	0

The *U* value obtained from Equation 4.1 along with the codes obtained from Part (1) “the method used for noise level estimation” and Part (2) “the auditory after-effects, temporary/permanent and site of symptoms” were added together to obtain an overall total number called the *Total Number of Units for Lifetime Cumulative Noise Exposure (Total U value)*. The *Total U value* was used to derive a *Noise Immission Rating (NIR) Value for occupational noise exposure* using Table 4.4. The form used to fill out and collect all the information needed for Parts (1), (2) and (3) along with the coding schemes were the same ones used in Lutman et al. (2008) (see Appendix E “Annex B Occupational noise exposure – at study worksite”).

**Table 4.4 Determination of Noise Immission Rating (NIR) values for occupational noise exposure.** The resulted Total Number of Units for Lifetime Cumulative Noise Exposure (Total U value) was used to derive NIR values. The table is adopted from Smith et al. (2000) – Table 4 & Lutman et al. (2008) - Table 6 (page 24).

Total number of units for lifetime cumulative noise exposure (Total U value)	NIR	Equivalent to continuous exposure 8 H/D, 5 D/W, 48 W/Y throughout a full-time 50 year working lifetime at the following levels in dB(A)
Up to 5	0	< 81
6 – 50	1	81 – 90
51 – 500	2	91 – 100
501 – 5000	3	101 – 110
5001+	4	> 110

H: hour, D: day, W: week, Y: year.

### ***Estimation of military noise exposure in soldiers***

Military noise exposure was estimated in 58 soldiers. Because military service often involves more variable noise sources compared to occupational noise, the method of estimating military noise exposure is different. To conduct an estimation of military noise levels, the following information was required:

- i. The number of rounds fired for each type of the following noises (this number should be recorded when hearing protection was not worn):
  1. Rifles including shotguns, military rifles, but not 0.22 rifles or air-guns
  2. Machine guns (i.e. Bren, GPMG)
  3. Large infantry weapons (i.e. Bazooka, mortars)
  4. Light artillery or anti-craft guns
  5. Large artillery weapons or naval guns
  6. Explosives (only reported if they caused permanent after-effects to hearing)

- ii. The shoulder from which the rifle was fired (right, left) because it is the opposite ear that receives the most noise exposure.
- iii. Whether the individual had noticed any immediate auditory after-effects (i.e. subjective reports of hearing loss, tinnitus, dizziness, others) and the individual's subjective rating of the severity of these symptoms (none, slight, moderate or severe).
- iv. The duration of symptoms (permanent, temporary).

Because the estimation was done retrospectively, some of the information was obtained individually from each participant, when the questionnaire was originally collected from participants and the rest of the information was obtained from the participants' work supervisors. For example, the types of noise the participant was exposed to in his current job was obtained from the answers to Q5 "*What are the most frequent noise sources encountered in your worksite?*". The shoulder used for firing (left = 1, right = 2) was obtained from the handedness information provided as part of the initial demographical information collected at the beginning of this study, so if the participant was right-handed, it was assumed that the shoulder used for firing was the right side and vice versa. As stated previously, some information was obtained by conducting formal interviews with two National Guard senior supervisors. Because military service requires military personnel to engage in regular annual military training, besides their regular daily military tasks, the interviews focused on collecting information about the type of noise each individual was exposed to, the approximate noise exposure duration (number of weeks/year, days/week and hours/day) for each noise type and the approximate number of rounds fired for each type of noise when hearing protection was not worn. The information provided by the military supervisors was based on the formal Saudi National Guard military annual shooting timetables and also on an individual basis according to the job title for each soldier.

Similar to hospital technicians, information on auditory after-effects and the duration of symptoms was obtained from the answers to Q10 "*Do you expect to have a hearing loss in today's exam?*" and Q13 "*Do you have ringing in your ear (tinnitus)? If yes, please describe it*". Information on the severity (none = 0, slight = 1, moderate = 2 or severe = 3) and

duration of symptoms (permanent = 1, temporary = 2) was inferred from the open-ended answers of the questionnaire. The form used to fill out and collect all the information needed for military noise estimation along with the coding schemes was the same one used in [Lutman et al. \(2008\)](#) (see Appendix H “Gunshot and Explosive Noises”). To calculate the total NIR, the values obtained from all types of noise the participant was exposed to (see sub-section “Estimation of military noise exposure in soldiers”, item “i” 1 to 5) were added together by converting all of them to the equivalent number of rounds. To obtain the number of rounds the participant was exposed to during his lifetime, the number of rounds for each noise type was multiplied by the total employment period. Then, for each noise type, this value was divided by 20 to yield a *Number of Units* that is comparable to the occupational noise exposure units (*U value* obtained by Equation 4.1). To obtain the *Total U value* for soldiers, these values were added to the values obtained for the severity of the auditory after-effects (none = 0, slight = 1, moderate = 2, severe = 4) and the duration of symptoms (permanent = 1, temporary = 2). Table 4.5 was used to derive the NIR equivalents.

**Table 4.5 Determination of Noise Immission Rating (NIR) values for military noise exposure “Gunshot and Explosive noises”.** The table is adopted from Lutman et al. (2008), Table 7 (page 24).

NIR	Approximate total number of rounds (unprotected)		Immediate permanent after-effects (one or both ears)
	Noise types 1 – 2* combined	Noise types 3 – 6** combined	
0	0 – 10	0	None
1	11 – 100	1 – 10	None
2	101 – 1000	11 – 100	Slight
3	1001 – 10,000	101 – 1000	Moderate
4	> 10,000	> 1000	Severe

\* Noise types 1 – 2 (1 = rifles, 2 = machine guns). \*\* Noise types 3 – 6 (3 = large infantry, 4 = light artillery or anti-aircraft guns, 5 = large artillery weapons or naval guns, 6 = explosives).

#### 4.9.4. Data analysis

##### *Analysis of closed-ended questions*

The majority of questionnaire items were closed-ended questions. The answers to these questions were in a multiple choice or "Yes/No" format. Thirteen questionnaire items (*Q9, Q10, Q12, Q13, Q14, Q16 to Q23*) were in a Yes/No format, so for analysis, a number was assigned for each answer option (1 = Yes, No = 2). The answers to *Q6* were also in a Yes/No format but with three additional responses, where that the participant could choose from (sometimes, recently/inconsistently). *Q7* and *Q14* had two parts; the answers to the first part were in a Yes/No format and if the participant's answer was "Yes", then he was asked to answer the second part which is in a multiple choice format. The multiple choice questions were constructed using Likert scales. For example, the following Likert scales were used for *Q1* and *Q2* (never = 1, strongly agree = 2, agree = 3, undecided = 4, disagree = 5 and strongly disagree = 6) and *Q4, Q7, Q14* and *Q15* (never = 1, a few times = 2, several times = 3, quite often = 4, very often = 5). A similar Likert scale was used for *Q3* and *Q11*.

For *Q6, Q12, Q13* and *Q20 to Q23*, if the participant's response was "Yes", then he would be asked to provide more details about his answer (i.e. specify or describe the problem). Therefore, although these questions were closed-ended and primarily quantitative, they were analyzed as open-ended questions if the answer was "Yes". Because the closed-ended questions were scalable and their components could be transformed into numbers, they could be dealt with as quantitative data. Thus, responses to the closed-ended questions in this study were analyzed using descriptive statistics and frequency tables in IBM SPSS 21.0 software (SPSS Software, SPSS Inc., Chicago, IL, USA). Because the questionnaire was a self-reported outcome measure related to the person and not the ear, unlike the previous studies described in Chapters 2 and 3, data here were not analyzed based on number of ears; instead, they were analyzed based on participants' responses.

### ***Analysis of open-ended questions***

Two types of open-ended questions were used in the questionnaire developed in this study. The first involved the explanations provided if the answer was “Yes” to the following questions (Q6, Q12, Q13 and Q20 to Q23). It involved also questions that had limited answer options (Q5: *what are the most frequent noise sources encountered in your worksite?*). Because the answers to these questions were expected to be very brief and list-like, they were analyzed using the *Word-based Analysis Method*. The word-based method is a common analysis method used in qualitative studies, which allows all the possible answer categories to emerge based on the co-occurrence of words or terms (Ryan and Bernard, 2000). A frequency count was done for each answer category.

The other type of open-ended question was the one used in Q8 “*If you do not use HPDs, please explain why*”. Because it was anticipated that the participants would provide a longer and more detailed answer to this question, the answers to this question were analyzed using *Thematic Coding or Code-based Analysis Method*, which is another common procedure used to analyze responses to open-ended survey questions (Jackson and Trochim, 2002; Hsieh and Shannon, 2005). This method is based on the idea of reducing text data into manageable summary categories or themes, which allows inferences to be made about a sample. The thematic coding method is suitable for denser types of text, such as those derived from interviews. First, the responses to Q8 were reviewed to identify themes, then each response was assigned to one or several categories to establish major patterns and trends (i.e. coding). The text was arranged in a table created in Microsoft Word in such a way that each response was distributed under the category heading in the appropriate column. After that, the data were checked again to ensure that the categories were actually appropriate, then the responses were reviewed to see which of the categories had the most responses and therefore represented major themes. To minimize the influence of researcher's bias on the data, the identified categories and themes were reviewed and refined by a colleague experienced in qualitative data analysis. Finally, frequency counts were done to see how many responses were available in each theme. A summary of this analysis is presented later in the results section of this chapter (Table 4.9).

### ***Analysis of estimated lifetime cumulative noise exposure***

With the use of the Microsoft Excel computer program, the lifetime cumulative occupational noise exposure for 27 noise-exposed hospital technicians and the lifetime cumulative military noise exposure for two noise types: 1) rifles/machine guns 2) light artillery/explosives, for 58 soldiers were calculated using the information obtained in Appendices E and F and the calculation described in section 4.9.3. All statistical analysis were performed using the IBM SPSS 21.0 software (SPSS Software, SPSS Inc., Chicago, IL, USA).

### ***Comparison of self-reported audio-vestibular data with diagnostic test findings and estimated lifetime cumulative noise exposure data***

Pearson's Chi-square test was applied to 2 x 2 cross-tabulation matrices to examine the association between self-reported audio-vestibular data and diagnostic test results (PTA, DPOAE and cVEMP), reported in Chapter 3. The test was used to determine statistical significance for every frequency count. An alpha level of ( $p < 0.05$ ) was used to determine significance. The following self-reported audio-vestibular data: Q1 "Do you consider the noise level where you are working now to be high?", Q2 "Do you have to shout to be heard at work because of noise?", Q3 "What is the approximate number of hours you spend in this noisy worksite?", Q7 "Do you use HPD at your worksite?", Q10 "Do you expect to have a hearing loss in today's exam?" and Q13 "Do you have ringing in your ear (tinnitus)?" were compared to participants' groups according to hearing status (NIHL group, noise-exposed NH group) and also according to DPOAE status (present/normal DP group, absent/abnormal DP group).

The test was performed also to compare the answers to Q14 "Did you experience dizziness over the last 6 or 12 months?" to cVEMP outcomes (present/normal, absent/abnormal). In addition, Pearson's Chi-square test was applied to 5 x 2 cross-tabulation matrices to examine the association between self-reported *audio-vestibular data* and the calculated *NIR values* (NIR = 0, NIR = 1, NIR = 2, NIR = 3, NIR = 4). To facilitate statistical analysis, for

questions which had several answer options (*Q1, Q2, Q6* and *Q7*), their answers were transformed into “Yes/No” format. For example, the answer options of *Q7* (never, a few times, several times, quite often, very often) were transformed into “Yes/No” format. Hence, participants who reported frequent uses of HPD (quite often, often), their answers were transformed to “Yes” and the remaining answers (never, a few times, several times) were transformed to “No”. The analysis was done separately for each noise type (occupational noise for hospital technicians and military noise for soldiers: rifles/machine guns and light artillery/explosives).

### ***Comparison of estimated lifetime cumulative noise exposure data with diagnostic test findings***

Because estimated lifetime cumulative noise exposure data (NIR values) were originally derived from numerical data, which were *the Total Number of Units for Lifetime Cumulative Noise Exposure “Total U values”* for hospital technicians and the *Total Lifetime Approximate Number of Rounds* for soldiers and the diagnostic test findings obtained in Chapter 3 were numerical data as well, these data were further examined to seek evidence for any possible correlation between them. Hence, *Total U values* for hospital technicians and the *Total Lifetime Approximate Number of Rounds* for soldiers were compared to *PTA thresholds, DPOAE amplitudes* and *cVEMP response parameters (P1 absolute latency, N1 absolute latency and P1-N1 normalized amplitude)*. Since most of the data obtained in both studies were not normally distributed, Spearman’s Correlation Coefficient (*r<sub>s</sub>*) was used to test the correlation between these variables (two test variables at a time).

Because only one *Total U value* was established for each participant, which reflected noise exposure for one or both ears and the audio-saccular test results were obtained for each ear separately, the Spearman’s Correlation Coefficient test was carried out for each ear separately, using the same binaural *Total U value* for each participant. The criteria used to determine the size of correlation was similar to the one used in Chapter 3 (section 3.4.5), which is very strong correlation ( $0.9 < r_s < 1.0$ ), strong correlation ( $0.7 < r_s \leq 0.9$ ), moderate



correlation ( $0.5 < r_s \leq 0.7$ ), weak correlation ( $0.3 < r_s \leq 0.5$ ) and no to very weak correlation ( $r_s \leq 0.3$ ). Scatter plots were generated to illustrate the direction and the strength of the established relationships between Total U values, the approximate lifetime number of rounds and the other tested variables (PTA thresholds at 2 kHz, 4 kHz, 6 kHz and PTA average of those three frequencies, P1 latency, N1 latency, P1-N1 normalized amplitude, DPOAE amplitudes at 2 kHz, 4 kHz, 6 kHz and DPOAE average of those three frequencies).

#### **4.10 Results**

Out of the 109 workers recruited in this study, 24 were excluded. Half of those 24 participants did not complete all investigations due to time constraints and the other half did not satisfy one or more of the inclusion criteria set in Chapter 3 (section 3.4.1). Thus, the data remaining from 85 participants were analyzed. Twenty seven participants were technicians working at the Utility and Maintenance Department at the main National Guard Hospital in Riyadh City, Saudi Arabia and the remaining 58 workers were soldiers working at two National Guard military units. A summary of demographic data of study participants is shown in Table 4.6. Participants were exposed to a minimum of one year and a maximum of 35 years of occupational noise (mean =  $15.5 \pm 8.2$ ). The occupational environments of the personnel included power plant in 15, water treatment in 11, artillery in 41 and weapons/explosives in 17. PTA results for the 85 noise-exposed participants reported in Chapter 3 (section 3.5.1) indicated that 46 of them (54.1 %) had normal hearing (NH) sensitivity (noise-exposed NH group) at least in one ear ( $\leq 25$  dB HL) and 39 (45.9 %) had abnormal hearing sensitivity (NIHL group) at least in one ear ( $> 25$  dB HL).

**Table 4.6 Summary of demographic data for study participants.**

Variable		N = 85
Gender	Males	85
Age; mean years (SD), min-max		38.42 (9), 22 - 60
Nationality	Saudi	71
	Non-Saudi (all hospital technicians)	14
Length of occupational noise exposure; mean year (SD), min-max		15.5 (8.2), 1 – 35
Job title	Soldiers (all Saudi)	58
	Hospital technicians	27

N = number of participants, SD (standard deviation)

#### 4.10.1 Questionnaire (Section A): self-reported noise exposure history

Table 4.7 shows participants' responses to noise exposure history questions (Q1 to Q4). The majority of participants (N = 80/85, 94.1 %) reported exposure to high levels of noise in their current worksites. The response figure of Q1 was similar between soldiers and hospital technicians in that the majority of both groups agreed/strongly agreed that their worksites contained significant levels of noise. More than half of participants (N = 56/85, 65.9 %) reported frequent use (quite often, very often) of shouting at their worksites to improve oral communication (Q2). When hospital technicians' responses were compared to soldiers' responses for Q2 by Pearson's Chi-square test, a highly statistically significant differences between the two groups were noted ( $\chi^2 = 31.07, p < 0.001$ ) because a significant proportion of soldiers (N = 48/58, 82.8 %) reported frequent use of shouting compared to relatively few hospital technicians (N = 8/27, 29.6 %). When the technicians were asked to explain why they were not frequently using shouting as a strategy to overcome noise levels, they reported that they often found this strategy ineffective and use hand signing or moving away from noise source was more effective if they wanted to communicate with each other.

About 35.3 % of participants (N = 30/85) reported a history of leisure noise exposure. The reported leisure noise sources included listening to loud music through loudspeakers or headphones, hunting and motorcycling. When participants were asked about the most frequent noise sources they were exposed to at their worksite (Q5), the majority of soldiers (N = 38/58, 65.5 %) reported exposure to heavy weapons, explosions and artillery while the remainder (N = 20/58, 34.5 %) reported small arms and light weapons. Hospital technicians reported exposure mainly to water treatment machinery, such as boilers, pumps and compressors (N = 14/27, 51.9 %), the remainder reported exposure to power generators located in hospital power plants (N = 12/27, 44.4 %) and 3.7 % of them (N = 1/27) reported exposure to fire alarms.

Responses to questions about the availability and the use of HPD (Q6 and Q7) are given in Table 4.8. More than half of the participants (N = 48/85, 56.5 %) reported the provision of HPDs in their worksites (Q6). The remainder (N = 25/85, 29.4 %) reported that HPDs were not provided in their worksites and 14.1 % (N = 12/85) reported that HPDs were sometimes provided, but inconsistently or had only been provided recently. Overall, only 40 % of participants (N = 34/85) reported a frequent use (often, quite often) of HPDs at their worksites and the remainder (N = 51/85, 60 %) reported partial (a few times, several times) or no use at all (never) of HPDs (Q7). When responses to the questions related to HPDs (Q6 and Q7) were compared across the two occupational groups by means of Pearson's Chi-square test, statistically significant differences were observed between hospital technicians and soldiers (Q6:  $\chi^2 = 21.243$ ,  $p < 0.001$ ; Q7:  $\chi^2 = 10.423$ ,  $p < 0.05$ ). Results showed that hospital technicians reported higher HPDs provision in their worksites and higher HPDs usage as well.

Table 4.7 Summary of 85 participants' responses to noise exposure history questions (Section A, Q1 to Q4).

Area assessed	Question	N = 85 (%)				
		No			Yes	
Worker's noise perspectives	Q1. "Do you consider the noise level where you are working now to be high?"	Never	Disagree	Strongly disagree	Strongly agree	Agree
		1 (1.2)	4 (4.7)	0 (0)	56 (65.9)	24 (28.2)
		No			Yes	
	Q2. "Do you have to shout to be heard at work because of noise?"	Never			A few times/several times	Quite often/very often
5 (5.9)			24 (28.2)	56 (65.9)		
Estimation of noise exposure	Q3. "What is the approximate number of hours you spend in this noisy worksite?"	< 8 hrs.		≤ 8 hrs.	> 8 hrs.	
		50 (58.8)		17 (20)	18 (21.2)	
	Q4. "How often do you use the following; small arms, portable listening devices, home tools, musical instruments?"	No		Yes		
		Never		A few times/several times		Quite often/very often
		55 (64.7)		23 (27.1)	7 (8.2)	

N = number of respondents. hrs. = hours

**Table 4.8 Highly statistically significant differences between the two occupational groups; soldiers and hospital technicians in questions related to the use of hearing protection devices "HPD" (Section A, Q6 & Q7).** The numbers in cells represent frequency or counts (%).

Area assessed	Question	Participant's Response	Occupational groups N = 85		Pearson's Chi-Squared and p-value
			Soldiers N = 58 (%)	Hospital technicians N = 27 (%)	
Use of Hearing protection devices (HPDs)	Q6. "Are HPDs are provided in your workplace?"	Yes	23 (39.7)	25 (92.6)	$\chi^2 = 21.243$ $p < 0.001$
		No	23 (39.7)	2 (7.4)	
		Sometimes/ recently/ inconsistently	12 (20.6)	0 (0)	
	Q7. "How often do you use your HPDs?"	Never	16 (27.6)	2 (7.4)	$\chi^2 = 10.423$ $p < 0.05$
		A few times	21 (36.2)	7 (25.9)	
		Several times	4 (6.9)	1 (3.7)	
		Quite often	5 (8.6)	3 (11.1)	
		Very often	12 (20.7)	14 (51.9)	

N = number of participants. HPD: hearing protection devices. Proportions are calculated based on the total number of respondents in each occupational sub-group (soldiers: N = 58; hospital technicians: N = 27). Significance level:  $p < 0.05$ .

