ASSESSMENT OF VESTIBULAR FUNCTIONS IN INDIVIDUALS WITH AUDITORY NEUROPATHY

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INTRODUCTION

Auditory neuropathy spectrum disorder (ANSD) is characterized by a unique pattern of hearing loss and absent or severely distorted auditory brainstem responses (ABRs) with preservation of outer hair cell function, as revealed by otoacoustic emissions (OAEs) and/or measurable cochlear microphonics (Starr, Sininger, Picton, Hood & Berlin, 1996). The abnormality of the VIII nerve could be at the level of the inner hair cells, the synapse between inner hair cells and VIII nerve fibers, the ganglion neurons, the nerve fibers, or may be a combination of the above (Sininger, 2002). Etiologies of ANSD include neonatal illnesses such as prematurity, low birth weight, anoxia, and hyperbilirubinemia (Sininger, 2002). Other possible causative factors include hydrocephalus, Charcot-Marie Tooth neuropathy syndrome, Friedreich's ataxia, ischemic-hypoxic neuropathy, and other hereditary sensory motor neuropathies (Cone-Wesson, 2003).

The physiological mechanisms underlying ANSD are varied in terms of the possible sites of lesions, which range from damage to selected inner hair cells, outer hair cells, the synapse between hair cells and the auditory nerve, neural dendrites or axons, the myelin sheath or spiral ganglion cells (Starr *et al.,* 1996). To neurologists, the term neuropathy has a precise connotation wherein it refers to a pathology involving the peripheral nerve fibres unlike pathologies such as neuronopathies affecting the neuronal cell bodies. Neuropathies can be divided into three broad types, demyelinating, axonal, and mixed (Rance, 2005). Each subcategory presents with clinical findings and symptoms that are distinct from the other. While demyelinating conditions result in the disruption of temporal synchrony causing difficulty in speech perception and clinically, absence of ABRs (Rance, 2005). The axonal involvement on the other hand results in the absence of adequate neural fibres resulting in the

inability to obtain middle ear muscle reflexes and olivocochlear reflexes (Starr, Picton & Kim, 2001).

In the Indian scenario, a prevalence rate of 1 in 183 (0.54%) individuals with sensorineural hearing loss has been reported (Kumar & Jayaram, 2006). Davis & Hirsh (1979) reported that 1 in 200 hearing impaired children exhibit an audiological pattern that is consistent with the contemporary diagnosis of ANSD. Rance, Beer, Cone-Wesson, Shepherd, Dowell , King, Rickards , and Clark (1999) presented results of 5,199 babies who were found to have risk factors for hearing loss. Upon extensive diagnostic evaluations, a prevalence of 0.23% or 1 in every 433 subjects was found. Higher ANSD prevalence levels of 4% (4 in 100 at risk neonates) have been reported by Stein et al.(1996) and Psarommatis, Tsakanikos, Kontorgianni, Ntouniadakis, and Apostolopoulos (1997) reported of 2 of their 102 (1.9%) high risk neonates, classified as such based on the JCIH position statement, were found to have characteristics typical of ANSD.

There are few reports available in the literature regarding the involvement of the vestibular nerve in individuals with ANSD (Starr, Picton, Sininger, Hood, & Berlin, 1996; Fujikawa & Starr, 2000; Sheykholeslami, Kaga, Murofushi, & Hughes, 2000; Sheykholeslami, Schmerber, Kermany, & Kaga, 2005; Kumar, Sinha, Singh, Bharti, & Barman). Starr et al.,(1996) initially described 10 subjects with AN, 2 of whom had absent responses to caloric testing, indicating a possible involvement of superior vestibular nerve and also 3 other subjects showed horizontal nystagmus on lateral gaze. All 5 patients had peripheral neuropathy which led the authors to suggest that the abnormal auditory and vestibular test results were part of a generalized neuropathic disorder affecting both the components of cranial nerve VIII.

Kumar *et al.* (2007) reported that 80% of the ears with auditory neuropathy assessed had abnormal Vestibular evoked myogenic responses (VEMP) results. This study has

reported of a possible involvement of inferior vestibular nerve in individuals with ANSD. Also, Kaga (2009) reported the involvement of superior as well as the inferior vestibular nerve of 8 individuals with ANSD in the absence of peripheral neuropathy. Kaga (2009) reported that ice water caloric stimulation failed to elicit any response on electronystagmography (ENG) and VEMPs were also abolished in 5 of the AN subjects. These subjects were therefore categorized to have 'auditory-vestibular neuropathy'. Three other subjects performed normally on the vestibular evaluations and were thereby diagnosed to have 'auditory neuropathy only'.

1.1 Need for the study

With such a wide range of possible pathological involvement in such subjects, the findings reported in literature have reflected this with varied and variable clinical findings. The heterogeneous nature of the disorder adds to the difficulty that exists in developing a comprehensive assessment protocol for these individuals. Of key concern in ANSD is the VIII nerve. The VIIIth nerve is a mixed nerve made up of three distinct nerve bundles: (a) the afferent auditory axons of the spiral ganglion neurons, (b) the afferent vestibular axons, and (c) the efferent axons of the olivo-cochlear bundle which travel with the vestibular division until they reach the cochlea and primarily innervate the outer hair cells. Comprehensive evaluation of the VIII nerve entails testing of altogether three divisions i.e. auditory, vestibular and olivo-cochlear, which, unfortunately is uncommon customarily.

Sub serving the abovementioned need is the fact that, in addition to the audiological findings, it has been suggested that in such disorders affecting the cochlear nerve it is highly probable that the vestibular nerve is involved as well, as both form a part of the same nerve bundle, the vestibulocochlear nerve (Akdogan, Selcuk, Ozcan, Dere, 2007). Correspondingly, ,a demyelinating neuropathy involving the VIII nerve could possibly result in impaired

conduction unselectively in all three of its divisions (afferent auditory and vestibular and efferent olivocochlear fibres). This may well be as biological differences among the schwann cells that ensheath axons in each of these three divisions have not been described.

Also anatomical changes of vestibular nerve in individuals with ANSD has been reported (Starr et a. 2003). It has been reported that the nerve itself had structural changes that were not found in the individuals with normal vestibular system. The overall vestibular nerve population between the receptor organ and the ganglion within the internal auditory meatus has been reported to be reduced (Starr et al. 2003). In the AN individuals who were found to have vestibular involvement, both the auditory as well as the vestibular nerve had an irregular beaded appearance (Starr et al. 2003). Further, fragmentation of the myelin layer with gaps nearly equal to the diameter of the nerve fibers has been reported along with the distortion of the nerve structure (Starr et al. 2003).

The vestibular branch of the vestibulocochlear nerve, comprising the superior and the inferior vestibular nerve, is a part of the system involved in maintaining a sense of equilibrium. Other structures involved include the vestibular nuclei, the semicircular canals and the central oculomotor systems. The functioning of the superior vestibular nerve and the end organ it innervates, the semicircular canals can be assessed by Electronystagmography (ENG). ENG also assess the vestibulo-occular reflexes and subsystems of vestibulo-occular reflexes. The status of the inferior vestibular nerve and the otolith organ it innervates, the saccule, can be assessed by means of obtaining cervical vestibular evoked myogenic Potentials (cVEMP). In individuals with ANSD assessment of vestibular functioning has been done by means of ENG test battery and recordings of vestibular evoked myogenic potentials.

1.1.1Need for Audiological evaluation

Currently, in a clinical setup, the diagnosis of ANSD is possible by means of audiologic evaluation. By conducting a thorough assessment of the functioning of the inner ear and the auditory nerve, it is possible to diagnose ANSD. In order to arrive at a reliable diagnosis, a test batter incorporating basic pure tone audiometry, speech audiometry in quiet and in noise, Otoacoustic emissions measurement and recording of the brainstem responses to auditory stimuli is utilized. Besides its utility in establishing the presence or absence of ANSD and distinguishing it from other possible conditions, basic audiological tests such as otoscopic examination and immittance evaluations are also a prerequisite to ENG, as it is essential that the presence of any middle ear or external ear conditions is ruled out.

1.1.2 Need for the dizziness questionnaire

A basic questionnaire incorporating the core features that exemplify vertigo provides the clinicians with valuable information at the outset of the assessment process. It represents a systematic attempt to determining the root of vertigo (Jacobson & Shepard, 2008). It is therefore important to collect adequate information about the quality of the dizziness, the timing of the attacks, provoking symptoms, concomitant symptoms and general medical problems. This information can inturn be correlated with quantitative vestibular assessment techniques such as ENG, vestibular evoked myogenic potential and tests of stability to determine its utility in the evaluation protocol. Additionally, no effort has been made to correlate vestibular symptoms with vestibular findings in ANSD. The outcome of such a correlational analysis would enable the development of a checklist which identifies the core features of vertigo or the most prevalent symptoms that that are specific to the vestibular findings in individuals with ANSD.