When participants were asked to indicate their experiences with HPD use (Q8, open ended question), only 42.4 % (N = 36/85) of them responded to this question. The remaining workers (N = 49/85, 57.6 %) did not answer this question because 69.4 % of them (N = 34/49) had previously reported reasonably good use of HPDs by selecting the “often” or “quite often” option to Q7. The remainder of these workers (N = 15/49, 30.6 %) did not give a clear response to this question. Some of them asked the investigator whether the answers to this question would reach their supervisors or not and because of this concern were reluctant to answer. Most of the participants who responded to Q8 were soldiers, since they were the group which reported lower availability of HPDs in their worksites and also lower frequencies of HPDs use. Thus, 36 workers' personal quotations were analyzed to identify major themes using *Thematic Coding Method* (Jackson and Trochim, 2002). Table 4.9 summarizes the main themes identified as barriers to HPDs use from the responses of these 36 workers, as well as examples of participants' quotations and the rate of response for each category. The barriers reported most frequently were: unavailability of HPDs at worksite (N = 35/36, 97.2%) followed by lack of safety, awareness and potential risks of damage from noise (N = 31/36, 86.1 %). The least reported barrier was comfort and compatibility issues (N = 20/36, 55.6 %).

**Table 4.9 Summary of the main themes identified as barriers to hearing protection devices (HPDs) use and examples of quotations obtained from 36 participants (Section A, Q8).** N = number of respondents.

Main Barriers	Barrier sub-category	Participants' quotations	N
Environmental	Unavailability of HPDs at worksite	"They were only provided at the start of employment but not afterwards" "They were only provided recently" "They do not provide them at my worksite, I buy them from the pharmacy" "They are provided only for certain employees with higher positions in my worksite" "When they wear out, I don't get a replacement for them" "I wear them only if they are provided to me"	35
	Lack of clear regulation to use hearing protection	"I see them at my worksite, but they were not given to us" "My employer does not ask me to wear them" "I have seen them in my worksite but only a few people use them" "Wearing them is optional in my worksite, it is a personal choice"	6
	Comfort and compatibility issues	"They do not sit well with my helmet" "They are heavy especially if I am wearing my helmet" "I still can hear noise very loudly even when I am wearing them" "They prevent me from hearing oral commands" "They are not comfortable" "Their quality is bad, they break very fast"	20
Individual	Lack of safety awareness and potential risks of damage from noise	"I only use them if I am close to the shooting" "I have more important safety things to care about like helmets" "Employee's safety protection is more important than noise protection" "I prefer to use tissues or my fingers to plug my ears to protect them from noise" "Sometimes, gun shooting starts and we are unaware of it"	31
	Personal issues and mistaken beliefs	"The noise does not bother me, I am accustomed to it" "We do not want soldiers to fear noise" "Why should I bother myself to wear them? I have been exposed to military noise all my life, if damage was going to occur to my ears, it would have occurred already" "I enjoy listening to high noise, it makes me feel I am in a real war"	5

#### 4.10.2 Questionnaire (Section B): self-reported auditory symptoms

Table 4.10 shows summary data and Chi-squared analysis of noise-exposed participants' responses to a range of auditory symptoms. A small number of participants (N = 27/85, 31.8 %) reported that they have had a hearing assessment done in the past. When responses to the hearing monitoring question (Q9) were compared between soldiers and hospital technicians, statistically significant differences were noted in that almost all the participants who reported having a previous hearing test were hospital technicians and the ones who reported that they had never had a hearing test were almost all soldiers. Approximately 42.4 % (N = 36/85) of participants anticipated that their hearing evaluations might reveal a hearing loss and the remainder (N = 49/85, 57.6 %) thought that their hearing was normal (Q10). Results also showed that soldiers demonstrated a significantly higher rate of expectation of hearing loss (N = 32/58, 55.2 %) compared to hospital technicians (N = 4/27, 14.8 %). Out of the 36 participants who expected to have a hearing loss, 30 (83.3 %) thought that excessive noise exposure was the cause of their hearing loss, the rest reported other causes: ear infection: (N = 1/36, 2.7 %), other reasons (N = 2/36, 5.6 %) and the remainder (N = 3/36, 8.3 %) did not really know what caused their hearing loss (Q11).

About 82.4 % (N = 70/85) of all participants reported the presence of tinnitus as a noise-associated symptom (Q13). Out of a total of 70 participants who reported tinnitus, more than half of them (N = 38/70, 54.3 %) were from the NIHL group and the rest (N = 32/70, 45.7 %) were from the noise-exposed normal hearing (NH) group. The incidence of tinnitus was higher in the participants who reported vestibular symptoms (N = 20/23, 86.9 %). Out of a total of 70 participants who reported tinnitus, 52.8 % of them (N = 37/70) described their tinnitus as "*noise-associated*", the remainder described it as "*bilateral*" (N = 21/70, 30 %) and only 17.1 % (N = 12/70) described it as "*unilateral or more on one side*". Results also showed statistically significant differences between the two occupational groups in tinnitus reporting as it was more frequently reported by soldiers (N = 52/58, 89.7 %) compared to hospital technicians (N = 18/27, 66.7 %). Describing tinnitus as "*noise-associated*" was more



frequent among soldiers (N = 37/58, 63.8 %) whereas hospital technicians described their tinnitus most frequently as "*bilateral*" (N = 13/27, 48.1 %).

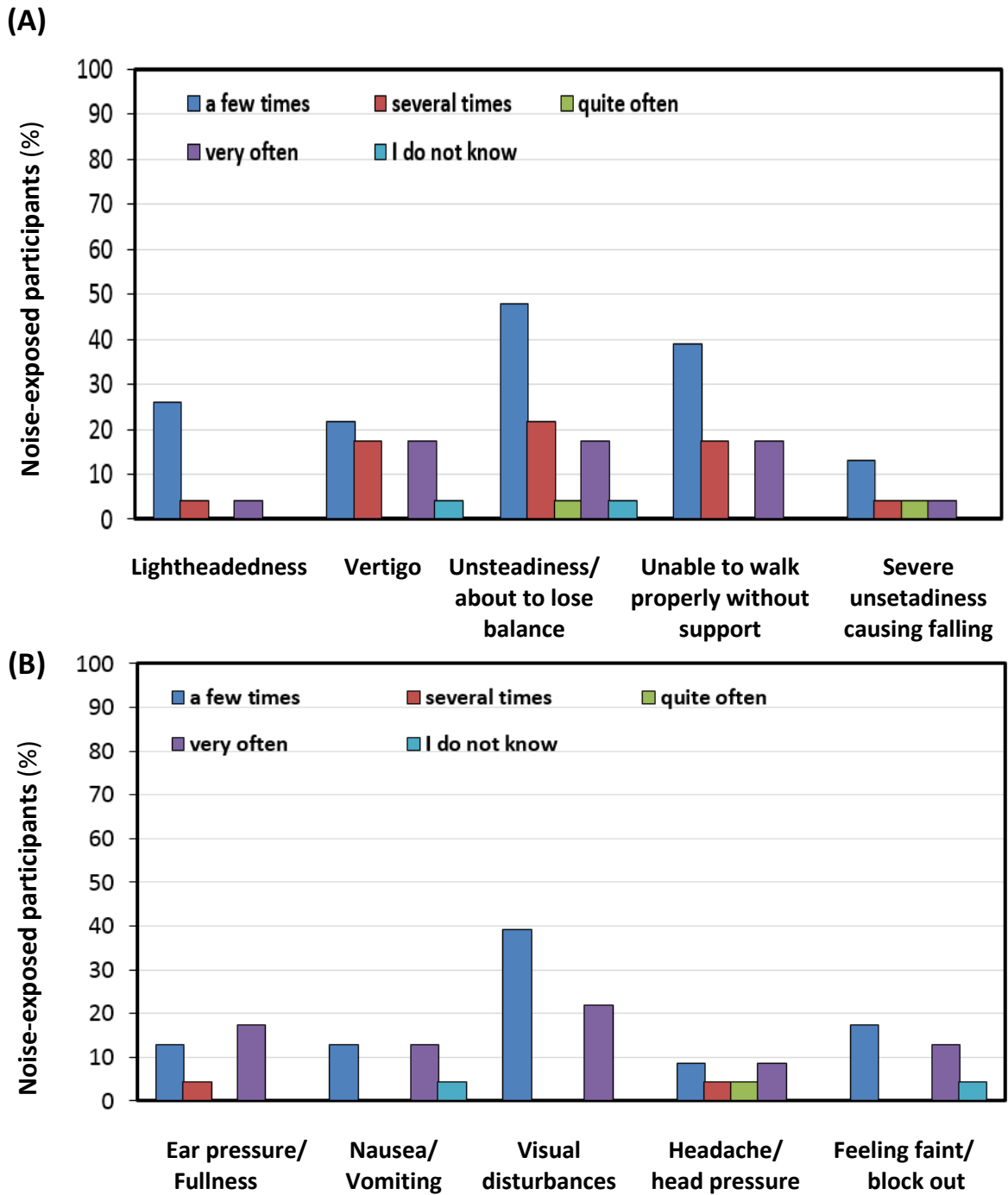
**Table 4.10 Summary of participants' responses to auditory history questions (Section B: Q9, Q10, Q12 and Q13).** Results showed statistically significant differences between the two occupational groups; soldiers and hospital technicians in all question responses except responses to Q12. The numbers in cells represent frequency or counts (%).

Area assessed and question	Participant's Response "Yes" N = 85		Pearson's Chi-Squared and p-value
	Soldiers N = 58 (%)	Hospital technicians N = 27 (%)	
<b>Hearing monitoring</b> <i>Q9. "Has your hearing been examined previously?"</i>	1 (1.7)	26 (96.3)	$\chi^2 = 76.023$ $p < 0.001$
<b>Expectation of hearing loss</b> <i>Q10. "Do you expect to have a hearing loss in today's exam?"</i>	32 (55.2)	4 (14.8)	$\chi^2 = 12.290$ $p < 0.001$
<b>Awareness of noise risks to hearing</b> <i>Q12. "Have you received any treatment/rehabilitation for your hearing loss?"</i>	1 (1.7)	0 (0)	$\chi^2 = 0.471$ $p > 0.05$
<b>Associated symptoms</b> <i>Q13. "Do you have ringing in your ear (tinnitus)?"</i>	52 (89.7)	18 (66.7)	$\chi^2 = 6.700$ $p < 0.05$

N = number of participants. Proportions are calculated based on the total number of respondents within each occupational sub-group (soldiers: N = 58; hospital technicians: N = 27). Significance level:  $p < 0.05$ .

#### 4.10.3 Questionnaire (Section C): self-reported vestibular symptoms

Figure 4.1 shows the frequency of noise-exposed participants' responses to vestibular symptoms history questions (Q14 and Q15). Vestibular symptoms rate was defined as the total number of participants who indicated the presence of vestibular symptoms (Q14: *Did you experience dizziness over the last 6 or 12 months? Yes/No*) divided by the total number of participants. Out of 85 participants, only 23 participants (N = 23/85, 27.1 %) indicated the presence of vestibular symptoms (soldiers: N = 17/85, 20 %; hospital technicians: N = 6/85, 7.1%). Pearson's Chi-Square test revealed statistically non-significant differences in frequencies of reporting vestibular symptoms among the two occupational groups ( $X^2 = 0.469$ ,  $p > 0.05$ ). Similarly, statistically non-significant differences were observed in vestibular symptoms rate between the two noise-exposed groups (noise-exposed NH group: N = 12/42, 28.5 %; NIHL group: N = 11/43, 25.6 %,  $X^2 = 0.096$ ,  $p > 0.05$ ). The most frequently reported vestibular symptom was *"unsteadiness or about to lose balance"* (N = 21/23, 91.3 %), followed by *"unable to walk properly without support/veering or staggering to one side"* (N = 17/23, 73.9 %) and then *"vertigo or spinning in the room"* (N = 13/23, 56.5 %). The least commonly reported vestibular symptoms were *"lightheadedness"* (N = 8/23, 34.8 %) and *"severe unsteadiness causing falling"* (N = 7/23, 30.4 %). When vestibular symptoms descriptions were compared across the two noise-exposed groups by Pearson's Chi-Square test, results showed statistically non-significant differences between the noise-exposed NH group and NIHL group (lightheadedness  $X^2 = 3.320$ , spinning in the room/vertigo  $X^2 = 6.254$ , unsteadiness or about to lose balance  $X^2 = 4.344$ , unable to walk properly without support  $X^2 = 5.831$ , severe unsteadiness causing falling  $X^2 = 2.636$ ,  $p > 0.05$  for all). Results also showed statistically non-significant differences in vestibular symptoms descriptions between hospital technicians and soldiers (lightheadedness  $X^2 = 1.706$ , spinning in the room/vertigo  $X^2 = 3.628$ , unsteadiness or about to lose balance  $X^2 = 7.172$ , unable to walk properly without support  $X^2 = 3.244$ , severe unsteadiness causing falling  $X^2 = 5.070$ ,  $p > 0.05$  for all).



**Figure 4.1 Summary of 23 noise-exposed participants' responses to vestibular symptoms history questions (Section C).** The bar graphs show the frequency of participants' responses (%) to vestibular symptoms description question (Q14, Panel A, top) and vestibular associated symptoms (Q15, Panel B, bottom).

The description *"unable to walk properly without support/veering or staggering to one side"* was equally reported by most noise-exposed NH group and the second most commonly reported symptom in the NIHL group and the description *"unsteadiness or about to lose balance"* continued to be the most commonly reported symptom in both groups. The least commonly reported symptoms in the noise-exposed NH group were *"severe unsteadiness causing falling"* and *"lightheadedness"* while for the NIHL group, they were *"severe unsteadiness causing falling"* and *"vertigo or spinning in the room"*. Out of 23 participants with vestibular symptoms, more than half of them (N = 14/23, 60.9 %) reported the existence of visual disturbances while they were dizzy. Workers had variable onset ranges for their vestibular symptoms, some had the first onset just a few weeks before the day of participating in the study and some had it 20 years previously. Almost all participants (N = 22/23, 95.7 %) reported that their symptoms were constant in nature, meaning that when they came they are unchanged, then they disappeared afterwards. On the other hand, only one participant (N = 1/23, 4.3 %) reported that symptoms came in attacks or episodes (Q16). For item (a) *"When did you first experience the sensation of dizziness or imbalance?"*, only a few participants could recall the start date of their vestibular symptoms. Thus, the question was excluded due to insufficient responses. Equally, only one participant reported the presence of his vestibular symptoms in attack form, so the question items regarding attacks: (b) length of the attack, (c) whether they were free of dizziness between attacks and (d) anticipation of an attack were not included in the analysis.

A summary of participants' responses to vestibular symptoms characteristic and triggers questions (Q17 to Q23) is provided in Table 4.11. Out of the 15 participants who reported their awareness of things that could stop their dizziness or make it better, only two participants (N = 2/15, 13.3 %) reported that moving away from noise would usually stop their vestibular symptoms or make them better while the majority (N = 13/15, 86.7 %) reported that if they lay down, sat down or limited motion, symptoms would usually decrease. Out of 12 participants who reported that they were aware of things that made their dizziness worse, only one participant (N = 1/12, 8.3 %) reported that prolonged exposure to noise usually increased symptoms or made them worse. The rest thought that increased body motion (N = 7/12, 58.4 %), changed head position (N = 3/12, 25 %)

and increased working hours and fatigue (N = 1/12, 8.3 %) usually provoked their vestibular symptoms. Answers to Q22 showed that the majority of participants who reported dizziness reported no exposure to irritating fumes, paints or other agents during their dizziness (N = 19/23, 82.6 %). Only four participants (N = 4/23, 17.4 %) reported exposure to irritating fumes while experiencing dizziness. Out of those 4 participants, two soldiers reported exposure to gunfire smoke (N = 2/4, 50 %), one hospital technician reported exposure to steam (N = 1/4, 25 %) and one to Chlorine (N = 1/4, 25 %). Answers to Q23 showed that out of the 20 participants who reported tinnitus, 9 participants (N = 9/20, 45 %) reported a change in their tinnitus during their dizziness attack. The changes were mainly described as an increase in tinnitus loudness (N = 3/9, 33.3 %). Some participants reported that tinnitus always accompanied their vestibular symptoms (N = 2/9, 22.2 %) and 44.4 % of them (N = 4/9) could not recall what happened to their tinnitus during their vestibular attack.

**Table 4.11 Summary of 23 participants' responses to vestibular symptoms history questions (Section C: Q17 to Q23).**

Areas assessed	Question	Yes	
		N	%
Characteristics of vestibular symptoms	<b>Q17.</b> <i>“Does change of position make your dizzy?”</i>	16	69.6
	<b>Q18.</b> <i>“Do you have trouble walking in the dark?”</i>	14	60.9
	<b>Q19.</b> <i>“ When you are dizzy, can you stand up unsupported?”</i>	18	78.3
Triggers of vestibular symptoms	<b>Q20.</b> <i>“Are you aware of anything that will stop your dizziness or make it better?”</i>	15	65.2
	<b>Q21.</b> <i>“Are you aware of anything that will make your dizziness worse?”</i>	12	52.2
	<b>Q22.</b> <i>“Were you exposed to any irritating fumes, paints, others at the onset of your dizziness?”</i>	4	17.4
	<b>Q23.</b> <i>“Does your tinnitus change with dizziness?”*</i>	9	45

N = number of respondents. Proportions are calculated based on the total number of participants who reported vestibular symptoms (total N = 23). \* The proportion was calculated based on the total number of participants who reported tinnitus (total N = 20).

#### 4.10.4 Estimation of lifetime cumulative noise exposure

Estimation of lifetime cumulative noise exposure using the *Method of Noise Immission Levels (NILs)* showed that the noise-exposed hospital technicians (N = 27) enrolled in this study had a mean total number of units for lifetime cumulative noise exposure (Total U value) of 40.9 ( $\pm$  47.4 SD) and that more than half of them (63 %) had a NIR of "1", which is equivalent to noise exposure at 81 – 90 dB(A) and about 22 % of them had a NIR of "2", which is equivalent to noise exposure at 91 – 100 dB(A). The mean approximate lifetime total number of rounds the noise-exposed soldiers (N = 58) had from rifles/machine guns was 55446.4 ( $\pm$  117586.7 SD) and 392.04 ( $\pm$  549.8 SD) from light artillery/explosives. More than half of the soldiers ( $\approx$  55 %) had a NIR of "2" from rifles/machine guns and only 27.6 % had a NIR of "4", which is equivalent to noise exposure level greater than 110 dB(A) from the same noise type. The great majority of soldiers ( $\approx$  88 %) had a NIR of "3", which is equivalent to noise exposure at 101 – 110 dB(A) from light artillery/explosives. Table 4.12 shows the frequency distribution of NIR values for both occupational groups.

**Table 4.12 Noise Immission Rating (NIR) values for 85 noise-exposed workers; 27 hospital technicians and 58 soldiers.**

Occupational group (N)		NIR values *					Total N (%)
		0	1	2	3	4	
Hospital technicians (N = 27)		4 (14.8)	17 (63)	6 (22.2)	0 (0)	0 (0)	27 (100)
Soldiers (N = 58)	Rifles/machine guns	0 (0)	8 (13.8)	32 (55.2)	2 (3.4)	16 (27.6)	58 (100)
	Light artillery/ explosives	2 (3.5)	1 (1.8)	1 (1.8)	49 (87.5)	3 (5.4)	56 ** (100)

Proportions are calculated based on the total number of respondents within each occupational group. \*NIR values are equivalent to continuous exposures 8 hours/day, 5 days/week, 48 weeks/year at the following levels throughout a full 50-year working lifetime. NIR = 0 is equivalent to continuous noise not exceeding 80 dB(A), NIR = 1 to 81 – 90 dB(A), NIR = 2 to 91 – 100 dB(A), NIR = 3 to 101 – 110 dB(A) and NIR = 4 to over 110 dB(A). \*\* Two soldiers reported no exposure to light artillery or explosives.

#### 4.10.5 The association between self-reported audio-vestibular symptoms and diagnostic test results

To determine if there is any association between the diagnostic test data reported in Chapter 3 and self-reported audio-vestibular symptoms data obtained in this study, several categorical variables were compared. The analysis included the following questions (Q1: *"Do you consider the noise level where you are working now to be high?"*, Q2: *"Do you have to shout to be heard at work because of noise?"*, Q3: *"What is the approximate number of hours you spend in this noisy worksite?"*, Q7: *"Do you use HPDs in your worksite?"*, Q10: *"Do you expect to have a hearing loss in today's exam?"*, Q13: *"Do you have ringing in your ear (tinnitus)?"* and Q14: *"Did you experience dizziness over the last 6 or 12 months?"*). Results showed statistically non-significant association between the answers of these questions and diagnostic test results reported in Chapter 3. However, some variables showed statistically significant associations. Table 4.13 shows a 2 x 2 cross tabulation matrix and associated Pearson's Chi-Squared analysis to test the association between self-reported expectation of hearing loss (Q10: *"Do you expect to have a hearing loss in today's exam?"*) and participants' groups according to hearing status (NIHL group, noise-exposed NH group). Results showed that the majority of noise-exposed participants who expected their hearing examination to reveal a hearing loss (N = 26/43, 60.5 %) were from the NIHL group.