1.1.3 Need for tests of stability

The tests of stability undertaken include the Romberg test, the fukuda stepping test, the tandem gait test and tests of cerebellar functioning such as finger o nose test, alternating hand movements test. These tests are a behavioural index of the extent to which an existing vestibular dysfunction manifests in a person's balance function during routine activities. They thus assess the functional integrity of all the systems responsible for balance maintenance in activities most commonly executed in day to day life. These tests have been shown to be sensitive to pathologies of the vestibular and cerebellar system as their procedures isolate the vestibular system by moderating or even limiting the involvement of the visual and proprioceptive system in the maintenance of balance. Thus, a behavioural representation of even subtle dysfunctions is made available to the clinician. This information can further be used to establish if a correlation exists with the objective tests of ENG and cVEMP, as there is a lack of information on such correlations. Such information on the presence of a good correlation between the behavioural and objective or not test could then be used to conclude if the tests of stability could be employed to determine the need for the more time involving objective tests.

1.1.4 Need for ENG test battery

In order to conduct a thorough examination of the status of the vestibular functioning, it is necessary to take into consideration its many pathways and divisional functions. Incorporating most of the different divisions as well as functional pathways of the system is the ENG test battery. The ENG test battery is inclusive of tests meant to assess the peripheral vestibular system (like caloric test, dix-hallpike manoeuvre, & positional test) and the central system (like gaze test, saccade test, Optokinetic test, as well as the caloric test). While the central sub-tests primarily look into the functional integrity of the ocular pathways of the

brainstem and cerebellum including the vestibular nuclei, medial longitudinal fasciculus, oculomotor nuclei and extra-ocular muscles, the peripheral subtests mainly deal with the assessment of one component of the peripheral vestibular organ, the semicircular canals, and its innervations, in particular, the superior vestibular nerve. A large part of research into the vestibular involvement in individuals with ANSD have focused cVEMP recordings which primarily provide information on the saccule and its neural support, the inferior vestibular nerve (Kumar, Sinha, Singh, Bharti & Barman., 2007, Sazgar, Yazdani, Rezazadeh & Yazdi., 2010), there is thus a dearth of information on the functioning of the superior vestibular nerve. Furthermore, this information is essential in order to provide collective information on the incidence of vestibular dysfunction n ANSD population.

1.1.5 Need for cVEMP

The determination of balance by the peripheral vestibular system is made possible by complex interplay between the organs involved, namely, semicircular canals and the otolith organs (Utricle and Saccule). Vertical acceleration accomplished by the functioning of the saccule. While the ENG test battery is tuned to determining dysfunctions of the superior vestibular nerve, it is not sensitivity to pathologies involving the integrity of otolith organs. cVEMP is one such test for the integrity of the Saccule, sacculocollic pathway (consisting of the inferior vestibular nerve) whose recording is by the stimulation of the saccule by sound. This is made possible by the saccule's connection to the cochlea by the ductus reuniens and also due to its close proximity to the cochlea itself.

cVEMPs have previously been successfully used in determining the presence of dysfunction along the sacculo-collic pathway in individuals with schwannoma's involving the vestibular nerve. Click cVEMPs were absent in 72.2 to 80% of subjects reporting of vestibular schwannomas (Murofushi, Matsuzaki, Mizuno, 1998; Takeichi, Sakamoto,

Fukuda, Inuyama, 2001; Ushio, Matsuzaki, Takegoshi, Murofushi, 2001). In a large study of 170 individuals presenting with vestibular schwannomas, 78.8% of the population had absent or low amplitude responses to clicks or 500-Hz short-tone bursts evoked cVEMPs. Statistical analysis revealed that, while 69.4% of all subjects were found to have absent click-evoked VEMPs, 23.5% of the entire group had absent click cVEMPs and normal or reduced cVEMPs to short-tone bursts, suggesting that tone burst evoked cVEMPs may be of value in detecting residual inferior vestibular nerve function (Patko, Vidal, Vibert, Tran Ba Huy, de Wael, 2003). Therefore, in addition to commenting on the prevalence of inferior vestibular nerve involvement, as previously mentioned, cVEMP is a reliable tool in addition to the ENG data to ascertain the incidence of vestibular dysfunction in ANSD.

1.2 Aim of the study

The aim of the present study is to compare the vestibular functions in individuals with ANSD with that of normal hearing subjects.

1.3 Objectives of the study

1. To establish a normative data for ENG and VEMP.
2. To assess the involvement of different peripheral vestibular pathways- Vestibulo-ocular as well as sacculo-collic pathways in individuals diagnosed to have ANSD
3. To assess the function of other central components of the balance system i.e. the saccade, Gaze and Optokinetic system in individuals with ANSD.
4. To statistically calculate the incidence of vestibular dysfunction in the ANSD population.
5. To reveal an association, if any, between vestibular abnormalities and the symptoms they present with.
6. To find out if any correlation between the vestibular findings and the type, degree and the configuration of hearing loss exists.

Chapter II

REVIEW OF LITERATURE

Auditory neuropathy (ANSD), a condition first described by Starr, Picton, Sininger, Hood, and Berlin (1996), is a disorder characterized by absent or severely abnormal auditory brainstem responses (ABR) with intact outer hair cell function, this, as evidenced by the presence of evoked otoacoustic emissions and/or cochlear microphonics.

Clinical profile of Individuals with ANSD

2.1 Onset and course

Rance (2005) suggested that the condition tended to present itself in individuals either in infancy, or develop in adolescence/early adulthood. Sininger and Oba (2001) reported that the mean age of onset of the condition in 75% of the 59 individuals assessed was less than 10 years old. Kumar and Jayaram (2006) reported that the average age of onset of the neuropathic symptoms was 16years. 59% of their 61 subjects demonstrated the onset of the condition to be between 14 to 24years. The course of the condition is unpredictable and may remain the same, resolve, fluctuate or worsen over time. Kumar and Jayaram (2006) additionally reported that 81% of their subject population reported that the conditions deteriorated progressively over time. Masuda & Kaga (2011) assessed the effect of age on auditory functions of 3 individuals with ANSD over a period f 10years. They concluded that with the progression of ANSD, elevation of the threshold of pure tone audiometry and marked decline in speech discrimination ability also occurred.

2.2 Prevalence

The prevalence of the condition has been found to vary from roughly 1% (Foerst, Beutner, Lang-Roth, Huttenbrink, Von Wedel & Walgner, 2006) to 10% in schools for the

deaf (Cheng *et al*., 2005) and between 10% in newborns (Sininger, 2002) and 40% in hearing impaired NICU Infants(Ria & Gibson, 2003). In adults with sensorineural hearing loss, in India, the prevalence has been reported at around 0.54% (Kumar & Jayram, 2006) with a female to male ratio of 2:1.

2.3 Pathophysiology

As the term ANSD suggests, the affected site in many patients has been reported to be the auditory nerve itself. Starr *et al.,* (1996) coined the expression based on the findings of their study wherein 8 of the 10 subjects had evidence of other peripheral nerve abnormality in addition to hearing loss. Neuropathic disorders of the auditory nerve can result in varying degrees of axon loss and myelin damage. Abnormal function in the auditory system resulting in the ANSD result pattern may therefore be related to disrupted neural synchrony resulting from myelin damage, a reduction in the number of functioning fibres caused by axonal loss, or in many cases, a combination of both.

Demyelination of the auditory nerve causes a change in the capacitance property of the nerve; in particular, it results in an increase in membrane capacitance and a decrease in membrane resistance. This in turn leads to a delayed excitation of the nerve upon stimulation, as well as slower propagation of the action potential (McDonald and Sears, 1970; Rasminsky and Sears, 1972; Pender and Sears, 1984). Fibres that are demyelinated to differing degrees conduct neural signals at different speeds therefore affecting the synchrony of the resulting discharges. As such demyelinated fibres are repeatedly activated; it causes an increase in the conduction time of the action potential, leading to an intermittent or total block in its propagation, termed as a conduction block (Rasminsky and Sears, 1972).

Axonal neuropathies on the other hand, while reducing the number of neural fibres available for discharge does not directly affect the conduction speed or properties of the nerve. A reduction in the amplitude of the whole nerve action potential and auditory brainstem response has been found to occur in such conditions.