Similarly, Table 4.14 shows a 3 x 2 (for Q3) and a 2 x 2 (for Q7) cross tabulation matrices and associated Pearson's Chi-Squared analysis to test the association between Q3 *"What is the approximate number of hours you spend in this noisy worksite?"*, Q7 *"Do you use HPD at your worksite?"* and participants' groups according to DPOAE status (present/normal DP group, absent/abnormal DP group). Results showed statistically significant association between the approximate number of hours spent in noise (Q3) and participants' groups according to DPOAE status because majority of participants who reported 8 hours (N = 15/17, 88 %) or less than 8 hours noise exposure (N = 37/50, 74 %) were from the absent/abnormal DP group. Unsurprisingly, all the participants who reported more than 8 hours noise exposure (N = 18/18, 100 %) were from the absent/abnormal DP group. Equally, results showed statistically significant association

between the use of HPDs (Q7) and participants' groups according to DPOAE status because majority of the participants who reported no use of HPDs were (N = 47/51, 92.2 %) were from the abnormal/absent DP group.

Table 4.15 shows a 2 x 2 cross tabulation matrix and associated Chi-squared analysis to test the association between the presence of vestibular symptoms (Q14: *"Did you experience dizziness over the last 6 or 12 months?"*) and cVEMPs response rate (present/normal, absent/abnormal). Results showed statistically non-significant association between those two variables because only 21.7 % (N = 5/23) of the noise-exposed participants who reported vestibular symptoms had absent/abnormal cVEMP findings. When the same comparison was repeated within each group (noise-exposed NH group and NIHL group), the association continued to be statistically non-significant. Results showed that among the 12 noise-exposed NH participants who reported vestibular symptoms, only one (N = 1/12, 8.3 %) had absent/abnormal cVEMPs and among the 11 noise-exposed participants with NIHL who reported vestibular symptoms, only four (N = 4/11, 36.4 %) had absent/abnormal cVEMPs. Because of the low established rate of vestibular symptoms among the participants who presented with absent/abnormal cVEMPs findings, the relationship between cVEMPs results and the other more specific categorical findings obtained in the vestibular symptoms history section was not further analyzed.



**Table 4.13 Highly statistically significant association between the self-reported expectation of hearing loss (Q10) and participants' groups according to hearing status reported in Chapter 3.** The numbers in cells represent frequency or counts (%).

Area assessed and question	Response	Groups according to hearing status		Total N (%)	Pearson's Chi-Squared and $p$ -value
		NIHL N (%)	Noise-exposed NH N (%)		
<b>Self-reported expectation of hearing loss</b> <i>Q10.</i> "Do you expect to have a hearing loss in today's exam?"	Yes	26 (60.5)	10 (23.8)	36 (42.4)	$\chi^2 = 11.693$ $p < 0.01$
	No	17 (39.5)	32 (76.2)	49 (57.7)	

N = number of participants. NIHL: noise-induced hearing loss. NH: normal hearing. Proportions are calculated based on the total number of respondents within each participants' sub-group (NIHL group: N = 43; noise-exposed NH group: N = 42, overall noise-exposed group: N = 85). Significance level:  $p < 0.05$ .

**Table 4.14 Statistically significant association observed between the self-reported approximate number of hours spent in noise (Q3), the self-reported use of hearing protection devices (Q7) and participants' groups according to DPOAE status reported in Chapter 3. The numbers in cells represent frequency or counts (%).**

Area assessed and question	Response	Groups according to DPOAE status		Total N (%)	Pearson's Chi-Squared and <i>p</i> -value
		Normal DP N (%)	Abnormal DP N (%)		
<b>Approximate number of hours spent in noise</b>  <i>Q3. "What is the approximate number of hours you spend in this noisy worksite?"</i>	<b>8 hr/day</b>	2 (13.3)	15 (21.4)	17 (20)	$\chi^2 = 6.662$ $p < 0.05$
	<b>&lt; 8 hr/day</b>	13 (86.7)	37 (52.9)	50 (58.8)	
	<b>&gt; 8 hr/day</b>	0 (0)	18 (25.7)	18 (21.2)	
<b>Use of hearing protection devices (HPDs)</b>  <i>Q7. "Do you use HPD at your worksite?"</i>	<b>Yes</b>	11 (73.3)	23 (32.9)	34 (40)	$\chi^2 = 8.433$ $p < 0.01$
	<b>No</b>	4 (26.7)	47 (67.1)	51 (60)	

N = number of participants, hr = hour. Normal DP group: normal/present DPOAE. Abnormal DP group: absent/abnormal DPOAE. Proportions are calculated based on the total number of respondents within each DP sub-group (Normal DP group: N = 15; abnormal DP group: N = 70, overall noise-exposed group: N = 85). Significance level:  $p < 0.05$ .

**Table 4.15** Statistically non-significant association observed between the self-reported presence of vestibular symptoms (Q14) and cVEMP response rate (present/normal, absent/abnormal) in noise-exposed NH group, NIHL group and overall noise-exposed sample (both groups). The numbers in cells represent frequency or counts (%).

Area assessed and question	Groups' responses (N)		cVEMP response rate		Total N (%)	Pearson's Chi-Squared and <i>p</i> -value
			Present/Normal N (%)	Absent/Abnormal N (%)		
<b>Self-reported presence of vestibular symptoms</b>  <i>Q14. "Did you experience dizziness over the last 6 or 12 months?"</i>	<b>Noise-exposed NH</b> (N = 42)	Yes	11 (26.2)	1 (2.4)	12 (28.6)	$\chi^2 = 2.218$  $p > 0.05$
		No	21 (50)	9 (21.4)	30 (71.4)	
	<b>NIHL</b> (N = 43)	Yes	7 (16.3)	4 (9.3)	11 (25.6)	$\chi^2 = 0.525$  $p > 0.05$
		No	24 (55.8)	8 (18.6)	32 (74.4)	
	<b>Both groups</b> (N = 85)	Yes	18 (21.2)	5 (5.9)	23 (27.1)	$\chi^2 = 0.282$  $p > 0.05$
		No	45 (52.9)	17 (20)	62 (72.9)	

N = number of participants. NIHL: noise-induced hearing loss. Noise-exposed NH (normal hearing). Proportions are calculated based on the total number of participants within each sub-group (noise-exposed NH: N = 42; NIHL: N = 43; both groups: N = 85). Significance level:  $p < 0.05$ .

#### 4.10.6 The association between self-reported audio-vestibular symptoms and estimated noise exposure data

To examine the association between *participants' estimated noise exposure data* and their *self-reported audio-vestibular data*, the questions, which may be related to noise exposure (Q1: "Do you consider the noise level where you are working now to be high?", Q2: "Do you have to shout to be heard at work because of noise?", Q3: "What is the approximate number of hours you spend in this noisy worksite?", Q6: "Are hearing protection devices (HPDs) provided at your worksite?", Q7: "Do you use HPDs in your worksite?", Q10: "Do you expect to have a hearing loss in today's exam?", Q13: "Do you have ringing in your ear (tinnitus)?" and Q14: "Did you experience dizziness over the last 6 or 12 months?") were compared to NIR values by means of Pearson Chi-Squared analysis.

Results showed statistically non-significant association between participants' NIR values and the answers of the questions listed above. However, a statistically significant association was observed between several variables. Table 4.16 shows a 2 x 5 (for Q2, Q7 and Q13) and a 3 x 5 (for Q3) cross tabulation matrices and associated Pearson's Chi-Squared analysis for the variables which showed statistically significant associations. Results showed a statistically significant association between *hospital technicians' NIR values* and Q2 "Do you have to shout to be heard at work because of noise?", *soldiers' NIR values* (both rifles/machine guns and light artillery/explosives) and Q7 "Do you use HPDs in your worksite?", *soldiers' NIR values* (rifles/machine guns) and Q3 "What is the approximate number of hours you spend in this noisy worksite?" and *soldiers' NIR values* (light artillery/explosives) and Q13 "Do you have ringing in your ear (tinnitus)?".

**Table 4.16** The association observed between self-reported audio-vestibular data (Q2, Q3, Q7 and Q13) and participants' Noise Immission Rating (NIR) values obtained for two occupational groups (hospital technicians and soldiers). The numbers in cells represent frequency or counts (%).

Occupational group (N)		Self-reported audio-vestibular data		NIR values					Pearson's Chi-Squared and <i>p</i> -value
				0	1	2	3	4	
Hospital technicians (N = 27)		Q2. "Do you have to shout to be heard at work because of noise?"	Yes	2	16	6	0	0	$X^2 = 7.346$ $p < 0.05$
			No	2	1	0	0	0	
Soldiers	Rifles/machine guns (N = 58)	Q3. "What is the approximate number of hours you spend in this noisy worksite?"	8 hr/day	0	0	10	1	2	$X^2 = 16.449$ $p < 0.05$
			< 8 hr/day	0	4	9	1	13	
			> 8 hr/day	0	4	13	0	1	
		Q7. "Do you use HPDs in your worksite?"	Yes	0	1	5	2	9	$X^2 = 14.412$ $p < 0.01$
			No	0	7	27	0	7	
	Light artillery/explosives (N = 56)*	Q7. "Do you use HPDs in your worksite?"	Yes	2	0	1	10	3	$X^2 = 17.173$ $p < 0.01$
			No	0	1	0	39	0	
		Q13. "Do you have ringing in your ear (tinnitus)?"	Yes	0	1	1	45	3	$X^2 = 18.392$ $p < 0.01$
			No	2	0	0	4	0	

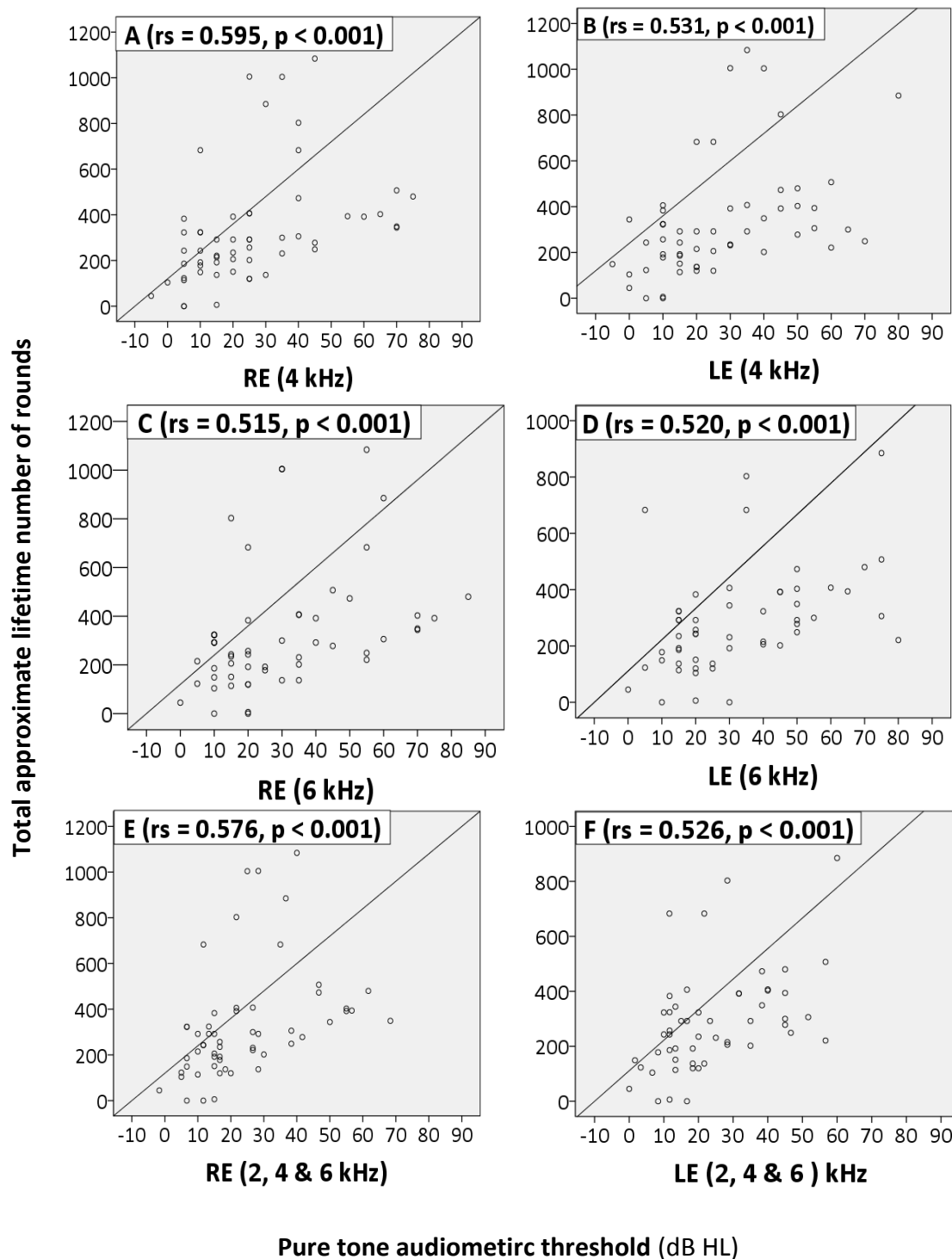
N = number of participants.\* Two soldiers reported no exposure to light artillery/explosives. NIR = 0 is equivalent to continuous noise not exceeding 80 dB (A), NIR = 1 to 81 – 90 dB(A), NIR = 2 to 91 – 100 dB(A), NIR = 3 to 101 – 110 dB(A) and NIR = 4 to over 110 dB(A). Significance level:  $p < 0.05$ .

#### 4.10.7 The relationship between estimated noise exposure data and diagnostic test results

Estimated noise exposure data were further inspected to seek evidence for a relationship between *hospital technicians' Total number of Unit for Lifetime Cumulative Noise Exposure (Total U value)* and the *diagnostic test results* obtained in Chapter 3 (PTA thresholds and DPOAE amplitude levels at 2, 4 and 6 kHz and at the average of these three frequencies, all cVEMP response parameters) by Spearman's Correlation Coefficient ( $r_s$ ). Hospital technicians' Total U value was derived from the sum of the followings: the U value obtained from Equation 4.1, the codes obtained from Part (1): the method used for noise level estimation and Part (2): the auditory after-effects, temporary/permanent and site of symptoms (see section 4.9.3). Results showed either no or weak correlation between *hospital technicians' Total U values* and all the above mentioned diagnostic test results. However, a significant positive moderate correlation was noted between *hospital technicians' Total U values* and *PTA average* (at 2, 4 and 6 kHz) only in the right ear ( $r_s = 0.524, p < 0.01$ ).

Spearman's Correlation Coefficient ( $r_s$ ) was also applied to examine the relationship between *soldiers' Total Approximate Lifetime Number of Rounds* for both noise types (rifles/machine guns, light artillery/explosives) and the *diagnostic test results* obtained in Chapter 3. To obtain the total approximate number of rounds the participant was exposed to during his lifetime, the reported number of rounds for each noise type was multiplied by the total employment period (see section 4.9.3). Results showed no correlation between *soldiers' Total Approximate Lifetime Number of Rounds* and all *cVEMP response parameters*. Results also showed either no or weak correlation between *soldiers' Total Approximate Lifetime Number of Rounds* (rifles/machine guns) and both *PTA thresholds* and *DPOAE amplitude levels*. However, a statistically significant positive correlation of moderate degree was observed between *soldiers' Total Approximate Lifetime Number of Rounds (light artillery/explosives)* and both *PTA thresholds* (at 4 and 6 kHz) and *PTA average* (at 2, 4 and 6 kHz) for both ears. Similarly, a statistically significant negative correlation of moderate degree was noted between

*soldiers' Total Approximate Lifetime Number of Rounds* (light artillery/explosives) and *DPOAE amplitude levels* (at 2, 4 and 6 kHz) only in the left ear and *DPOAE average* (at 2, 4 and 6 kHz) for both ears. Scatter plots, Spearman's correlation coefficient values ( $r_s$ ) along with  $p$ -values for the variables, which revealed moderate correlations in soldiers' data are shown in Figures 4.2 and 4.3.



**Figure 4.2** Panels A-F show scatter plots demonstrating statistically significant moderate positive correlation ( $0.5 < r_s \leq 0.7$ ) between total approximate lifetime number of rounds from light artillery/explosive noise and pure tone audiometric (PTA) thresholds for 58 noise-exposed soldiers at 4 kHz (Panels A & B), 6 kHz (Panels C & D) and PTA average at 2, 4 & 6 kHz (Panels E & F) in the right and left ears by Spearman's Correlation Coefficient test at  $p < 0.05$  significance level. RE: right ear, LE: left ear.



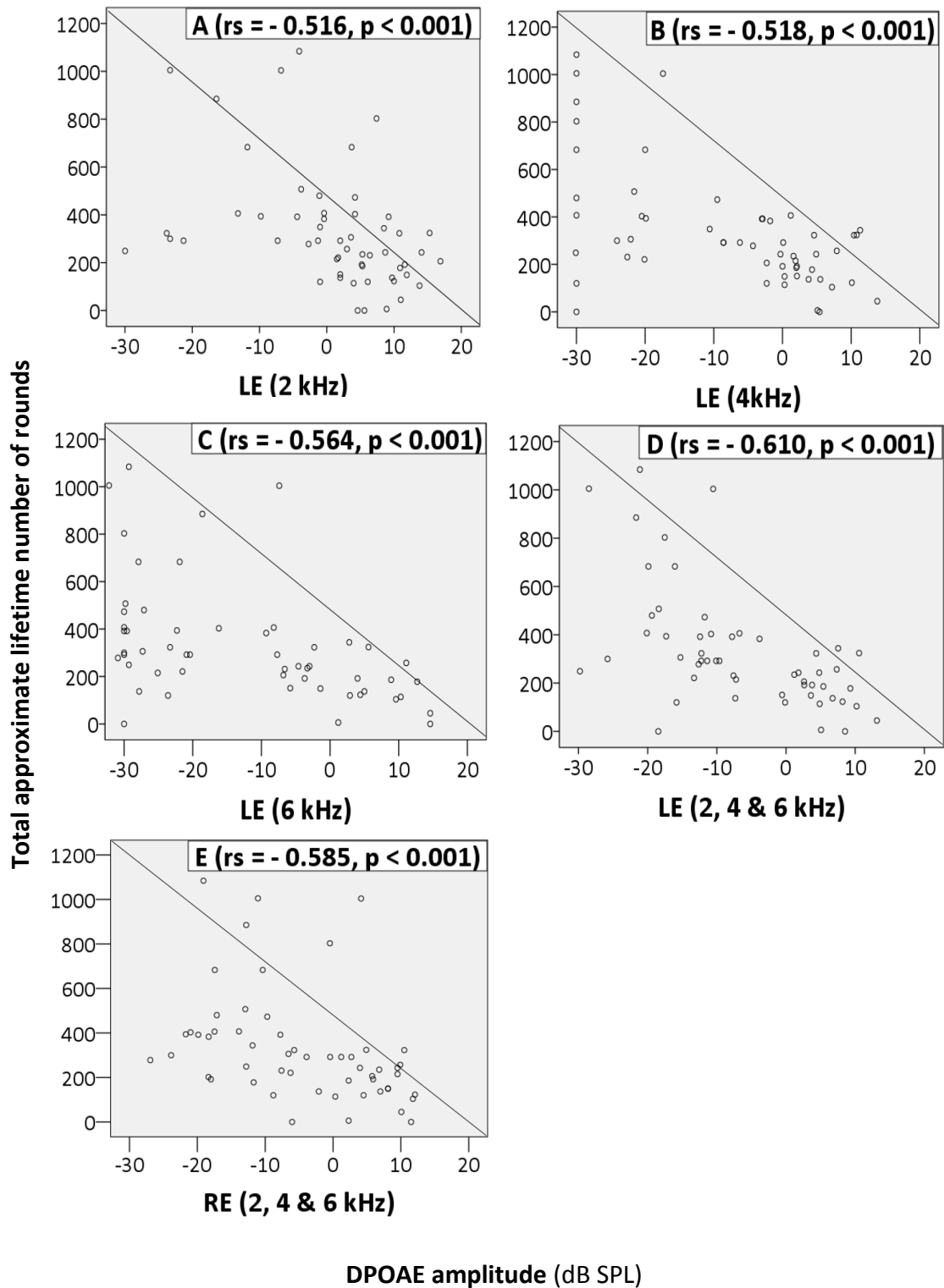


Figure 4.3 Panels A-E show scatter plots demonstrating statistically significant moderate negative correlation ( $0.5 < r_s \leq 0.7$ ) between total approximate lifetime number of rounds from light artillery/explosive noise and DPOAE amplitudes for 58 noise-exposed soldiers in the left ear at 2 kHz (Panel A), 4 kHz (Panel B), 6 kHz (Panel C) and DPOAE amplitude average (at 2, 4 & 6 kHz) in both ears (Panels D & E) demonstrated by Spearman's Correlation Coefficient test at  $p < 0.05$  significance level. RE: right ear, LE: left ear.

#### 4.11 Discussion

The study reported in this chapter examined the behavioural manifestations of vestibular damage caused by excessive noise exposure. Since audio-saccular dysfunction evident by abnormal cVEMP and NIHL has been identified in some of the noise-exposed workers investigated in Chapter 3, it was first hypothesized in this chapter that this damage would manifest itself in audio-vestibular symptoms reported by these individuals. Second, given that results from Chapter 3 suggest that saccular dysfunction is possible in noise-exposed individuals who are at risk of developing NIHL but still have normal hearing (noise-exposed NH group), it was hypothesized that these individuals might report vestibular symptoms related to noise exposure as well. Third, it was hypothesized that there would be an association between the self-reported audio-vestibular data obtained in this study and the diagnostic test data obtained in Chapter 3. Fourth, it was hypothesized that there would be an association between the self-reported audio-vestibular data and the estimated noise exposure data collected in the current study. Finally, it was hypothesized that there would be a relationship between the estimated noise exposure data and the diagnostic test data obtained in Chapter 3.

In addition, the vestibular symptoms obtained in this study were inspected to see if the reported symptoms could be distinguished from symptoms commonly reported by individuals affected by semicircular canal lesions. To examine these hypotheses, self-reported audio-vestibular symptoms data were collected from the same noise-exposed cohort investigated previously in Chapter 3 (85 workers: 58 soldiers and 27 hospital technicians). The nature and frequency of noise-induced vestibular symptoms were investigated in this study using both closed-ended and open-ended questionnaire. Additional noise exposure data were collected from all participants to estimate the lifetime cumulative noise exposure levels for each participant. The estimated noise exposure data were compared with the diagnostic test results and also with the self-reported audio-vestibular data to elucidate any relationship between estimated noise levels and these data.

#### 4.11.1 Auditory and noise exposure data reported by noise-exposed individuals

The great majority of participants' responses to the noise exposure history questions indicated that the investigated sample was probably exposed to significant noise levels (Table 4.7). The evidence came from the fact that most of these workers reported exposure to significant noise levels in their worksites and the use of strategies to facilitate communication, such as shouting and hand signing. In addition, the types of noise sources reported by soldiers (i.e. weapons, explosions, artillery, etc.) are known to generate significant impulse noise up to 150 dB sound pressure peak level or more (Ylikoski and Pääkkönen, 1986; Ylikoski et al., 1995). Hospital technicians reported exposure to industrial noise sources (i.e. water treatment machinery, power generators, etc.) which are also documented to produce significant noise levels (Eleftheriou, 2002). Thus, all the noise exposure data reported by these workers suggest that they have been exposed to significant levels of noise in their place of work.

Although all the noise exposure data obtained in this study were self-reported and no actual physical noise measurements were obtained, it is unlikely that the investigated workers under-reported or over-reported their noise exposure because most of them (N = 58/85, 68.2 %) were unaware of their hearing impairment, since they never had their hearing tested before their enrolment in this study (Q9). Most of the questions used in this investigation were closed-ended. However, the inclusion of some open-ended questions was extremely useful to understand many of participants' responses to closed-ended questions. For example, although the majority of hospital technicians reported exposure to high levels of noise in their worksites (Q1) and expressed difficulties with using oral communication in noise, only 29.6 % of them (N = 8/27) reported frequent use of shouting as a strategy to overcome noise levels, as opposed to 82.8 % (N = 48/58) of soldiers (Q2). When the technicians were asked to elaborate, they mentioned that shouting is often ineffective and instead, they prefer to do hand signing or they moved away from noise if they wanted to engage in oral communication. This suggests that extremely high noise levels existed in technicians' worksites up to the point that attempting the use of high level oral communication was unhelpful. If no clarification or explanations had been sought for the answer of this question (Q2) by the

use of open-ended questions (i.e. explain why?), there would have been a discrepancy between the technicians' answers to Q1 and Q2. Thus, the use of both closed-ended and open-ended questions helped gain a better picture of the underlying problem.

Results also showed that both soldiers and hospital technicians underestimated their hearing loss. This is consistent with previous studies, which suggested that adults tend to underestimate rather than overestimate their hearing loss (Westbrook et al., 1992; Hallberg, 1998). The reported usage rate of HPDs among the noise-exposed sample in the present study was 40 %. Interestingly, this rate was in close agreement with the rate obtained for responses of personal expectation of hearing loss (Q10) which was 42 %. This could be explained by the fact that if a person believes that he/she is vulnerable to hearing loss, he/she will be more tempted to use HPDs to preserve hearing, which is in accordance with the Health Belief Model in that perceived vulnerability is one of the factors related to taking preventive actions (Becker et al., 1977). Hence, published literature including the current study suggests that people tend to accurately predict if they have a hearing loss or not and the likelihood of accepting the use of HPDs increases if the individual is considering himself/herself vulnerable to hearing loss. In addition, the present study findings suggest that lack of availability of HPDs in the workplace and lack of safety, awareness and potential risks of damage from noise were the main reasons why the noise-exposed workers of this study were not using HPDs consistently (see Table 4.9).

Several published studies have found that self-reported noise exposure data correlate well with physical noise measurements. For example, Ahmed et al. (2004) compared self-reported noise exposure data of 259 factory workers to measured physical noise intensity levels obtained from the same worksites in Eastern Saudi Arabia and found a strong agreement between the two sets of data. A number of other investigations have shown similar findings (Ahmed et al., 2001b; Ayr et al., 2003; Gerostergiou et al., 2008). Although the present investigation did not involve direct physical noise measurements due to legislative and security restrictions in accessing National Guard worksites, the established association between self-reported noise exposure data and the physical noise measurements in the literature supports the potential of the used self-reported

data to provide accurate predication of actual noise intensity levels. Furthermore, the amount of noise exposure the participants were exposed to was estimated by calculating the lifetime cumulative noise exposure levels. The results of these calculations are discussed later in section 4.11.3. The fact that about half of the cohort included in this investigation had NIHL and the rest had hearing thresholds within normal limits supports that variability in hearing thresholds among noise-exposed groups is likely (NIOSH, 1998; Sliwinska-Kowalska and Davis, 2012). The variability could arise also from several factors. First, the noise intensity level they were exposed to might be variable. Second, the length of noise exposure (the number of years they were exposed to noise or their employment length) is another important factor to consider when looking at the effect of noise on these individuals. Among other factors to consider are the inconsistent use of HPDs by these individuals and the differences in the noise type experienced by the two occupational groups (continuous noise versus impulse/impact noise).

#### **4.11.2 Vestibular symptoms reported by noise-exposed individuals**

##### ***The Incidence of vestibular symptoms reported by noise-exposed individuals***

The findings described in this chapter suggest that vestibular symptoms might be reported by individuals with self-reported noise exposure. As previously mentioned in section 4.2, the incidence of vestibular symptoms in the general population averaged across lifespan is about 20 to 30 % (Hannaford et al., 2005; Karatas, 2008; Mendel et al., 2010). However, the reported incidence of vestibular symptoms in noise-exposed individuals with or without NIHL reported in the literature (16 to 60 %) is much more variable (Shupak et al., 1993; Golz et al., 2001; Cassandro et al., 2003; Atmaca et al., 2005; Scherer et al., 2007; Raghunath et al., 2012; Akin et al., 2012). In the present study, vestibular symptoms were reported in approximately 27 % of the overall investigated sample (noise-exposed NH group: 29 %, NIHL group: 26 %) which is in close agreement with the 24 % reported by Scherer et al. (2007) and the 35 % (only noise-exposed NH group) reported by Raghunath et al. (2012). In contrast, Akin et al. (2012) reported a higher incidence of vestibular symptoms (57 %) among 43 military personnel with a history of rifle shooting and asymmetrical NIHL. Methodological differences may

account for the observed differences between the current study and the above mentioned studies. While the majority of these studies included only cases of NIHL, only about half of the current study's sample had NIHL. The findings of normal hearing sensitivity in about half of the present study sample suggest that those individuals experienced insufficient noise exposure to cause damage to their vestibular system. Alternatively, the reported vestibular symptoms rate in the present study (27 %) might just be indicative of the general dizziness rate reported in the literature (20 to 30 %) rather than noise-induced saccular damage.

Since noise is typically diffused in the environment rather than directed more to one side than the other, as in rifle/gun shooting, the damage in the environment of noise-exposed individuals is expected to be bilateral and symmetrical and this is the typical configuration seen in cases of NIHL. According to participants' responses to Q5, the majority of the investigated noise-exposed workers in this study (76.5 %) reported exposure to noise types that lead to a fairly equal chance of developing symmetrical NIHL (i.e. for soldiers: heavy weapons, explosions and artillery; for hospital technicians: boilers, pumps, compressors and power generators). On the other hand, only a small number of workers (23 %, all soldiers) reported exposure to noise sources, which could potentially cause asymmetrical NIHL, such as rifle or small arms and light weapons. This finding is in line with their audiometric configuration, because all participants had bilateral and fairly symmetrical NIHL.

Consequently, if saccular damage had occurred in these cohorts, it would logically be expected to be bilateral and symmetrical. Published literature suggests that due to the absence of neural asymmetries, individuals who suffer from long term bilateral or symmetrical vestibular dysfunction are less likely to experience troublesome symptoms compared to those who experience acute unilateral or asymmetrical vestibular loss (Jen, 2009; Kim et al., 2011). On the other hand, if individuals have long-term asymmetric vestibular lesion, then compensation can occur, which could reduce the severity of the vestibular symptoms reported. If the likelihood of the present study's participants having bilateral or symmetrical saccular damage was high, then neural asymmetries would be absent, resulting in few or no symptoms reported by these individuals. Hence,

the existence of vestibular compensation strategies in the central nervous system of individuals suffering from NIHL along with potential absence of neural asymmetries is potentially likely and this might also explain the low incidence of vestibular symptoms obtained in this study.

### ***Characteristics of vestibular symptoms reported by noise-exposed individuals***

The noise-exposed participants of the present study mostly described their vestibular symptoms as *“unsteadiness, about to lose balance or disequilibrium”*. In contrast, several other investigations found that the most frequently reported description of vestibular symptoms in noise-exposed individuals was *“lightheadedness”* (Spitzer, 1990; Akin et al., 2012; Raghunath et al., 2012). However, Akin et al. (2012) found *“imbalance”* the second most commonly reported vestibular symptom in 43 noise-exposed military personnel and since disequilibrium is defined as unsteadiness, impaired balance or gait in the literature (Kentala and Rauch, 2003; Lee, 2012), it can be inferred that the nature of vestibular symptoms reported by the present study's participants is in broad agreement with those reported by Akin et al. (2012). Similarly, Raghunath et al. (2012) found that the symptom *“unable to stand or walk properly without support/veering or staggering to one side”* was the second most frequent description of vestibular symptoms reported by noise-exposed participants. Hence, the present study findings are in broad agreement with both Akin's and Raghunath's studies.

The least commonly reported symptoms in the current study were *“severe unsteadiness causing falling”* and *“lightheadedness”*. Reports of *“vertigo”* were noted in more than half (57.5 %) of study's participants. In contrast, *“lightheadedness”* was the most frequently reported vestibular symptom and *“vertigo”* was the least commonly reported symptom in Akin's and Raghunath's studies. Vertigo or spinning in the room is a common symptom described by patients suffering from conditions caused by vestibular pathologies located in the semicircular canals (Lee, 2012). The higher rate of vertigo reports observed in the present study compared to other studies could be explained by the possibility of involvement of semicircular canals lesion in these individuals, in addition to their noise-induced saccular lesions, which could not be ruled out since no semicircular canal testing was carried out in this study. Although the present study's

noise-exposed NH group described their symptoms in a similar way to the NIHL group, "*vertigo*" was reported far less in the NIHL group. Since noise-induced vestibular damage has been documented in the saccule, the low rate of reporting "*vertigo*" in this study and Akin's study was not unexpected because semicircular canal function has proven to be intact in individuals affected by noise exposure (Wuyts et al., 2007; Lang and McConn Walsh, 2010). The only plausible explanation for the low reported rate of "*lightheadedness*" in the present study is the variation in the terminology used by patients, so it could be that this kind of vestibular symptom description was not comprehensible to a large number of our participants.

One of the major challenges for investigators when trying to use self-report measures to evaluate balance-related symptoms is the difficulty in obtaining accurate descriptions of symptoms due to the differences in the terminology used by patients. Some terms could be confusing for patients. For example, some patients might report "*lightheadedness*" whereas someone else may report the same sensation as "*unsteadiness*", also the word "*vertigo*" may have different meanings to different individuals. Some individuals might use the term "*vertigo*" to describe "*lightheadedness*", whereas others might use it to describe a "*spinning*" sensation, which is the correct term to describe vertigo. Hence, caution should be exercised when constructing words and terms used in self-reported measures to avoid patients' confusion over terms. One of the interesting findings also in the present study was the presence of visual disturbances (i.e. oscillopsia, loss of visual acuity and blurred vision) in 61 % of participants. This could be due to altered vestibule-ocular reflex (VOR) as a result of altered vestibular (saccular) function. The VOR coordinates eye movement by rotating the eyes to compensate for the movement of the head. This results in the eyes remain still in space during head motion enabling clear vision. The VOR involves three reflex arc from the semicircular canals to the vestibular nuclei and then to the extraocular muscles causing eye motion in a direction opposite to head turning. If a lesion exists anywhere along the VOR pathway, the compensatory eye movements normally performed by the VOR during head rotation could possibly be affected (Fetter, 2007). Although saccular input contributes less to ocular movement than do semicircular canals and utricular inputs (Chan et al., 1977; Isu et al., 2000), the presence



of vertical and torsional eye movements in guinea pigs (Curthoys, 1987) and vertical eye movements in cats (Goto et al., 2004), evoked by selective, unilateral saccular nerve stimulation supports the presence of sacculo-ocular anatomical connections. Thus, the existence of visual disturbances in the noise-exposed individuals of this study suggests that perhaps not only the vestibule-collic reflex pathway is affected by noise exposure; the VOR pathway might be affected as well. Furthermore, reports of nausea and vomiting from 26 % of study participants suggest the existence of a sensory mismatch between the vestibular and the visual systems in these individuals, which probably caused a stimulation of the autonomic nervous system. Almost all participants reported that their dizziness was constant in nature, meaning that if it comes, it stays unchanged for some time then it disappears. The absence of dizziness episodes suggests a permanent vestibular pathology rather than a fluctuating one commonly seen in other peripheral vestibular lesions like benign paroxysmal positional vertigo, perilymphatic fistula and Meniere's disease.

The studies which have investigated vestibular symptoms in noise-exposed individuals (Shupak et al., 1993; Golz et al., 2001; Cassandro et al., 2003; Atmaca et al., 2005; Scherer et al., 2007; Raghunath et al., 2012; Akin et al., 2012) had several limitations. Most of these studies used routine vestibular diagnostic procedures, such as ocular-motor tests using ENG, videonystagmography or caloric testing, which are not suitable to evaluate the saccule, the most likely affected site of lesion in the vestibular system as a result of noise exposure. Unfortunately, even studies which have investigated noise-induced vestibular symptoms using both cVEMP and self-reported data (Cassandro et al., 2003; Akin et al., 2012) did not describe these symptoms in great detail. Rather, these studies only either reported the rate of the vestibular symptoms found in their sample or provided a very general description of these symptoms. The present study provides further detailed description of vestibular symptoms possibly arising from noise-induced saccular damage. Based on the findings discussed above, the present study hypothesizes “*i. The noise-exposed NIHL group will report vestibular symptoms which reflect saccular dysfunction as a result of noise exposure*” was accepted.

***Can self-reported vestibular data be used to differentiate between individuals affected by otolith lesions and semicircular canal lesions?***

As explained in the introduction of this chapter, vertigo, a spinning or rotary sensation has traditionally been accepted as the primary description of peripheral vestibular dysfunction arising from semicircular canal lesions (Lee, 2012; Roland et al., 2016). The rotary sensation experienced by these individuals has been explained by the angular position of the semicircular canals and their responsiveness to angular acceleration. Since the neurophysiology of the semicircular canals and the otolith organs is distinct in terms of each one's contribution to perceived head positions and balance tasks, it is logical to expect that lesions affecting these organs will result in different symptoms. While the saccule is able to detect linear movements in the vertical plane because it is positioned vertically, the horizontal position of the utricle allows it to detect accelerations and deceleration more in the lateral/horizontal plane. Since detecting motions in the direction of the sagittal plane is a function of the saccule, the description of symptoms as "unsteadiness", "about to lose balance", "disequilibrium", "general imbalance" and "swaying" suggests that these symptoms probably originate from the saccule. Thus, the nature of the symptoms reported in the current study (i.e. more linear and less rotary) is consistent with a lesion in the otolith organs, which is also in line with what is currently thought about the origin of noise-induced vestibular damage (i.e. saccule). The usefulness of using linear and rotary descriptions of perceived dizziness to distinguish between canal versus otolith lesions was recently demonstrated in 14 patients suffering from vestibular symptoms due to variable vestibular pathologies (Farrell and Rine, 2014).

***Vestibular symptoms reported by noise-exposed individuals with normal hearing***

Another important finding from the current investigation was that approximately half of participants who reported vestibular symptoms had normal hearing (52 %) and the other half (48 %) had NIHL. This finding is in line with our previous findings obtained in Chapter 3, in that saccular dysfunction evident by absent/abnormal cVEMPs responses was observed in noise-exposed participants with and without hearing loss. The existence

of vestibular symptoms with and without hearing loss suggests that long-term noise exposure might cause vestibular changes leading to self-reported vestibular symptoms before cochlear damage becomes evident in the audiogram, which was previously reported by [Raghunath et al. \(2012\)](#). Nonetheless, the results from Raghunath's study were confounded by the use of a small sample size (20 workers recruited from one single factory) and there was no saccular function assessment performed in this study. Hence, the findings demonstrated in the present study and in Chapter 3 provided stronger evidence of early saccular dysfunction and symptoms in noise-exposed individuals who are at risk of developing NIHL but still have normal audiograms. Hence, based on the finding discussed above, the present study hypothesis *“ii. The noise-exposed group with normal hearing (NH group) will report vestibular symptoms which reflect saccular dysfunction as a result of noise exposure”* was accepted.

#### **4.11.3 Estimation of occupational and military noise exposure in Saudi National Guard personnel**

In the present study, the lifetime cumulative noise exposure for 85 workers; 27 hospital technicians exposed to occupational noise and 58 soldiers exposed to military noise (rifles/machine guns, light artillery/explosives) was estimated. The noise exposure estimation done in this study was based on the self-reported noise exposure data obtained from a large population and has been used widely in research to calculate Noise Immission Levels (NILs) ([Lutman and Spencer, 1991](#); [Jokitulppo et al., 1997](#); [Smith et al., 2000](#); [Jokitulppo et al., 2006b](#); [Jokitulppo et al., 2008](#); [Lutman et al., 2008](#)). According to the calculated Noise Immission Rating (NIR) values obtained from the noise-exposed hospital technicians (see Table 4.12), more than half of the technicians (63 %) had a NIR of “1”, which suggests that they were exposed to occupational noise amounting to the energy equivalent of up to 81 – 90 dB(A) during a full 50-year working lifetime. Results also showed that only about a quarter of hospital technicians (22 %) had a NIR of “2”, which suggests that a small number of those technicians acquired occupational noise exposure at energy levels equivalent of up to 91 – 100 dB(A) during a full 50-year working lifetime.

While estimation of military noise exposure showed that more than half of the investigated soldiers ( $\approx 55\%$ ) had a NIR of “2” from exposure to rifles/machine guns noise, which suggests that they were exposed to noise levels equivalent of up to 91 – 100 dB(A), the majority of them ( $\approx 88\%$ ) had higher noise immission levels (NIR = 3) equivalent to 101 – 110 dB(A) from light artillery/explosive noise compared to hospital technicians (see Table 4.12). Overall, the majority of hospital technicians (85.2 %) had NILs (NIR = 0, 1 or 2) equivalent of up to 80 – 100 dB(A) or less. On the other hand, all soldiers (100 %) demonstrated NILs (NIR  $\geq 1$ ) equivalent of up to 81 – 110 dB(A) or more from exposure to rifles/machine guns and approximately all of them (96.4 %) acquired the same NIL figure from exposure to light artillery/explosives noise. As explained in Chapter 1 (section 1.7.1), most international guidelines agree upon the criterion of 85 to 90 dB(A) averaged across 8-hour workday as the maximum permissible exposure level (PEL) for noise exposure in worksites (OSHA, 1983; NIOSH, 1998; EU, 2003). Hence, the noise exposure levels of the majority of the workers investigated in this study exceeded the worldwide limit of 85 or 90 dB(A), which put these individuals at high risk of developing noise-induced damage, particularly NIHL. Under these circumstances, those personnel would normally be required to use hearing protectors in their worksite to preserve their hearing and to prevent further deterioration of hearing thresholds. Because most of the aspects of the noise exposure level calculation were reliant on self-reports of exposure based on typical or average duration of tasks, rather than minimum or maximum durations, it is unlikely that the obtained NILs resulted in under-estimation or over-estimation of noise exposure for those individuals.