2.4 Audiological profile

2.4.1 Degree and configuration of hearing loss.

According to Rance (2005), earlier reports on ANSD described subjects with losses concentrated in the mild to moderate hearing loss category (Davis and Hirsh, 1979; Worthington and Peters, 1980; Lenhardt, 1981).The subsequent review of literature has yielded results wherein the behavioural thresholds range from normal levels to profound hearing loss. One such study was by Starr, Sininger and Pratt (2000) who described the audiometric findings of 67 individuals with ANSD. They found that 31% had average hearing levels less than 35dB HL, 39% of ears between 35 and 70 dB HL, and 30% of ears at more than 70dBHL. With respect to the configuration, 41% had audiograms with low frequency emphasis, 29% had irregular saw tooth pattern, 5% had a 'U' shaped audiogram, 5% showed a tent shaped loss with a peak at 2 kHz and the remaining 11% had a high frequency sloping loss.

Kumar and Jayaram (2006) reported the audiometric findings of 61 subjects with AN. Of 61 patients, 26 showed a peaked audiogram (sharp peak at a single frequency with worsening of thresholds at immediately adjacent frequencies), 11 showed flat, 11 showed rising, eight showed saucer shaped and three showed a sloping audiogram in both ears. Amongst those who showed a peaked audiogram, 77% had a peak at 2000 Hz. The degree of hearing loss varied from mild to severe.

An earlier study by the same authors on 14 subjects found that five had a rising audiometric pattern, eight subjects had a peaked audiometric pattern and one subject had a flat loss. The hearing loss averaged from 5dB HL to 75dB HL in the subjects assessed. Inherently characteristic of subjects with ANSD are the fluctuations in hearing level. 5 of the 14 children reported by Rance, Beer and Cone-Wesson (1999), showed significant hearing level fluctuations with threshold variances of approximately 20 dB The Sininger and Oba (2001) showed 29% of ears assessed to have significant hearing level fluctuations.

2.4.2 Acoustic Reflexes.

The classic clinical triad of findings in ANSD is combined with the absence, or threshold elevation of middle ear reflexes to both ipsilateral and contralateral tones (Starr, Sininger, Winter, Derebery, Oba, & Michalewski, 1998; Xu, Liu, Lian, Yang, & Tang, 2002). Kumar and Jayaram (2006) reported of the absence of reflex findings in the 61 subjects retrospectively analysed by them. With respect to the paediatric population, Berlin, Hood, Morlet, Wilensky, Li, Mattingly, Taylor-Jeanfreau, Keats, John, Montgomery, Shallop , Russell, Frisch (2005) extracted the database of 136 subjects with ANSD that had undergone middle ear reflex measurements, revealed that none of the evaluated children showed normal reflex at all frequencies tested. Of the 136, only three subjects showed any reflexes at 95 dB HL or below, but never at both 1 and 2 kHz in both ears whether elicited ipsilaterally or contralaterally.

Shivashankar, Satishchandra, Shashikala,& Gore (2003) also reported absent acoustic reflexes in 24 patients determined to have ANSD. Konradsson (1996) reported of the positive presence of a response in the ear diagnosed to have ANSD, but only when probe stimulation was in the contralateral normal hearing ear. This was obtained in the absence of responses (ipsilateral and contralateral) with stimulation of ANSD ear. Such a

finding in cases of unilateral ANSD suggests that the primary disruption in the middle ear reflexes loop is in the afferent pathway (Tibesar and Shallop, 2005). Acoustic middle ear muscle reflexes are absent in ANSD, whereas their activation by nonacoustic stimuli is preserved (Starr *et al*., 1998).

Intense sounds, as used in reflex elicitation normally activate a large proportion of auditory nerve fibres causing them to discharge at high rates for several seconds, thus leading to reflex excitation via the stapedial motor neurons. The absence of acoustic middle ear muscle reflexes in ANSD subjects is consistent with reduced numbers of auditory nerve fibres being activated and/or their ability to discharge at high rates. Exceptions to these findings were reported in 3 of 44 subjects in Sininger and Oba (2001).

2.4.3 Otoacoustic Emissions and Cochlear microphonics (OAE & CM).

Cochlear microphonics and otoacoustic emissions tests have been used as indicators of cochlear (outer) hair cell functioning in individuals with ANSD. Normal functioning of the outer hair cells as evinced by robust OAEs have been reported in ANSD individuals. Transient evoked otoacoustic emissions (TEOAE's) were present in all the subjects assessed by Kumar and Jayaram (2006). The mean amplitude of the obtained TEOAE's in the subjects was found to be higher than those obtained for other adults with normal hearing sensitivity (16 dB SPL as compared to11.5 dB SPL).