The elevated NIL figure obtained for soldiers in this study indicates that soldiers had a greater noise exposure compared to hospital technicians and thus, are at higher risk of developing noise-induced damage. The findings reported in Chapter 3 showed that soldiers had greater PTA thresholds, lower DPOAE amplitude levels and longer cVEMP latencies compared to hospital technicians (see Figures 3.9, 3.10 and 3.11). Hence, the higher estimated noise exposure levels obtained for soldiers in this study explains the differences observed in diagnostic test results between the two occupational groups. It is important to mention here that this agreement suggests that the method used here in this study to estimate participants’ noise exposure was probably robust. However,

due to the variability that could take place in working schedules, particularly in such a highly diverse working environment as the military sector, it is often difficult to get very accurate information for each estimated noisy task from participants, so many of the noise exposure data obtained in this present study relied on participants' ability to recall information and thus, most of the collected noise exposure data from participants were approximate.

#### **4.11.4 Is there an association between self-reported audio-vestibular symptoms data and diagnostic test findings?**

When the results of PTA obtained in Chapter 3 and the responses to the question regarding hearing loss expectation (Q10) were considered together, the findings showed a close agreement between the two variable outcomes because 60.5 % (N = 26/43) of the participants who had been diagnosed with NIHL reported that they expected their hearing evaluation to reveal a hearing loss. Similarly, about three quarters (N = 32/42, 76.2 %) of the noise-exposed participants who had been diagnosed with normal hearing reported that they were not expecting their hearing evaluations to reveal a hearing loss (see Table 4.13). The ability of noise-exposed individuals to predict their hearing loss has been previously documented (Williams et al., 2004; Muhr and Rosenhall, 2010). Hence, the present study's participants were able to anticipate correctly both the presence and absence of hearing loss, even though the majority of them had not had any previous hearing evaluation before the study was conducted. This illustrates the value of obtaining auditory symptoms from noise exposed individuals as they might be used as good predictors of audiometric findings. Thus, the present study hypothesis "iii. (a) *If the identified audio-vestibular dysfunction can express itself as audio-vestibular manifestations, then an association would be expected between the self-reported audio-vestibular symptoms and PTA findings reported in Chapter 3*" was partially supported.

The demonstrated association between participants' DPOAE status (present/normal DP group, absent/abnormal DP group) and the approximate number of hours/day spent in noise (Q3) suggests that noise-exposed participants who reported longer duration of daily noise exposure ( $\geq 8$  hours), had more noise damage evident by their

absent/abnormal DPOAE findings. Since it is widely accepted that the daily duration of noise exposure and the level of noise are the two main factors commonly employed to determine if the individual is exposed to excessive noise exposure or not, the significant association found between the daily duration of noise exposure and DPOAE results in this study was unsurprising. Equally, the finding that the majority of noise-exposed participants who reported frequent use of HPDs (Q7) had normal cochlear function demonstrated by present/normal DPOAE findings (N = 11/15, 73.3 %) suggests that the use of hearing protection had played an important role in preventing noise-induced OHC dysfunction in those individuals (see Table 4.14). This finding supports the notion that HPDs can reduce the amount and level of noise entering the cochlea and consequently reduce hazardous noise to prevent against noise effects, such as OHC dysfunction and NIHL. Hence, the present study hypothesis "iii. (b) *If the identified audio-vestibular dysfunction can express itself as audio-vestibular manifestations, then an association would be expected between the self-reported audio-vestibular symptoms and DPOAE findings reported in Chapter 3*" was partially supported.

Comparison of cVEMP findings from Chapter 3 with self-reported vestibular symptoms (Q14) indicated a weak association between those two variables. This finding was not unexpected, since only a few participants (N = 5/23, 21.7 %) who had reported vestibular symptoms had absent/abnormal cVEMP (see Table 4.15). This could reflect the overall low rate of self-reported vestibular symptoms observed in this study (N = 23/85, 27.1 %). As explained previously, the rate of self-reported vestibular symptoms in this study might not be entirely due to saccular dysfunction, as semicircular canal lesions cannot be ruled out, especially given the presence of vertigo in 56.5 % (N = 13/23) of study participants. Hence, the present study hypothesis "iii. (c) *There will be an association between the self-reported audio-vestibular symptoms and cVEMP findings reported in Chapter 3*" was rejected. There is emerging evidence from published studies, of a relationship between self-reported data and cVEMPs findings. However, the available evidence is limited. [Akin et al. \(2012\)](#) reported that vestibular symptoms were most commonly reported in individuals suffering from asymmetric NIHL with abnormal cVEMPs. Despite the weak association observed in the present study between saccular dysfunction evident by abnormal cVEMP and vestibular symptoms, the coincidence

between those two variables was higher in the NIHL group (N = 4/43, 9.3 %) compared to the noise-exposed NH group (N = 1/42, 2.4 %). This could be due to the fact that the NIHL group might have been exposed to excessive noise sufficient to alter both their cochlear and saccular function, which consequently resulted in audio-saccular dysfunction identified by both cVEMP and self-reported data.

#### **4.11.5 Is there an association between self-reported audio-vestibular symptoms data and estimated noise exposure data?**

The findings presented in Table 4.16 indicate that the majority of hospital technicians who reported the use of shouting in their noisy worksites (N = 22/27, 81.5 %) as a strategy to improve communication (Q2) were exposed to high noise levels (NIR = 1 or 2, equivalent to 81 - 100 dBA). This finding suggests that seeking information about the speech level noise-exposed individuals tend to use while they are in noise is important and can provide accurate prediction of actual noise levels. The use of the vocal effort required to hold a conversation as a way of estimating typical noise level ranges based on the expected difficulty in communication (see Table 4.2) has been previously suggested in the literature (Smith et al., 2000; Lutman et al., 2008).

Results also showed an association between soldiers' estimated noise levels from exposure to light artillery/explosive noise and noise-related symptoms like tinnitus (Q 13) which means that the majority of soldiers (N = 50/56, 89.3 %) who reported tinnitus after exposure to this type of noise had NIR values of either "3" (equivalent to 101 - 110) or "4" (equivalent to over 110 dBA). The connection between self-reported symptoms and estimated personal noise exposure levels has been reported previously in the literature. For example, Jokitulppo et al. (2006b) showed that noise-exposed individuals who had higher personal lifetime noise levels resulting from leisure-time activities reported auditory symptoms including tinnitus, distortion and sound annoyance more often than those who had lower estimated noise levels. Similar findings were reported by the same group of authors in a subsequent study (Jokitulppo et al., 2008). The study involved the estimation of two noise types: leisure-time noise and military noise. The

study demonstrated that individuals with high lifetime cumulative noise exposure resulting from leisure-time noise had more frequent noise-related complaints, such as tinnitus, pain in the ear and temporary hearing loss. What is interesting about this study is that only estimated military noise levels resulting from exposure to explosives were found to be related to personal experiences of tinnitus, while other symptoms like sound distortion were associated more with military noise levels resulting from exposure to mortar noise. This finding is in good agreement with the present study findings, because the observed association between tinnitus reports and estimated noise levels were demonstrated for exposure to light artillery/explosive noise as well.

Further evidence for the connection between self-reported data and estimated noise exposure levels came from the association observed between the approximate duration of noise exposure (hour/day) reported by soldiers (Q3) and soldiers' estimated noise levels from exposure to rifles and machine guns. Results showed that soldiers who reported a daily exposure of 8 hours/day or more to rifles and machine gun noise had acquired a NIR of "2" or more (equivalent to 91 – 110 dB(A) or more, see Table 4.16). This association was expected because the duration of noise exposure is one of the main aspects required to conduct the noise level estimation procedure. Results also indicate that use of hearing protection devices (Q7) was related to participants' estimated noise levels. Results showed that most of the soldiers who reported no use of hearing protection devices (HPDs) during exposure to rifles and machine guns noise (N = 34/41, 82.9 %) had a NIR value of "2" or more (equivalent to 91 – 100 dB(A) or more). The association between self-reported HPD use and estimated noise levels was even greater for exposure to light artillery and explosive noise because almost all soldiers who reported no use of HPDs for this noise type (N = 39/40, 97.5 %) showed a NIR value of "3" (equivalent to 101 – 110 dB(A)). These results support the notion that the less frequently noise-exposed individuals use HPDs, the more sound energy will reach the ear and hence, the more likely those individuals are to be exposed to high noise intensity levels and consequently they are more prone to noise damage.

Hence, the present study hypothesis "iv. *If the self-reported audio-vestibular symptoms are related to noise exposure, then an association would be expected between the self-*



*reported audio-vestibular symptoms data and participants' estimated lifetime cumulative noise exposure data*'' was partially accepted. Although the data presented in the current study regarding noise exposure and audio-vestibular symptoms are self-reported and potentially prone to inaccuracy and bias like any other subjective self-reported measures, the aforementioned consistency between the two sets of data and the agreement between the present study findings and the published literature support the accuracy of these finding.

#### **4.11.6 Is there a relationship between estimated noise exposure data and diagnostic test results?**

An attempt was made in this study to investigate a possible relationship between participants' estimated noise exposure levels demonstrated by NILs for occupational noise in hospital technicians and military noise in soldiers and PTA, DPOAE and cVEMP findings obtained in Chapter 3. The numerical data revealed by the NIL calculation (*Total U values* for hospital technicians and *Approximate Total Lifetime Number of Rounds* for soldiers) were tested against *PTA thresholds, DPOAE amplitudes and cVEMP response parameters* obtained in Chapter 3 by Spearman's Correlation Coefficient (see section 4.10.7). Correlation analysis revealed no relationship between estimated lifetime cumulative noise exposure data and cVEMP response parameters in both occupational groups. Thus, the present study hypotheses "v. (c) *There will be a relationship between hospital technicians' estimated lifetime cumulative noise exposure data and cVEMP response parameters*", "vi (c) *There will be a relationship between soldiers' estimated lifetime cumulative noise exposure data (rifles/machine guns) and their cVEMP response parameters reported in Chapter 3*" and "vii. (c) *There will be a relationship between soldiers' estimated lifetime cumulative noise exposure data (light artillery/explosives) and their cVEMP response parameters reported in Chapter 3*" were rejected. The lack of a relationship between estimated noise data and cVEMP findings could be related to the low rate of cVEMP abnormality found in this study. The author is unaware of any study that has attempted to correlate cVEMP data for noise-exposed individuals to their estimated noise exposure data using the NIL method.

However, analysis of participants' Total U values, PTA thresholds and DPOAE amplitudes revealed some interesting findings. Results showed a moderate positive correlation between hospital technicians' Total U values and the PTA average of the right ear (at 2, 4 and 6 kHz). Hence, the present study hypothesis "v. (a) *There will be a relationship between hospital technicians' estimated lifetime cumulative noise exposure data and their PTA thresholds reported in Chapter 3*" was accepted. However, no correlation was found between hospital technicians' Total U values and their DPOAE amplitudes. Hence, the present study hypothesis "v. (b) *There will be a relationship between hospital technicians' estimated lifetime cumulative noise exposure data and their DPOAE amplitudes reported in Chapter 3*" was rejected. The evidence for a relationship between PTA thresholds/DPOAE amplitudes and estimated noise exposure data, was more evident in soldiers' data. Results showed a moderate positive correlation between soldiers' approximate total number of rounds (light artillery/explosives) and their PTA thresholds (see Figure 4.2). In addition, a moderate negative correlation was documented between soldiers' approximate total number of rounds (light artillery/explosives) and their DPOAE amplitudes (see Figure 4.3). Hence, the present study hypothesis "vi. *There will be a relationship between soldiers' estimated lifetime cumulative noise exposure data (rifles/machine guns) and their (a) PTA thresholds (b) DPOAE amplitudes reported in Chapter 3*" was rejected and "vii. *There will be a relationship between soldiers' estimated lifetime cumulative noise exposure data (light artillery/explosives) and their (a) PTA thresholds (b) DPOAE amplitudes reported in Chapter 3*" was accepted. Overall, these findings indicate that the higher the estimated noise levels, the smaller the DPOAE amplitudes due to OHC damage and further, the greater the PTA thresholds and likelihood of developing NIHL.

These findings are in line with the findings of other investigations. For example, [Jokitulppo et al. \(2008\)](#) found that the mean estimated noise exposure levels for 416 Finnish conscripts were 85.3 dB(A) from military noise exposure and 80.2 dB(A) from leisure-time noise exposure. The investigators also found that the hearing thresholds correlated well with their estimated noise exposure levels from pistols and machine guns. Another study attempted to compare transient evoked otoacoustic emission (TEOAE) findings of 154 participants to estimated noise levels obtained for occupational,

social and gunfire noise (Lutman et al., 2008). Although there was a tendency for TEOAE responses to be lower in the participants with higher noise exposure, the analysis revealed a lack of significant correlation between TEOAE data and participants' accumulated number of noise exposure units. Conducting an accurate comparison with the present literature in this subject area is hard to accomplish, because often there are differences between studies in-terms of the subjects being investigated, the noise sources, the calculations used to estimate noise exposure and methods of data analysis.

The statistically significant moderate correlation found in the present study, between the approximate total number of rounds the soldiers reported and their PTA and DPOAE data only for light artillery and explosive noise data, suggests that the data obtained for this noise type might have been more accurately reported by the military supervisors compared to the data obtained for rifles and machine guns. Another explanation for the lack of a relationship between rifles and machine guns data and soldiers' diagnostic findings is the fact that military training, particularly tasks involving the use of personal weapons like rifles and guns, may vary and according to the task and the distance of the individual from the noise source, the noise energy reaching the soldier's ear would be more variable compared to training with larger weapons like artillery and explosives. Hence, it might be difficult for the military personnel to provide an accurate estimation of the total number of rounds for rifles and machine guns and thus, no relationship was observed between the estimated noise levels from this noise type and PTA and DPOAE results.

#### **4.12 Conclusion**

The experimental findings reported in this chapter suggest that long-term noise exposure may lead to vestibular damage manifesting itself as vestibular symptoms. The present findings suggest that noise-exposed individuals, who may or may not have showed noise-induced saccular damage evident by cVEMP testing, are more likely to experience linear-type vestibular symptoms, such as "unsteadiness", "about to lose balance", "disequilibrium", "general imbalance" and "swaying". Since the saccule has been identified in the literature as a potential site of damage from noise exposure, the

linear-type vestibular descriptions reported in this study are consistent with the saccular dysfunction evident among these individuals. Additionally, noise-exposed individuals are less likely to experience rotary-type vestibular symptoms, such as vertigo, commonly seen in individuals affected by semicircular canal lesions. Although there is evidence for a relationship between NIHL and noise-induced saccular damage, the vestibular symptoms in this study were equally reported by individuals affected by NIHL as well as those with similar noise exposure but normal hearing. Thus, the findings reported in this chapter support the conclusion in Chapter 3 that noise-induced saccular dysfunction and vestibular symptoms, predominantly saccular in nature, could occur before hearing loss is evident on the PTA. The estimated lifetime cumulative noise exposure data and the self-reported data presented in this study suggest that individuals, particularly soldiers, were exposed to noise levels reaching or exceeding maximum allowable noise limits.

The consistency observed between questionnaire outcomes and diagnostic test results (PTA and DPOAE) supports the evidence that self-reported data can provide accurate information about the clinical picture of noise-exposed individuals. The present study could not identify a relationship between cVEMP and either self-reported data or estimated noise levels. However, a consistency has been identified between several questionnaire findings, PTA/DPOAE findings and estimated noise exposure data. Finally, the identified moderate correlation between PTA/DPOAE findings and estimated military noise exposure levels suggests the potential use of self-reported noise exposure data to identify groups at risk of noise hazards. The findings obtained in this chapter will be further discussed in relation to the other findings obtained in the previous chapters, Chapters 2 and 3, in the following chapter, Chapter 5.

## **Chapter 5**

### **Overall discussion and conclusions**

## 5.1 Introduction

The aim of this thesis was to examine the effect of noise exposure on the human vestibular system, particularly saccular function, using a variety of diagnostic test procedures and self-reported measures. The overall research question was *“Does noise exposure affect vestibular function?”*. Several hypotheses were derived to address this question and were tested by studies reported in Chapters 2, 3 and 4. This thesis reports a number of novel findings that contribute to our understanding of how noise might affect human vestibular function.

The first study in this work (Chapter 2) aimed to establish an optimal biofeedback method and cVEMP data analysis technique. The identification of these optimal methods and techniques were then used to ensure a reliable cVEMP methodology for use in the second study (Chapter 3). Chapter 2 identified that the head rotation-sitting (HR-S) as a muscle activation procedure, blood pressure manometer (BPM) as a biofeedback method and amplitude normalization as a data analysis technique, were the optimal recording process, eliciting robust and reproducible cVEMP responses in 90 healthy adults. In Chapter 3, this optimal cVEMP protocol was used to investigate the effect of noise exposure on saccular function among individuals working in noisy environments and with a self-reported history of occupational noise exposure. In addition, the work in Chapter 3 explored the possibility of saccular dysfunction in individuals affected by noise-induced hearing loss (NIHL) as well as normally hearing individuals with a similar history of noise exposure and at risk of developing NIHL. cVEMP responses were obtained from 85 participants (58 soldiers and 27 hospital technicians working for the Saudi National Guard organization) who presented with a self-reported history of occupational noise exposure, with and without NIHL. Findings suggest the existence of noise-induced audio-saccular dysfunctions in these workers evidenced by DPOAE, PTA and cVEMP measurements. cVEMP abnormality was noted in both noise-exposed workers with NIHL and noise-exposed workers with normal audiometric hearing.

The third study, reported in Chapter 4, explored the presence of vestibular symptoms, in the same noise-exposed individuals studied in Chapter 3, to gain more understanding of how noise-induced saccular dysfunction might manifest itself behaviourally. This led to a better understanding of the relationship between the self-reported data described in Chapter 4 and the diagnostic test results obtained in Chapter 3. In addition, to inform the discussion of the overall findings of Chapters 3 and 4, the lifetime cumulative noise exposure levels these individuals were exposed to in their worksites were estimated. Audio-vestibular symptoms were reported by some of these noise-exposed workers and were described in Chapter 4. The behavioural nature of the vestibular symptoms described by these individuals supports saccule dysfunction rather than utricle or semicircular canal dysfunctions. The calculated lifetime cumulative noise exposure levels suggest that the level of noise exposure those individuals were exposed to was considerably greater than the maximum values recommended by international organizations. The results and the implications of the three studies conducted in this thesis are discussed in the following sections. The limitations of each study are also highlighted at the end of each section. This chapter concludes by providing recommendations for future investigations along with recommendations for the Saudi National Guard health organization.

## **5.2 Cervical vestibular evoked myogenic potential (cVEMP): determination of an optimal biofeedback method and data analysis technique using the head rotation – sitting (HR-S) procedure**

The findings of this study were reported in Chapter 2. Although both blood pressure manometer (BPM) and electromyogenic monitoring (EMGM) methods were capable of producing clear and robust cVEMP responses in all the 90 healthy adults, the BPM method produced significantly higher non-normalized amplitudes and pre-stimulus EMG levels compared to the EMGM method. The use of the BPM method to monitor and control SCM muscle contraction variability in conjunction with the HR-sitting (HR-S) procedure produced the highest cVEMP non-normalized amplitude data and the lowest inter-aural amplitude asymmetry ratio (IAR). The BPM method was identified as the optimal biofeedback method

to control cVEMP within-subject variability (i.e. inter-aural amplitude variability) in this study and thus, this method was adopted in the second study reported in Chapter 3. On the other hand, cVEMP data produced with the use of EMGM method yielded the lowest amplitude variability between subjects, because it produced the lowest standard deviation (SD) values, so this method was better in reducing inter-subject amplitude variability. Interestingly, the statistically significant amplitude difference between the two biofeedback methods was not observed in normalized amplitude data, meaning that the amplitude normalization technique was able to remove differences in amplitude with the use of a biofeedback method. This is the first study that has investigated differences in cVEMP data obtained by two different biofeedback methods (BPM and EMGM) with and without amplitude normalization, so the current findings are novel and add new insight to current cVEMP recording protocols. These findings are in broad agreement with the recent findings of [Meyer et al. \(2015\)](#). Meyer and colleagues conducted a systematic review and meta-analysis of 66 cVEMP normative data publications and found that different methods to control EMG levels in cVEMP testing might reveal significantly different response parameters.