Similar findings of robust amplitude responses were also reported by Berlin and Hood (2001).This phenomenon was explained to be due to the lack of efferent suppression of otoacoustic emissions occurring in subjects with ANSD by Kumar and Jayaram (2006). However, studies, such as by Starr, Sininger & Pratt, 2000 have suggested that OAEs may disappear over time in such individuals as it did in 9 individuals with ANSD who participated in their study. Such deterioration in the obtained OAE amplitude could be

explained due to factors such as middle ear disease or due to the prescription and use of amplification devices.

CMs are typically found to be robust and present for several milliseconds (Berlin, 1999; Santarelli & Arslan, 2002), possibly reflecting the normal functioning of the outer hair cells.. The recording of CM while recording ABR is possible by reversing the polarity of the presented stimuli. In 1999, Rance, Beer and Cone-Wesson reported the presence of CMs in all of their 33 ears, with OAEs being present only in 16 of the ears. In their study recording of CM was in fact the primary mode of detection of ANSD. They discussed the obtained responses in terms of possible factors that predominantly affect OAE recording rather than CM such as subtle middle ear pathology. Another hypothesis was that, the presence of significant OHC dysfunction/loss could have resulted in the absence of OAE's, with the CM recording showing a good response due to purely the contribution of the IHC cells. However, Rance (2005) in his review article noted that the most apt explanation to be the differential physiological process necessary to generate the two responses, i.e. the explanation that outer hair cells were present and were able to polarize and depolarize thus resulting in the production and subsequent recording of CM, but that their function was impaired to the extent that they could not generate the mechanical cochlear processes of which the OAE's are a reflection.

Deltenre , Mansbach ,& Bozet (1999) previously reported a similar result when they described the findings for 2 children who were identified with auditory neuropathy in infancy based on the criteria for diagnosing ANSD provided by Starr *et al*., 2001, but who subsequently lost their emissions. Cochlear microphonic responses in these children were relatively unchanged, with similar amplitudes obtained before and after emission loss and only a slight morphologic change reported in one case

A unique distinguishing trait of CM's in individuals with ANSD is its large amplitude and its increased latency. Starr *et al*., (1991, 1998) in both his studies reported of CM recorded in 4 subjects with ANSD lasting for duration of 5ms. Starr *et al*., 2001 also reported of findings of enhanced amplitudes of CM in 33 subjects with ANSD below the age of 10yrs. The amplitude seemed to correlate with the presence of TEOAE, such that, an amplitude of 0.46μv was found on an average if TEOAE's were present, and 0.38 μv if absent.

2.4.4Auditory Brainstem Responses (ABR).

ABRs are generally absent in individuals with ANSD. However, if present, they have been found to be severely abnormal. Starr, Sininger, and Pratt reported that 73% of their subjects did not show ant component of ABR regardless of the level of stimulation, 21% showed abnormal wave V, characterized by abnormal latency and amplitude, 6% of the subjects did show wave III and V, but with grossly abnormal morphology and latency and amplitude. Subsequent studies have all published of the absence of replicable ABR peaks (Starr *et al.*, 1996; Rance *et al.*, 1999; Sininger and Oba, 2001).Starr. Sininger, Nguyen, Michalewski, Oba, and Abdala (2001) reported of 21% of their clinical population of 60 ears exhibiting the presence of wave V alone. The mean amplitude of the responses were significantly reduced in comparison to that obtained in normal hearing individuals (0.01μv as compared to 0.51 μv) Additionally, the latency of the wave was delayed a portion of the subjects.

The obtained responses could reflect the dysfunction that occurs in the physiological functioning of the auditory nerve in subjects with ANSD. Thus, abnormal responses could occur due to reduced number of neural elements responsible for the generation of the response, thus leading to reduced latency and morphological variations or even the absence of responses. Another reason deals with a disruption in the temporal

aspects of the neural signal generated, such as asynchronous firings or prolongation of refractory period. Dys-synchrony in the neural firing of the order of fractions of a millisecond (Starr, McPherson, Patterson,Don, Luxford , Shannon ,Sininger, Tonakawa, and Waring, 1991) has been known to be sufficient to disrupt ABR responses and render the averaged potentials unrecognizable

2.4.5 Speech perception.

Difficulties in perceiving speech has been widely reported in subjects with sensorineural hearing loss. The speech scores obtained in such cases correlate with their puretone threshold. However, a distinctive trait of individuals with ANSD is the disproportionate speech scores with respect to the degree of loss (Starr *et al.,* 2000)