In the current study, the increased cVEMP amplitude observed with the use of the BPM method compared to the EMGM method could be explained by the fact that the pushing task involved in this method produces greater muscular contraction and tension in the SCM muscle. In contrast, the EMGM method involves only looking at the screen to maintain EMG levels at target levels. Although both methods were performed using the HR-S procedure, the slight difference in head positions between the two methods might also have induced differences in the tonic muscle contraction. The findings of this study also indicated that due to the ease and simplicity of the EMGM method and the reduced muscle contraction tension required, the great majority of participants preferred the use of EMGM over the BPM method. However, because cVEMP misdiagnosis (i.e. obtaining reduced cVEMP amplitude due to insufficient muscle contraction and labelling it as abnormal) is a common pitfall, the current study suggests that it is better to use the BPM method to ensure sufficient muscle contraction is applied throughout cVEMP recording. The use of the EMGM



method is a good alternative for patients who cannot tolerate great muscular tension, such as children, the elderly and patients with past history of impacting musculo-skeletal problems or injuries. It should be noted that in order to use the EMGM method, either special equipment capable of recording EMG (i.e. stand-alone EMG recording equipment) or an integrated EMG recording feature within the evoked potential system, used to record cVEMP, is required. For the BPM method, only a simple blood pressure cuff with a manometer screen, which is readily available at low cost in many clinical settings, is needed.

The present study revealed statistically non-significant differences between cVEMP non-normalized and normalized amplitudes. This finding was observed on the IAR data for both biofeedback methods. The inability of amplitude normalization to reduce inter-aural amplitude variability was previously reported in the literature (Bogle et al., 2013; McCaslin et al., 2013; Kim et al., 2013; van Tilburg et al., 2014). Some investigators explained that the imprecise non-linear relationship between cVEMP amplitude and EMG level might be the reason why correcting for baseline EMG background levels does not always stabilize cVEMP amplitude data and reduce the large observed amplitude variability (Bogle et al., 2013; Kim et al., 2013). Hence, the present thesis finding that amplitude normalization had no apparent effect on IAR data with the use of either BPM or EMGM method is consistent with the investigations discussed above. However, the findings presented in this thesis support the evidence that the use of an amplitude normalization technique could stabilize cVEMP amplitude data, particularly inter-subject amplitude variability arising from differences in muscle strength across genders. In addition, an amplitude normalization technique was found useful in-terms of reducing amplitude differences possibly arising from the use of different biofeedback methods in cVEMP testing.

The only investigations that the author is aware of which have supported the use of an amplitude normalization technique, are the ones done by Lee et al. (2008a) and Isaacson et al. (2006). In Lee's study, the effect of amplitude normalization on cVEMP responses of 22 normal subjects was examined using two testing conditions: 1) HR-supine alone (without a biofeedback method) and 2) HR-S with a BPM method. The study found that in both testing

conditions, the normalized IARs were significantly reduced compared to non-normalized IARs. Equally, the present study showed a general trend of reduction in IAR data with the use of amplitude normalization, only in the BPM method condition. The trend of slightly reduced normalized IARs has been previously reported with and without the use of biofeedback methods (Welgampola and Colebatch, 2001a; Suh et al., 2009; McCaslin et al., 2013). Interestingly, Isaacson's study (2006) found that amplitude differences between several SCM muscle activation procedures: HR-S, HE-supine and HR-supine disappeared after applying amplitude normalization. Similarly, the present study found that the amplitude differences observed with the use of different biofeedback methods disappeared after applying amplitude normalization. Based on the findings reported in Chapter 2 and the evidence derived from published literature, it seems that amplitude normalization does sometimes work well, especially if differences in muscle contraction levels across subjects were caused by gender or affected by the application of different methods (i.e. biofeedback methods) or procedures (i.e. SCM muscle activation procedures). However, the assumption that this technique can reduce cVEMP inter-aural amplitude variability and possibly result in lower IAR is not supported by the current study findings. Hence, it could be concluded that the amplitude normalization technique seems to have an impact on cVEMP inter-subject amplitude variability rather than inter-aural amplitude variability. Nevertheless, because of the complex relationship between cVEMP amplitude level and EMG levels and until we better understand the influence of muscle contraction on cVEMP amplitude (i.e. threshold and saturation levels), the interpretation of cVEMP data obtained using an amplitude normalization technique with or with or without a biofeedback method should be performed with caution.

One of the most interesting findings of this study was the gender effect shown in cVEMP amplitude measures in both biofeedback methods testing conditions. The findings reported in Chapter 2 suggest that in both biofeedback methods, males had statistically significantly higher non-normalized amplitude compared to females. The literature has provided contradictory findings with regard to cVEMP gender-related differences. The majority of studies reported no gender effect on cVEMP amplitude or threshold measures (Brantberg

and Fransson, 2001; Ochi and Ohashi, 2003; Basta et al., 2005b; Tourtillott et al., 2010; de Oliveira Barreto et al., 2011). In contrast, Lee et al. (2008b) found that females had higher cVEMP amplitudes compared to males. Some studies found that cVEMP amplitude correlated negatively with subcutaneous tissue (i.e. neck thickness) (Farina et al., 2002; Chang et al., 2007). The authors of these studies explained that the thicker the neck muscles, the smaller the cVEMP amplitude possibly due to increased distance between the surface electrodes and actual recorded EMG signals from muscles. The present study found no gender-related latency differences in cVEMP data, which agrees well with some published studies (Akin et al., 2003; Basta et al., 2005b). However, Brantberg and Fransson et al. (2001) documented shorter P1 latencies in females whereas Lee et al. (2008b) found that females had significantly longer latencies compared to males. Chang et al. (2007) found that P1 latency correlated positively with neck length in both adults and children, meaning that the longer the neck length, the more likely it is that P1 latency will be delayed. The authors of this study suggest that structural differences, such as muscle thickness, neck length and possibly head size, could potentially contribute to the cVEMP latency and amplitude differences among subjects.

The author is unaware of any published study that has looked at the influence of anatomical features like head size on cVEMP latencies and amplitudes across genders. However, the above mentioned structural differences between adults and children have been suggested as the most likely explanation for the finding of shorter P1 and N1 latencies in children compared to adults (Sheykholelami et al., 2001; Phillips and Backous, 2002; Kelsch et al., 2006; Rodriguez et al., 2018). In addition, the fact that statistically significant gender differences in the strength of head and neck muscles have been documented previously in the literature (Lee et al., 1994; Ueda et al., 2002), makes anatomical and structural differences between males and females the most plausible explanation for the cVEMP amplitude difference observed in this study. Importantly, the gender differences demonstrated in the current study were only observed in non-normalized amplitude data in both biofeedback methods testing conditions. The absence of gender-related differences in the present study's normalized amplitude data suggests that amplitude normalization

was able to factor out inter-subject amplitude variability arising from natural differences between the two genders. These results agree relatively well with the findings of [Chang et al. \(2007\)](#) reported a relationship between subcutaneous tissue and cVEMP non-normalized amplitude and this relationship was lacking in normalized amplitude data, meaning that amplitude normalization in Chang's study was able to exclude the influence of subcutaneous thickness on the recorded muscle potential.

As explained in Chapters 1 and 2, although published research indicated the need to control cVEMP amplitude variability by applying certain methods or techniques to reduce the variability, the possibility of a gender effect on cVEMP amplitude data as a function of method is unknown. Hence, the findings that different biofeedback methods applied in cVEMP recording reveal variable cVEMP amplitude levels across genders might explain some of the cVEMP amplitude variability observed among subjects (i.e. inter-subject or between subject variability). However, within-gender amplitude variability will still be observed if the other influencing factors are variable, such as the muscle contraction level, SCM muscle activation procedure and biofeedback method. Hence, based on the evidence from this study, it is recommended that each clinic uses a standard method to control SCM muscle contraction levels along with gender-specific normative data, particularly if amplitude normalization technique is not applied, and of course age-appropriate data as indicated by published data, to interpret their patients' cVEMP findings.

### **5.3 Noise-induced audio-vestibular dysfunction in Saudi National Guard personnel**

The study reported in Chapter 3 evaluated 27 hospital technicians and 58 soldiers using routine PTA, DPOAE and the newly developed saccular function test, cVEMP. The objective was to provide evidence of impaired audio-saccular function due to excessive occupational noise exposure. Data from this cohort were compared with 90 participants with normal hearing, normal saccular function and no history of either occupational or leisure noise

exposure. The noise-exposed group had outer hair cell (OHC) dysfunction, abnormal hearing thresholds consistent with NIHL as well as abnormal saccular dysfunction evident by cVEMP. The abnormal cVEMP findings demonstrated in the NIHL group in this study are consistent with the findings of a small number of studies that reported variable rates (33 to 75 %) of abnormal cVEMP in NIHL groups (Wang and Young, 2007; Wu and Young, 2009; Kumar et al., 2010; Akin et al., 2012; Tseng and Young, 2013). The use of different cVEMP protocols and methodological differences, including differences between the studied NIHL groups, are the most likely explanation for the wide range of reported cVEMP abnormality rate in NIHL cases. The majority of these studies were unfortunately of low quality, predominantly due to small sample sizes, making their findings difficult to apply to the general population. Furthermore, most of these studies used a less than optimal cVEMP protocol. In contrast, the present study used a relatively large sample size (N = 85) as well as a highly feasible effective approach to record and analyze cVEMPs as determined in Chapter 2. Other studies' methods were probably less than optimal and the reported cVEMP amplitude values and IARs in these studies may have had a high level of variability.

One of the most novel and interesting findings of this study was the existence of abnormal/absent cVEMP responses indicating a likely saccule dysfunction in normal hearing noise-exposed individuals who are at risk of developing NIHL. This suggests that noise exposure may affect saccular function in humans before cochlear damage is evident in the audiogram. Based on the general medical history obtained from these workers and the significant noise exposure history reported by them, it can be presumed that the observed abnormal cVEMP findings in this group are due to noise and not to any other factor. The self-reported audio-vestibular data along with the estimated noise exposure levels reported in the third study described in Chapter 4 also supported this conclusion. It is important to note here that this study is the first one to report saccular changes in noise-exposed individuals with normal hearing. The only study the author is aware of that has investigated vestibular disturbances in noise-exposed individuals without hearing loss was the one carried out by Raghunath et al. (2012). However, Raghunath's study investigated vestibular symptoms reported by normal hearing workers exposed to long-term occupational noise

using subjective measures (i.e. questionnaires) and no objective vestibular testing (i.e. cVEMP) was carried out in the study. Another limitation of this study was the limited size of the investigated sample (N = 20). The present study findings have an important clinical implication in that clinicians should be aware that vestibular pathology, particularly saccular dysfunction, can occur in individuals presenting with a history of noise exposure prior to any audiometric hearing loss. When interpreting cVEMP responses for noise-exposed individuals with normal hearing, similar to noise-exposed individuals with NIHL, clinicians should not only look at cVEMP presence/absence, but should also examine the response parameters by comparing them to age and gender appropriate cVEMP norms to determine whether they are normal or not.

Given that DPOAE has been identified as a more sensitive measure to noise damage than PTA (Desai et al., 1999; Seixas et al., 2005; Atcharyasathian et al., 2008; Baradarnfar et al., 2012), comparing the noise-exposed cVEMP data with DPOAE results revealed some interesting findings. The finding of absent/abnormal DPOAE findings in about 73 % of the overall noise-exposed sample and in 80 % of the total 10 ears identified with absent cVEMP responses indicates a high consistency between DPOAE and cVEMP findings. Despite the low correlation found between cVEMP response parameters and DPOAE amplitudes and the findings of normal DPOAE in some ears with absent/abnormal cVEMP, the likelihood of developing absent cVEMP was higher in cases with abnormal DPOAE results. Although correlational analysis suggests no relationship between DPOAE amplitudes or PTA thresholds and cVEMP amplitudes, DPOAE amplitudes and cVEMP amplitude showed higher correlational values compared to those obtained for PTA thresholds and cVEMP amplitudes. These findings may suggest that noise-exposed individuals with reduced OHC function evident by DPOAE, with or without NIHL, are more likely to develop saccular dysfunction compared to those who have similar noise exposure but still have normal DPOAE. Hence, it could be inferred that saccular dysfunction evident by cVEMP may be associated with OHC dysfunction defined by DPOAE more than hearing loss defined by PTA. The investigation described in Chapter 3 is the first study to apply PTA, DPOAE and cVEMP, to evaluate audio-saccular dysfunction in noise-exposed individuals.

Although VEMP and OAE are two totally different test procedures, the identified relationship between cVEMP and DPOAE was not unexpected. The close proximity of the origins of these two test procedures (i.e. cVEMP originates from the saccule and OAE originates from the OHCs in the cochlea) and the similarity between the anatomy and physiology of the sensory receptors, the hair cells, from which the responses of these assessment tools originate, explains why their results might give a better indication of hair cell dysfunction due to noise exposure compared to routine audiometric testing. Hence, the findings of this study suggest that combining cVEMP data with DPOAE data might facilitate the detection of early noise-induced saccular damage as opposed to the common clinical practice of combining cVEMP with PTA findings. If the patient presents with a long-term history of noise exposure, reduced or absent OHCs function evident by OAEs, with or without NIHL, this should alert clinicians to look for the possibility of saccular involvement.

The statistically significant differences in PTA and DPOAE findings between the two occupational groups suggest that OHC dysfunction and NIHL were more evident among soldiers compared to hospital technicians. Furthermore, the finding that the cVEMP absence rate was higher among soldiers (8 %) compared to that observed among hospital technicians (4%) indicates that the saccular function of soldiers may be more affected compared to that of the hospital technicians. As explained in Chapter 3, the observed differences in the findings (DPOAE, PTA and cVEMP) of these occupational groups could be explained by the natural differences between the two professions' noise exposure environments. The information gathered in Chapter 4 helped to understand the origins of these differences. The author of this thesis is unaware of any previous published study indicating possible differences in saccular, or even cochlear function between military and technical personnel. Thus, these findings are novel and important as they indicate that different noise-exposed groups, depending on the characteristics of their noise exposure environments, might present with different profiles of audio-saccular dysfunction. This finding also provides additional support for the suggestion that differences in the investigated groups among studies might have played an important role in the differences of cVEMP results reported in the literature. Because the noise exposure data of the

investigated groups in this research were all based on self-reported data and no actual physical noise measurements were performed, the possible effects of variable frequency and spectral characteristics of noise on the obtained audio-saccular findings could not be assessed or discounted.

Conducting physical noise measurements is extremely useful to identify the groups and the worksites with the most significant noise exposure. According to international standards, if workers are exposed to noise at intensity levels equal to or greater than 85 dB(A) for an average working day of 8 hours, then a hearing conservation programme in the worksite becomes mandatory (NIOSH, 1998; EU, 2003). Unfortunately, direct noise measurements could not be done in this study due to safety and security restrictions in accessing the Saudi National Guard worksites. The inclusion of physical noise measurements would have given the current findings more weight and would also have allowed an evaluation of the effect of different noise exposure aspects on cVEMP findings. As an alternative, detailed self-reported noise exposure data were collected and participants' lifetime cumulative noise exposure levels were calculated in the third study described in Chapter 4.

#### **5.4 Audio-vestibular symptoms and noise-exposure data reported by noise-exposed individuals**

The study reported in Chapter 4 revealed vestibular symptoms in 27 % of noise-exposed participants (those with NIHL and normal hearing). Published literature has reported a wide range for the rate of vestibular symptoms in noise-exposed individuals (16 to 60 %), with or without hearing loss (Shupak et al., 1993; Golz et al., 2001; Cassandro et al., 2003; Atmaca et al., 2005; Scherer et al., 2007; Akin et al., 2012; Raghunath et al., 2012). The great majority of this study's participants (76.5 %) reported exposure to noise sources which are more likely to cause bilateral rather than unilateral damage and this was evident in their audiograms as all of them had bilateral, primarily symmetrical NIHL. The low incidence of vestibular symptoms reported in this study might be explained by the absence of neural asymmetries.



When the characteristics of noise-induced vestibular symptoms were explored in the questionnaire, some interesting findings were revealed. The most frequent symptom reported by the present study's participants was *"unsteadiness or about to lose balance"* (91 %). On the contrary, some authors found that *"light-headedness"* was the most frequently reported vestibular symptom by their noise-exposed participants (Spitzer, 1990; Akin et al., 2012; Raghunath et al., 2012). Akin's and Raghunath's studies found that *"imbalance"* and *"unable to stand or walk properly without support/veering or staggering to one side"* were the second most reported vestibular symptoms. Thus, the findings of the present study are in broad agreement with those two studies. Furthermore, Akin's and Raghunath's studies found that *"vertigo"* was the least common reported symptom. Given that vertigo is a common symptom reported by patients with semicircular canal lesions (Lee, 2012), the low incidence of vertigo in these studies is not unexpected and is consistent with the findings of normal horizontal semicircular canal function in noise-exposed individuals (Perez et al., 2002). However, 57 % of the current study's participants reported symptoms of vertigo. One explanation is the possibility of our participants having additional undiagnosed semicircular canal lesions. The existence of canal lesions in those participants could not be ruled out unless a canal function test, such as caloric testing was performed. Unfortunately, the setup for performing caloric testing was not available in the clinic where data collection of this study took place; therefore, it was not part of the assessment procedures included in this study. The inclusion of tests like Calorics would have been useful to identify any possible horizontal canal pathology and could possibly have provided a clearer explanation of the vertigo symptoms reports in this study. Alternatively, it is likely also that a lack of a rigorous definition of the term *"vertigo"* caused the participants to confuse this term with the term *"unsteadiness"*.

The use of self-reported measures to evaluate balance-related symptoms is often challenging because of the different terms used by patients to describe symptoms. Therefore, to avoid patients' confusion over terms, clinicians should be careful in the choice of words and terms used in these measures. Translation of questionnaire items from one language to another is also another important issue to consider, so an influence of

questions' translation from English to Arabic cannot be ruled out in this study. One of the major challenges in conducting such research is the lack of robust or validated tools to evaluate vestibular dysfunction caused by noise exposure. Because of the nature of this kind of research, the assessment tool used has to be linguistically appropriate. Although there have been attempts by some investigators to adapt some existing standardized self-reported vestibular tools like the *Dizziness Handicap Inventory (DHI)* for the Arabic speaking population (Alsanosi, 2012), the author is unaware of any published questionnaire designed to evaluate noise-related vestibular symptoms in Arabic speaking population. Similarly, the author is not aware of any published questionnaire in English, specifically developed to evaluate noise-induced vestibular symptoms. Therefore, the questionnaire developed in the current investigation should open the door for other researchers to design both linguistically and culturally appropriate subjective tools to evaluate noise-induced audio-vestibular symptoms.

The studies which have investigated vestibular symptoms in noise-exposed individuals are very limited and were confounded by lack of detailed description of these symptoms. Most of the existing studies either only evaluated saccular function in the case of NIHL by cVEMP or only investigated vestibular symptoms in noise. The only studies the author is aware of that have investigated saccular function using cVEMP and obtained vestibular symptoms as well, in one single study are those carried out by [Cassandro et al. \(2003\)](#) and [Akin et al. \(2012\)](#). Nonetheless, even those two studies did not describe noise-induced vestibular symptoms in any great detail. Rather, they only either reported the rate of the vestibular symptoms found in their noise-exposed sample or simply provided a very general description of these symptoms. Hence, the findings obtained in Chapters 3 and 4 would help to better define saccular symptoms resulting from noise damage. In Chapter 4 (section 4.11.2), the question, "*Can self-reported vestibular data be used to differentiate between individuals affected by otolith lesions and semicircular canal lesions?*" was posed. The findings reported in this study that individuals with noise-induced saccular pathology are likely to report symptoms which are less rotary (e.g. spinning, vertigo) and more linear in nature (e.g. swaying and general imbalance) are supported by the evidence available from

other published data (Farrell and Rine, 2014). In this study, the usefulness of using linear and rotary descriptions of perceived dizziness to distinguish between canal and otolith lesions was demonstrated in 14 patients suffering from vestibular symptoms due to a variety of vestibular pathologies. The linear-type symptoms commonly reported by individuals affected by noise-induced saccular pathology reflect the function of the otolith organs, particularly the saccule, rather than the semicircular canals, which is in line with what is currently thought about the origin of noise-induced vestibular damage (i.e. the saccule).

The noise-induced vestibular symptoms reported in Chapter 4, which seem primarily saccular in nature, were observed equally in noise-exposed individuals affected by NIHL and those who had a similar history of noise exposure but normal hearing. Based on the abnormal cVEMP data reported in Chapter 3 and the self-reported symptoms reported in Chapter 4, both noise-exposed cohorts showed evidence of noise-induced saccular dysfunction and symptoms. These findings support indications in published data that saccular damage is likely to occur in individuals affected by NIHL, and also indicates that noise-induced saccular damage and symptoms could occur before hearing loss becomes evident in the audiogram. Although vestibular symptoms in noise-exposed individuals with normal hearing have been documented only by one study (Raghunath et al., 2012), the study had a small number of subjects (20 factory workers) and involved no saccular function testing. Thus, the present study findings are novel as they provide stronger evidence of saccular dysfunction and symptoms in a broader cohort of noise-exposed individuals at risk of developing NIHL but showing no audiometric hearing loss. This finding advances our current knowledge on the adverse effects of noise exposure on the human vestibular system and alerts clinicians to the possibility of noise-exposed patients developing saccular damage without evidence of NIHL.

In addition, the self-reported noise exposure data collected in Chapter 4 demonstrated the value of obtaining self-reported noise exposure data in identifying workers at risk of occupational noise exposure, which has been reported previously by several studies

(Scherer et al., 2007; Hong et al., 2008a; Hoffer et al., 2010). Calculation of Noise Immission Levels (NILs) for 27 noise-exposed hospital technicians showed that the majority of those technicians ( $\approx 85\%$ ) acquired a NIR of "1" or more, which is equivalent to noise levels of at least 81 – 100 dB(A). Similar findings were observed in 58 noise-exposed soldiers. However, the NIL figure was higher in soldiers because all soldiers (100 %) had a NIR of "1" or more. Overall, these findings indicate that the noise exposure levels for the participants of this study were high and greater than the guideline values set by international organizations (OSHA, 1983; NIOSH, 1998; EU, 2003). The higher NIR values for soldiers compared to those obtained for hospital technicians suggest that the Saudi National Guard military personnel are at higher risk of developing noise-induced damage compared to other occupational groups like technicians. These results were not surprising, because worldwide, military personnel are well-known to be exposed to both, continuous and impulse noises (Durch et al., 2005; Humes et al., 2006; Saunders and Griest, 2009; Yong and Wang, 2015). Although the time of exposure to military noise is short, the noise sources involved in military training are documented to be powerful. These findings are in agreement with the literature in that military service and armed forces are identified among the top occupational categories, which involve a high risk of noise exposure (NIOSH, 1998; Paoli and Merllié, 2001). The unprotected exposure, lack of enforcement of wearing hearing protection devices and the low awareness of the risks of excessive noise exposure are the most plausible explanations for why soldiers were identified as having more detrimental effects of noise exposure in this thesis. This explanation is supported by the self-reported data obtained in Chapter 4 (see Table 4.9).

The findings reported in Chapter 4 showed that several participants' questionnaire answers were significantly associated with the diagnostic test results (PTA/DPOAE status) obtained in Chapter 3 (see sections 4.10.5 and 4.11.4). For example, the significant association observed between the self-reported approximate number of hours spent in noise (Q3), the HPD use (Q7) and DPOAE outcomes (present normal DP, absent/abnormal DP) agrees with the notion that the duration of noise exposure and the use of HPDs are both significant factors in the development of reduced cochlear function among noise-exposed individuals.

In addition, the findings in Chapter 4 showed that participants' estimated noise exposure data (NIR values) were significantly associated with several self-reported data (see sections 4.10.6 and 4.11.5), such as the level of vocal efforts (*Q2*), the approximate number of hours spent in noise (*Q3*), HPDs use (*Q7*) and tinnitus (*Q13*). These associations suggest that noise-exposed individuals who are exposed to potentially damaging noise would exhibit the following behaviours and symptoms: the tendency to raise the voice or shout to improve oral communication, a higher number of reported hours spent in noise, less frequent reported HPD use and higher complaints of tinnitus, compared to those who do not. The correlational analysis reported in Chapter 4 provides further evidence for the link between self-reported data and diagnostic test results (see sections 4.10.7 and 4.11.6). The positive correlations observed between hospital technicians' estimated noise exposure levels (the total number of units for lifetime cumulative noise exposure "Total U values") and PTA thresholds and between soldiers' estimated noise exposure levels (the approximate total number of rounds) and PTA thresholds/DPOAE amplitudes support the well-established finding of reduced hearing levels and OHC function in individuals with high noise exposure. These findings agree well with the findings of some investigations, which have demonstrated a consistency between self-reported audio-vestibular symptoms data and estimated noise exposure levels (Jokitulppo et al., 2006b; Jokitulppo et al., 2008).

The link identified between the three sets of data obtained in this thesis: the questionnaire results, the estimated noise exposure levels and PTA/DPOAE findings suggests that the individuals studied in this thesis had excessive noise exposure, which was enough to alter their auditory system and result in behavioural manifestations. Despite the subjective nature of the data collected in Chapter 4, the relationship demonstrated among these data suggests that self-reported measures are accurate and can be reliably applied to study noise-exposed individuals. Although both the questionnaire data and the other self-reported noise exposure data collected for the purpose of NIR calculation (duration of exposure: hour/day, days/week, weeks/year, total number of rounds for each military noise type) describe well the noise exposure characteristics of those workers, it should be noted that the present study did not obtain a full picture of those individual's noise exposure

history. For example, it was brought to the author's attention that there may be some seasonal occasions, which require the workers to be involved in certain extra activities (e.g. military training and military shows for soldiers and special industrial projects for technicians). These activities were not included in the noise exposure estimation because it was hard for participants to provide accurate details of these activities. Similarly, no detailed information was gathered on participants' leisure-time noise exposure and therefore this was not included in the calculation.

The fact that in most occupational settings, particularly in the military, the noise levels may vary during the workday according to the task and the distance of the worker from the noise source makes obtaining an accurate estimation of noise levels challenging. Hence, any self-reported noise exposure information obtained from noise-exposed individuals is approximate. However, because the noise exposure estimation conducted in this study was based on the typical duration of tasks, not a maximum, and due to the identified relationship between the diagnostic test data obtained in Chapter 3 (PTA, DPOAEs) and the calculated lifetime cumulative noise exposure levels obtained in Chapter 4, it seems unlikely that those workers significantly under-reported or over-reported their noise exposure. In brief, it could be concluded that the majority of the investigated workers in this thesis had been exposed to significant occupational noise hazards. The cumulative effect of noise during the occupational service of those personnel opens a question about the progression of noise-induced audio-vestibular damage in these individuals. The methodology used in Chapter 4 provides a good example of alternative methods for estimating lifetime cumulative noise exposure levels in occupational and military settings.

## 5.5 Recommendations

### 5.5.1 Recommendations for future experimental work

#### *cVEMP future research*

As noted earlier at the start of this chapter (section 5.2), the study described in Chapter 2 is the first study to compare cVEMP findings obtained by two biofeedback methods (BPM, EMGM) and one data analysis technique (amplitude normalization) all in one single study. Based on the findings reported in this thesis and the evidence available from published literature, the application of these biofeedback methods ensures that enough muscle contraction is taking place, which is an essential step clinicians should ensure they accomplish while recording cVEMP. However, to increase the reliability of using the amplitude response in cVEMP interpretation, the variability of this response measure has to be minimized. The current state of the available data analysis technique (i.e. amplitude normalization) seems to provide some control of cVEMP amplitude variability (inter-subject amplitude variability). Nevertheless, amplitude normalization has little influence on cVEMP inter-aural amplitude variability, which is an important aspect of diagnosis to determine the side affected with vestibular dysfunction. The inability of this data analysis technique to provide full control of cVEMP amplitude variability may largely be caused by the complex relationship between SCM muscle contraction level and the resulting surface EMG level, as well as between EMG amplitude and cVEMP amplitude reported in the literature. Hence, future research should be directed towards conducting further examination of the relationship between cVEMP amplitude, SCM muscle contraction level and surface EMG activity. For example, instead of the common practice of increasing the level of muscle contraction to obtain a robust cVEMP waveform for all subjects, which has been found to reduce the signal to noise ratio (SNR) and increase amplitude variability, researchers should look at the possibility of determining the minimum required muscle contraction level for each subject according to individual's cVEMP threshold and amplitude/EMG growth

function and then possibly integrate this information into the amplitude normalization technique before conducting cVEMP.

Because of the cVEMP gender effect reported in Chapter 2, it is recommended that every clinic develop its own gender-specific biofeedback normative data. Alternatively, the use of amplitude normalization may assist in providing a more stabilized inter-subject amplitude data if gender-specific comparative data is not available. Future advances in cVEMP technology might yield new biofeedback methods to control muscle contraction variability. Hence, the effect of gender should be tested whenever a new method/technique is being developed. It would be also worthwhile investigating whether there will be any difference in cVEMP amplitudes and pre-stimulus EMG levels with and without the use of visual biofeedback methods using the same cVEMP protocol used in Chapter 2. This question can be answered by adding an additional third testing condition (i.e. control condition), where we only apply HR-S procedure to activate the sternocleidomastoid muscle in cVEMP testing without the inclusion of a biofeedback method. The addition of this control condition would allow comparison of cVEMP response parameters with and without the use of biofeedback methods so it will help us to better evaluate the usefulness of applying these methods in cVEMP testing. Unfortunately, a control condition was infeasible to include in this study, because of the time constraints of the participants' data collection session. Moreover, this was not one of the questions the present author attempted to answer at the beginning of this study. cVEMP only evaluates the saccule and inferior vestibular nerve. Thus, the findings of cVEMP should be viewed in conjunction with a battery of other vestibular tests, to gain a full picture of the overall vestibular function of these individuals.

### ***Early detection of noise-induced saccular dysfunction***

As explained earlier, the present thesis reports the first research to document both saccular damage and saccular symptoms, in noise-exposed individuals with normal hearing. Further investigations of these groups will help to clarify the nature and characteristics of cVEMP abnormality in this group. For example, it is currently unknown if these individuals have



different cVEMP thresholds compared to controls or noise-exposed individuals with NIHL. Thus, noise-induced saccular damage in noise-exposed individuals without NIHL is a new area of research that requires further exploration. Because of the demonstrated relationship between cVEMP and DPOAE findings in Chapter 3, it would be useful to consider OAE findings while interpreting cVEMP findings in noise-exposed individuals. This could be done by performing OAE assessment prior to cVEMP testing for individuals suspected to have noise-induced saccular dysfunction.

### ***Evaluation of noise-exposed individuals using self-reported data***

Conducting physical noise level measurements using common methods like dosimetry would allow a direct comparison with estimated noise levels, such as those calculated in conducted in this thesis. If the comparison showed that differences between methods were not extremely large, this would demonstrate that the use of self-reported noise exposure information to estimate noise levels is appropriate and should be applied whenever direct noise measurement is not feasible. [Lutman et al. \(2008\)](#) compared noise dosimetry data with estimates of noise exposure and found that the differences between them were within 3 dB in 43 % and 6 dB in 84 % of their studied cases. Although the importance of obtaining case history information and self-reported data in patients' diagnostic process has been well recognized in many medical conditions including management of patients suffering from dizziness, a reliable comprehensive questionnaire targeting noise-induced vestibular dysfunction has not yet been developed.

The questionnaire developed in Chapter 4 opens the door for other investigators to develop a comprehensive subjective noise-induced vestibular dysfunction tool, currently unavailable. This questionnaire is a preliminary work that should undergo further evaluations in terms of checking its reliability, validity and suitability to use with both Arabic and English speakers before it becomes ready for clinical use. Further work also has to be done to examine the sensitivity and the specificity of this questionnaire to detect audio-saccular dysfunction in noise-exposed individuals. When developing such tools, the nature

of utricle and saccule-related symptoms ought to be characterized, to differentiate them from semicircular canal-related symptoms. Finally, further study of more groups in the Saudi National Guard organization at similar facilities with potential noise exposure is highly recommended. Such research will help to identify more workers at high risk of noise hazards and will assist in the development of noise control programmes where needed in worksites.

### **5.5.2 Recommendations for Saudi National Guard Organization**

- i. The present thesis clearly indicates that military personnel and hospital technicians working at the Saudi National Guard facilities in Riyadh have a high prevalence of OHC dysfunction (72 %) and NIHL (46 %) which suggests that these workers are exposed to significant noise hazards. Findings also showed a higher prevalence of OHC dysfunction (77 %) and NIHL (54 %) in soldiers compared to hospital technicians (54 %, 28 %), which indicates that soldiers had more significant noise exposure, probably caused by the presence of extremely high noise intensity levels in military sectors (i.e. weapon fire, explosives) and minimal use of hearing protection in this group. The impact that these levels of noise exposure are having on those workers' health, communication abilities, work performance and quality of life as well as the economic impact in terms of reduced workers' productivity should be considered.
- ii. Other adverse noise affects have been identified among the Saudi National Guard personnel, such as balance disturbances resulting from reduced saccular function. The existence of such pathology in these workers makes them at high risk of injury from falling which could have significant impact on their work safety.
- iii. A hearing conservation programme should be implemented at the Saudi National Guard military services as well as at the Utility and Maintenance Department at King Abdulaziz Medical City (National Guard hospital in Riyadh). The programme should be compatible with the worldwide established international noise exposure guidelines and regulations and should include physical noise measurements to identify areas of high risk of noise

exposure, audio-vestibular baseline evaluations, annual follow up monitoring and suitable hearing protection devices with proper training on how to use them efficiently. Finally, training about the hazards of noise exposure should take place periodically across these facilities to improve employees' awareness of the adverse effects of noise on human health.

## 5.6 Conclusions

The aim of the work described in this thesis was to determine the effects of noise exposure on the human balance function using various diagnostic test procedures and self-reported measures. The overall research question of this thesis was *“Does noise exposure affect vestibular function?”*. This question was addressed by proposing a number of hypotheses tested via a series of studies and described in several chapters. The first work described in this thesis aimed to compare cVEMP responses of 90 normal adults using the HR-S procedure and two biofeedback methods (BPM and EMGM), with and without one data analysis technique (amplitude normalization). First, it was hypothesized in this study that since both biofeedback methods involve monitoring the level of EMG activities, which are related to cVEMP amplitude levels, then there would be no difference in cVEMP response parameters between the two methods. Second, it was hypothesized that the combined use of both biofeedback methods (BPM or EMGM) and amplitude normalization would stabilize cVEMP inter-aural amplitude variability and produce lower IARs. Third, it was hypothesized that the combined use of these methods and this technique would reduce the expected large cVEMP inter-subject amplitude variability. The conclusion of this study supports the use of the BPM method in cVEMP testing to obtain high cVEMP amplitudes and reasonably well-stabilized inter-aural amplitude differences. The study also indicates that combining an amplitude normalization technique with a biofeedback method (BPM or EMGM) resulted in more stable cVEMP amplitude data and reduced possible inter-subject amplitude variations caused by differences in muscle strength across genders or the use of different biofeedback methods. Finally, the study found that amplitude normalization had no apparent effect on cVEMP inter-aural amplitude asymmetry data.

The second piece of work, described in Chapter 3, aimed to determine the effects of noise exposure on cVEMP among two noise-exposed workers: 1) noise-exposed workers with a self-reported history of occupational noise exposure and confirmed cochlear damage (NIHL group) and 2) noise-exposed workers who had a similar self-reported history of occupational noise exposure but intact auditory structures (noise-exposed normal hearing "NH" group). This study aimed also to examine the relationship between the three diagnostic test procedures utilized in this study (PTA, DPOAE and cVEMP). First, it was hypothesized that cVEMP response parameters of the *noise-exposed NIHL group* would be different from those obtained from individuals with normal audio-vestibular function without a history of noise exposure (controls). Second, it was hypothesized that cVEMP response parameters of the *noise-exposed NH group* would be different from those obtained from controls. Third, it was hypothesized that cVEMP response parameters of the *NIHL group* would be different from those obtained from the *noise-exposed NH group*. The study identified cochlear and saccular damage in 85 adults working at potentially noisy worksites at the Saudi National Guard organization. cVEMP abnormality was detected not only in workers diagnosed with NIHL, but also in workers who were at risk of developing NIHL but still had normal hearing evident by audiograms. In addition to the well-documented sensitivity of OAE in identifying early noise-induced cochlear changes reported in the literature, the study suggests that combining DPOAE and cVEMP findings seems to increase the likelihood of detecting noise-induced saccular damage. These findings are novel as they indicate that long-term noise exposure can impair saccular function, before clinically detectable cochlear dysfunction or hearing loss. The data collected in this study help in understanding the relative sensitivity of the cochlea and the sacculle to excessive noise exposure.

The third piece of work, described in Chapter 4, aimed to determine the frequency and nature of vestibular symptoms among the same noise-exposed groups enrolled in the second study: 1) noise-exposed NIHL group and 2) noise-exposed-normal hearing NH group. The study aimed also to estimate the lifetime cumulative noise exposure of two noise-exposed occupational groups (hospital technicians and soldiers) and to examine as well the

relationship between the self-reported data obtained in this study and the diagnostic test results obtained in Chapter 3. First, it was hypothesized in this study that the *noise-exposed NIHL group* would report vestibular symptoms which reflect saccular dysfunction as a result of noise exposure. Second, it was hypothesized that the *noise-exposed NH group* would report vestibular symptoms which reflect saccular dysfunction as a result of noise exposure. Third, it was hypothesized that there would be a consistency among the three sets of data collected in this thesis: the audio-vestibular symptoms data, the estimated lifetime cumulative noise exposure data, obtained in Chapter 4 and the diagnostic test results obtained in Chapter 3.

The third study documented vestibular symptoms, most likely related to saccular damage, reported by noise-exposed individuals with and without NIHL. The results of this study help to better define as well as differentiate noise-induced saccular symptoms from other pathologies affecting the vestibular system. The documented abnormal cVEMP and saccular symptoms are likely to be attributable to the impact of long-term noise exposure on the inner ear of these workers. The estimated noise exposure levels of the investigated group exceeded safety limits and are regarded as the levels above which exposure to noise is detrimental to human health. The overall findings reported in this study demonstrate the importance of obtaining case history information and self-reported data in the clinical management of noise-exposed patients. Thus, based on the overall findings obtained in the works presented in this thesis, it can be concluded that noise affects the human vestibular function by damaging the saccule, which may be apparent before peripheral hearing damage is observed and possibly resulting in reported symptoms.

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### List of abbreviations

BPM	blood pressure manometer
cVEMP	cervical vestibular evoked myogenic potential
daPa	decapascals
dB	decibel – a unit of sound intensity based on a logarithmic relationship of one intensity to a reference intensity
dB(A)	decibel expressed in sound pressure level and measured on the A-weighted scale of a sound level meter filtering network
dB(C)	decibel expressed in sound pressure level as measured on the C-weighted scale of a sound level meter filtering network
dB HL	decibel hearing level – a sound level relative to the average hearing threshold obtained from normally hearing population, hence, 0 dB HL refers to audiometric zero and also to normal hearing
dB nHL	decibel normal hearing level – a sound level relative to the behavioural thresholds of a sample of normal hearing persons, used most often to describe the intensity level of stimuli used in evoked potential testing
dB pSPL	decibel peak sound pressure level – a sound level of a 1000 Hz tone at an amplitude equivalent to the peak of a transient signal often used to express the intensity level of a click stimuli in auditory evoked potential testing
dB SPL	decibel sound pressure level – is a logarithmic measure of the effective pressure of a sound relative to a reference value and is expressed in dB. dB SPL equals 20 times the log of the ratio of an observed sound pressure level of 20 micropascals (or 0.0002 dyne/cm <sup>2</sup> , 0.0002 microbar, 20 micro-Newtons/m <sup>2</sup> )
DP	distortion product
DPOAE	distortion product otoacoustic emission
EMG	electromyogenic
EMGM	electromyogenic monitoring
ENG	electronystagmography
HE	head elevation
HPD	hearing protection device
hrs.	hours
HR-S	head rotation-sitting
Hz	Hertz
IAR	inter-aural amplitude asymmetry ratio

IHCs	inner hair cells
kHz	Kilohertz
$\Omega$ k	Kiloohm
mmHg	millimeters of mercury
Ms	milliseconds
$\mu$ V	microvolt
N	number
NH	normal hearing
NIHL	noise-induced hearing loss
NIL	noise emission level
NIOSH	National Institute for Occupational Safety and Health
NIR	noise immision rating
NITTS	noise-induced temporary threshold shift
OAE	otoacoustic emission
OHCs	outer hair cells
oVEMP	ocular vestibular evoked myogenic potential
PEL	permissible exposure limit – is a legal limit for noise exposure established by occupational safety and health agencies which is the highest intensity level in A-weighted sound level (dBA) to which an employee can be exposed for a specified duration of time (usually 8 hour/working day) and still meet occupational safety guidelines
PTA	pure tone audiometry
Q	question
SCD	semicircular canal dehiscence
SCM	sternocleidomastoid
SD	standard deviation
SNR	signal to noise ratio
TEOAE	transient-evoked otoacoustic emission
Total U value	total units of lifetime cumulative noise exposure
U value	units of lifetime cumulative noise exposure
VEMP	vestibular evoked myogenic potential
VOR	vestibulo-ocular reflex



- Precipitate an attack?  
  11. Were you exposed to any irritating fumes, paints, etc. at the onset of dizziness?  
  12. Do you have any allergies?  
  13. Did you ever injure your head?  
  Were you unconscious?  
  14. Do you take any medications regularly? What .....  
  15. Do you use tobacco in any form?  
  How much?.....

iii. Do you have any of the following symptoms? Check either YES or NO and circle ear involved.

- | Yes                      | No                       |  |           |       |      |
|--------------------------|--------------------------|--|-----------|-------|------|
| <input type="checkbox"/> | <input type="checkbox"/> | 1. Difficulty in hearing?                          | Both ears | Right | Left |
| <input type="checkbox"/> | <input type="checkbox"/> | 2. Noise in your ears?                             | Both ears | Right | Left |
|                          |                          | Describe the noise.....                            |           |       |      |
| <input type="checkbox"/> | <input type="checkbox"/> | Does noise change with dizziness? If so, how?..... |           |       |      |
| <input type="checkbox"/> | <input type="checkbox"/> | 3. Fullness or stuffiness in your ears?            | Both ears | Right | Left |
| <input type="checkbox"/> | <input type="checkbox"/> | Does this change when you are dizzy?               |           |       |      |
| <input type="checkbox"/> | <input type="checkbox"/> | 4. Pain in your ears?                              | Both ears | Right | Left |
| <input type="checkbox"/> | <input type="checkbox"/> | 5. Discharge from your ears?                       | Both ears | Right | Left |

iv. Have you experienced any of the following symptoms? Please check either YES or NO and CIRCLE either CONSTANT or IN EPISODES.

- | YES                      | NO                       |                                       |          |             |
|--------------------------|--------------------------|---------------------------------------|----------|-------------|
| <input type="checkbox"/> | <input type="checkbox"/> | 1. Double vision                      | Constant | In episodes |
| <input type="checkbox"/> | <input type="checkbox"/> | 2. Numbness of face or extremities    | Constant | In episodes |
| <input type="checkbox"/> | <input type="checkbox"/> | 3. Blurred vision or blindness        | Constant | In episodes |
| <input type="checkbox"/> | <input type="checkbox"/> | 4. Weakness in arms or legs           | Constant | In episodes |
| <input type="checkbox"/> | <input type="checkbox"/> | 5. Clumsiness in arms or legs         | Constant | In episodes |
| <input type="checkbox"/> | <input type="checkbox"/> | 6. Confusion or loss of consciousness | Constant | In episodes |
| <input type="checkbox"/> | <input type="checkbox"/> | 7. Difficulty with speech             | Constant | In episodes |
| <input type="checkbox"/> | <input type="checkbox"/> | 8. Difficulty with swallowing         | Constant | In episodes |

**Appendix B Noise at Work Questionnaires (Purdy and Williams, 2002)**

**126 Greville Street  
Chatswood  
NSW 2067 Australia**



*National*  
**Acoustic**  
*Laboratories*

Date questionnaire completed:

Code Number:

**Noise at Work Questionnaire**

*We are interested in your experience of noise at work.  
This questionnaire will be given a code number by the researchers so that your  
answers cannot identify you.  
If you have any comments about the questionnaire, we have left space at the end  
for you to use.  
If you have any questions about the research please contact your Safety Office  
.....  
or Warwick Williams or Suzanne Purdy at National Acoustic  
Laboratories (02-9412 6800).*

**SECTION A**

**We're interested in what you think about noise. Below are sentences about noise at work. Please look at each sentence and put a cross in one of the boxes provided according to how much you agree with the sentence. If you completely disagree with this example sentence, you would rate it like this:**

	Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree
It is never noisy at work.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>

1. My hearing will <u>not</u> be damaged by noise at work.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2. The noise at work does <u>not</u> bother me.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3. Work would be less stressful if it was quieter.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4. I do not have time to do anything about the noise at work.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
5. Hearing protectors stop me from hearing what I want to hear.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
6. I will feel better if my worksite is less noisy.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
7. I can <u>not</u> reduce noise at work.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
8. Hearing protectors are uncomfortable.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
9. I like it when it is noisy.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
10. I am <u>not</u> sure that I can use hearing protectors correctly.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
11. Management is <u>not</u> interested in Occupational Health and Safety.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>





**SECTION B**

*This section is for research purposes only.*

*No feedback will be given to your employer that may be used to identify you.*

Please tell us whether you are: Male , or Female

What year were you born? 19\_\_\_\_\_

What is the main language you speak at home?.....

What is the highest level of education you have attained?

Primary school

High school  Technical or business school

University

Trade qualification (TAFE, apprenticeship, etc)

What sort of work do you do?

.....

Which of these describes your work?

Manager

Plant or equipment operator

Trades work

Labourer

Supervisor

How long have you been doing this type of work?.....

How long have you been in your current job?.....

Do you feel you have a hearing loss?

No

Yes

Do you have any noises/ringing in your ears?

Never

Occasionally

Frequently

Always

During the past month in your work area what percentage of the time during the working day were you exposed to loud noise (loud enough to require you to raise your voice)?

.....%

During the past month in your work area what percentage of the time during the working day did you wear hearing protectors ( earmuffs or earplugs)?.....%

Does an immediate family member or friend feel that you have a hearing loss?

No

Yes

Have you ever had a hearing test?

No

Yes

If you had a hearing test was it organized through your work?

No

Yes

If you had a hearing test did someone explain the results to you?

No

Yes

Do you find it very difficult to follow a conversation at home if there is background noise, e.g., TV, radio, children playing?

No

Yes

**COMMENTS**.....



**3. Use of Hearing Protection Devices (HPDs)**

Do you wear any kind of HPDs at work?

Yes Please mention type:  ear plugs and/or earmuffs  anything  No

If yes, how often you use your HPD?

Never  A few times  Several times  Quite often  Very often

**Section (B): Auditory History**

---

**1. Expectation of hearing loss:**

Do you expect to have a hearing loss in today's hearing exam?  Yes  No

**2. Hearing monitoring:**

Has your hearing been examined previously?  Yes  No

If yes, what was the result?

Normal  Hearing loss (circle; unilateral or bilateral)  I don't know

If you have chosen 'hearing loss', please answer the following questions in this section:  
When was your hearing loss diagnosed? .....

**3. Awareness of noise risks to hearing:**

Do you know the cause of your hearing loss?

Hereditary  Ear infection  Exposure to Noise  I don't know

other reason (mention :.....)

Did you receive any treatment/rehabilitation for it?.....

**4. Associated symptoms:**

Do you have tinnitus (ringing in your ear)?  Yes (unilateral or bilateral)

Please describe:.....  No

**Section (C): Vestibular History**

---

**1. Symptoms Description:**

Have you ever experienced any of the following?

A feeling of being light-headed, 'swimmy' or giddy

Never  A few times  Several times  Quite often  Very often

A sensation of 'spinning' in the room or the room/things in the room is 'spinning' around you (vertigo)

Never  A few times  Several times  Quite often  Very often

Feeling unsteady, about to lose balance

Never  A few times  Several times  Quite often  Very often

Unable to walk properly without support, veering or staggering to one side

Never  A few times  Several times  Quite often  Very often

Unsteadiness so severe that you actually fall

Never  A few times  Several times  Quite often  Very often

**2. Associated Symptoms:**

Is your dizziness ever associated with any of the following symptom?

- Pressure or fullness in your ears  
 Never             A few times             Several times             Quite often             Very often
- Nausea or vomiting  
 Never             A few times             Several times             Quite often             Very often
- Visual disturbances (double vision or blindness)  
 Never             A few times             Several times             Quite often             Very often
- Headache or pressure in your head  
 Never             A few times             Several times             Quite often             Very often
- Feeling faint or about to black out  
 Never             A few times             Several times             Quite often             Very often

**3. Characteristics:**

When did you first experience the sensation of dizziness or imbalance?.....

Is your dizziness constant or does it come in attacks?.....

If in attacks, how often do they last?.....

- Can you tell when an attack is about to start?             Yes             No             Sometimes
- Are you completely free of dizziness between attacks?  Yes             No             Sometimes
- Does change of position make you dizzy?             Yes             No             Sometimes
- Do you have trouble walking in the dark?             Yes             No             Sometimes
- When you are dizzy, can you stand up unsupported?  Yes             No             Sometimes

**4. Triggers:**

Do you know of anything that will:  
Stop your dizziness or make it better.....

Make your dizziness worse .....

Precipitate an attack? .....

Were you exposed to any irritating fumes, paints, or others at the onset of dizziness?.....

If you have tinnitus, does it change with dizziness? If so, how?.....

*Thank you for completing this form.*

Investigator's Notes:.....  
.....

## Appendix D Audio-vestibular symptoms in noise – Arabic version

### (أعراض إختلال جهازي السمع و التوازن الناتج عن الضوضاء/الضحيج: دراسة إستبائية)

التاريخ : .....  
رقم الهوية في البحث:.....

#### المعلومات الشخصية:

العمر:	30-18 □	40-31 □	50-41 □	60-51 □
المسمى الوظيفي :	.....			
عدد السنوات التي قضيتها في الوظيفة الحالية:	.....			
□ أقل من سنة	□ 1-5 سنوات	□ 5-10 سنوات	□ أكثر من 10 سنوات	□ أكثر من 10 سنوات
وظائف سابقة ( اذكرها.....)	.....			
عدد السنوات التي قضيتها في الوظيفة السابقة:	.....			
□ أقل من سنة	□ 1-5 سنوات	□ 5-10 سنوات	□ أكثر من 10 سنوات	□ أكثر من 10 سنوات

#### التاريخ الصحي:

الرجاء الإشارة اذا كنت تعاني من إحدى الأمراض التالية, في الوقت الحالي أو في ما مضى:

□ إصابه في الرأس □ مرض عصبي-عضلي □ مرض عصبي

□ الدوخة/الدوار ناتج عن مرض معروف في جهاز التوازن في الأذن الداخلية

(أذكر:.....)

هل تستخدم أي أدوية بانتظام ؟ □ لا □ نعم

(أذكر:.....)

هل لديك أي مشاكل صحية رئيسيه أخرى :.....

#### أ- تاريخ التعرض للضوضاء / الضحيج:

##### 1. الإنطباع الشخصي عن الضوضاء/الضحيج في بيئة العمل:

هل مستوى الضوضاء/الإزعاج في بيئة عملك الحالي مرتفع جدا؟

□ أبدا □ أوافق بشدة □ أوافق □ لا أستطيع تحديد ذلك /لا أعرف □ لا أوافق

□ لا أوافق بشدة

هل تحتاج أن ترفع صوتك في العمل (تصرخ) حتى يسمعك الآخريين بسبب

الضوضاء/الضحيج؟

□ أبدا □ مرات قليلة □ مرات كثيره □ في كثير من الأحيان □ في أغلب الأحيان

##### 2. تقدير مستويات الضوضاء/الضحيج:

تقريبا كم عدد الساعات التي تقضيها في الأماكن المزعجه في عملك؟

□ 8 ساعات في اليوم □ أقل من 8 ساعات في اليوم □ أكثر من 8 ساعات في اليوم

□ لا أعرف

**3. استخدام وسائل حماية الأذن:**

- هل يوفر لك عملك أي أداة/وسيلة لحماية أذنك/سمعك؟  
 نعم (أذكر النوع: .....)  
 لا  
 إذا كانت إجابتك بنعم , كم مره تستخدم هذه الأداة/الوسيلة ؟  
 لم يسبق لي إستخدامها  بعض المرات  مرات كثيرة  في كثير من الأحيان  
 في أغلب الأحيان  
 كم في الغالب تستخدم هذه الوسائل (الأسلحة اليدوية الصغيره - وسائل الاستماع المحمولة (مثال: الهاتف المتنقل) - المعدات المنزلية – أدوات/الآت موسيقية -أخرى (حدد:.....)  
 لا أستخدامها أبداً  مرات قليلة  مرات كثيرة  في كثير من الأحيان  
 في أغلب الأحيان  
 ما هي أكثر مصادر الضوضاء/الضجيج التي تتكرر عليك في مجال عملك؟  
 .....  
 هل كنت في مكان به ضوضاء/ضجيج خلال ال 24 ساعة الماضية سواء في عملك أو خارج العمل الى الحد الذي تحتاج فيه أن ترفع صوتك من أجل المحادثة؟  
 نعم  لا

**ب- التاريخ السمعي:****1. متابعة حالة السمع**

- هل سبق و أجريت اختبار للسمع؟  
 نعم  لا  
 إذا كانت الإجابة نعم , ماذا كانت النتيجة ؟  
 طبيعي  يوجد ضعف سمع (إختر: الأذن اليمنى / الأذن اليسرى)  لا أعرف  
 إذا اخترت "يوجد ضعف سمع" , نرجو الإجابة على الأسئلة الآتية في هذه الفقرة:  
 متى تم تشخيص ضعف السمع لديك ؟ .....

**2. مدى معرفة مخاطر الضوضاء/الضجيج على السمع:**

- هل تعرف سبب ضعف السمع لديك؟  
 وراثي  التهاب في الأذن  التعرض للأصوات العالية (الضجيج/الضوضاء)  
 لا أعرف  سبب آخر (أذكر:.....)  
 هل تلقيت أي علاج أو تأهيل للسمع في السابق؟ .....

**3. الأعراض المصاحبة:**

- هل لديك طنين (أصوات/وشوشه) في الأذن؟  
 نعم (الأذن اليمنى/الأذن اليسرى)  لا  
 وصف الطنين: .....

**ت- تاريخ الشعور بالدوخة:****1- وصف الشعور بالدوخة:**

- هل سبق أن تعرضت لأي من التالي؟  
 على وشك الإغماء أو فقد الوعي للحظات قصيره جداً (خفه في الرأس):  
 أبداً  مرات قليلة  مرات كثيرة  في كثير من الأحيان  في أغلب الأحيان  
 الشعور أنك تدور في الغرفة, أو أن الأشياء في الغرفة تدور حولك:  
 أبداً  مرات قليلة  مرات كثيرة  في كثير من الأحيان  في أغلب الأحيان

الشعور بعدم التوازن أو أنك سوف تفقد توازنك:

□ أبدا □ مرات قليلة □ مرات كثيرة □ في كثير من الأحيان □ في أغلب الأحيان  
عدم القدرة على المشي جيداً دون الاعتماد/الإرتكاز على شيء أو الشعور بالإنحراف  
على إحدى الجانبين:

□ أبدا □ مرات قليلة □ مرات كثيرة □ في كثير من الأحيان □ في أغلب الأحيان  
عدم التوازن الشديد الى درجة السقوط:  
□ أبدا □ مرات قليلة □ مرات كثيرة □ في كثير من الأحيان □ في أغلب الأحيان

## 2- الأعراض المصاحبة للدوخة:

هل الشعور بالدوخة لديك مرتبط بإحدى الأعراض التالية:

الشعور بالضغط أو الامتلاء في الأذن

□ أبدا □ مرات قليلة □ مرات كثيرة □ في كثير من الأحيان □ في أغلب الأحيان  
الغثيان والتقيؤ

□ أبدا □ مرات قليلة □ مرات كثيرة □ في كثير من الأحيان □ في أغلب الأحيان  
اضطرابات في الرؤية (الرؤيا المزدوجة أو العمى)

□ أبدا □ مرات قليلة □ مرات كثيرة □ في كثير من الأحيان □ في أغلب الأحيان  
صداع أو ضغط في الرأس

□ أبدا □ مرات قليلة □ مرات كثيرة □ في كثير من الأحيان □ في أغلب الأحيان  
الشعور بالإغماء

□ أبدا □ مرات قليلة □ مرات كثيرة □ في كثير من الأحيان □ في أغلب الأحيان

## 3- الأسباب المثيرة للشعور بالدوخة:

هل تعرف الأشياء التي ممكن أن تؤدي إلى:

توقف شعورك بالدوخة أو تخفيف الشعور بالدوخة؟ .....

زيادة شعورالدوخة لديك؟ .....

تعجيل نوبات الدوخة؟ .....

خلال وجود الدوخة, هل كنت متعرضاً لأي روائح/أبخره مهيجة، دخان، دهان،

أشياء أخرى ؟ .....

إذا كان لديك طنين في الأذن, هل يطرأ عليه أي تغيير مع حدوث الدوخة؟ إذا كانت

إجابتك نعم فماذا يحدث للطنين؟ .....

## ملاحظات الباحث

.....



## Appendix E Estimation of Occupational Noise Exposure

Adopted from Lutman et al. (2008) – Appendix 6 Noise Exposure and Rating Questionnaire (page 82)

Annex B (i) Occupational noise exposure – at study worksite

	1	2	3	4	5
1. Job					
2. Task					
3. Noise level estimate dB (A)					
4. Method					
5. Duration					
6. Weeks/year					
7. Days/week					
8. Hours/day applies					
9. Hearing protection type					
10a. Hearing protector attenuation					
10b. % time hearing protection worn*					
11. After effects					
12. Temporary/permanent					
13. Side of effect(s)					

Method of estimation: 1 = actual knowledge, 2 = personal/documentary knowledge, 3 = examples table, 4 = speech communication table

After effects: 1 = dullness of hearing, 2 = tinnitus, 3 = both

Temporary/permanent: 1 = permanent, 2 = temporary

Site: 1 = left, 2 = right, 3 = both/central

\* % hearing protection worn is for each task. If hearing protection is less than 100 %, enter the % time worn in the column that discusses noise + HP. This value is not included in the NIR calculation.

## Appendix F Estimation of Military Noise Exposure

Adopted from Lutman et al. (2008) – Appendix 6 Noise Exposure and Rating Questionnaire (page 85)

### Annex D Gunshot and explosive noises

Type of noise	Approximate total rounds (without proper hearing protection)	Immediately noticed auditory after-effects (see below for coding)	After-effects (temporary or permanent) See below for coding
1. Rifles (include shotguns, military rifles, but not 0.22 rifles or air-guns)	Fired from shoulder RIGHT / LEFT		
2. Machine guns (e.g. Bren, GPMG)			
3. Large infantry weapons (Bazooka, mortars)			
4. Light artillery or anti-aircraft guns			
5. Large artillery weapons or naval guns			
6. Explosives	Specify circumstances		

NIR \_\_\_\_\_

#### *Coding:*

Immediately noticed auditory after-effects

0 = none, 1 = slight, 2 = moderate, 3 = severe

Temporary/permanent

1 = permanent, 2 = temporary

## Appendix G Dissemination strategy

The studies described in Chapters 2, 3 and 4 will be submitted as papers for publication in a peer-reviewed journals later in 2018 and 2019. The methodology and data described in this thesis have been disseminated in the following forums:

*“The effect of noise on balance Function: a preliminary pilot data findings”* was presented as a poster in the Post Graduate Research (PGR) Student Conference at the School of Healthcare, University of Leeds, Leeds, UK. June 22, 2011.

*“Cervical vestibular evoked myogenic potentials (cVEMPs) normative data in adults: selecting the appropriate methodology to control sternocleidomastoid muscle contraction variability”* (as described in Chapter 2 of this thesis) was presented as a poster at Faculty of Health and Medicine (FHM) Conference, Weetwood Hall, University of Leeds, Leeds, UK. June 23, 2014.

*“Cervical vestibular evoked myogenic potentials (cVEMP): Determination of an optimal biofeedback method and data analysis technique using head rotation-sitting procedure”* (as described in Chapter 2 of this thesis) was presented as an oral presentation at the International Conference for Audiology and Neuro-otology (iCAN) held at Alfaisalia Hotel, Riyadh, KSA. March 1 – 5, 2015.

*“Noise-induced audio-vestibular dysfunction in Saudi National Guard personnel”* (as described in Chapter 3 of this thesis) was presented as a poster at the 33<sup>rd</sup> World Congress of Audiology (WCA) held at Sheraton Wall Centre in Vancouver, British Columbia, Canada. September 19, 2016. The abstract of this presentation was peer reviewed and published in the congress proceedings.

*“Cervical vestibular evoked myogenic potentials (cVEMP): Determination of an optimal biofeedback method and data analysis technique using head rotation-sitting procedure”* (as described in Chapter 2 of this thesis) was presented as an oral presentation at the 24<sup>th</sup> SORL (Saudi otorhinolaryngology) held at Fairmont Makkah Hotel, Makkah, KSA. December 12 –13, 2017.