Word recognition scores ranged from 0% to 92% in 8 subjects assessed by Starr *et al*., (1996). Poor speech perception abilities in these patients have been ascribed to abnormal temporal coding and asynchrony (Rance, McKay, & Grayden, 2004; Zeng, Kong, Michalewski, & Starr, 2004). Kumar and Jayaram (2006) in their retrospective analysis of 60 subjects fitting the ANSD criteria stated that the speech perception abilities of their cases varied from no measurable perception ability (as assessed by means of speech identification scores) to 90% scores. All in all, 60% of their subjects did not have measurable speech identification scores. Additionally, the obtained scores correlated with the pure tone thresholds at 250 and 500Hz. They hypothesized that this could be due to the differential physiology involved in the coding of high frequency and low frequency sounds. Thus, they inferred that the low frequency hearing sensitivity could indicate the extent of dysfunction of the temporal integrity of the auditory system which in turn indicates the extent of possible speech perception deficits such individuals would suffer from.

However, at the other end of the spectrum are those individuals whose speech perception deficits are in line with that predicted for a particular degree of sensorineural loss. 25% of the ears presented by Starr *et al.* (1996) and 30% of the Sininger and Oba (2001) subjects were assessed and found to have speech perception scores in quiet within the normal range for sensorineural losses of an equivalent degree. The authors believed that this possibly indicated a lesser extent of neuropathic involvement of the nerves in these subjects compared to the rest.

2.5 ENG findings in individuals with ANSD

The initial report on the functioning of the vestibular system in individuals diagnosed to have ANSD was by Starr *et al.,* (1996) who described 10 patients with auditory neuropathy. Of the 10 subjects assessed 3 subjects showed horizontal nystagmus on lateral gaze, and 2 others had absent responses to caloric vestibular testing. These 5 patients were also asymptomatic with regard to vestibular dysfunction. In addition to neuropathic changes in the vestibulocochlear nerve, all 5 patients had evidence of a generalized peripheral neuropathy which led the authors to suggest that the abnormal auditory and vestibular test results formed a part of a generalized neuropathic disorder affecting both components of cranial nerve VIII. Kaga, Nakamura, Shinogami, Tsuzuku, Yamada, & Shindo (1966) in the same year, reported on two subjects diagnosed to have an 'Auditory nerve disease', who also suffered complained of vestibular symptoms, wherein ice water caloric testing failed to elicit any nystagmus in both the subjects. The performances of the two subjects in the central tests as well as the positional and positioning tests were normal. The obtained results were attributed to a slight involvement of the vestibular organs and the brainstem in such subjects having a possible lesion of the cochlear nerve.

Sheykholeslami, Kaga, Murofushi & Hughes in 2000 assessed 3 subjects who fit the criteria for AN. These subjects also complained of balance disorders and on subsequent testing by the Romberg, Mann and stepping tests showed abnormal results with their eyes closed. Spontaneous nystagmus was not found in any patient ruling out a central involvement of the vestibular tract. Ice water caloric stimulation elicited horizontal nystagmus without vertigo only in the right ear of one of the subjects, but was ineffective at provoking responses from other ears. They concluded that, in patients with isolated auditory neuropathy, the vestibular branch of the VIII cranial nerve and its innervated structures can also be affected. They also provided evidence that in subjects with unprogressed isolated auditory neuropathy, the auditory system as well as the vestibular system may be affected which led to their suggestion of using the term 'cochlear neuropathy' to characterize those patients with involvement of only the auditory branch of the VIIIth cranial nerve and its innervations.

Fujikawa & Starr (2000) report the incidence of abnormal peripheral vestibular test results in 14 individuals with auditory and peripheral neuropathies when symptoms of vestibular dysfunction were absent. Auditory neuropathy was identified bilaterally in all subjects. Eight subjects had concomitant peripheral neuropathies as well. Vestibular abnormalities occurred in 9 of the 14 patients, 7 of whom had concomitant peripheral neuropathies. In the abnormal group, 5 had absent responses, and 3 had asymmetrical responses. Saccadic test results were within the normal range for all subjects. All results for the 5 subjects tested with the sinusoidal tracking test, the optokinetic test, and the gaze test were within normal range. These results provide evidence that certain types of degenerative peripheral neuropathies are associated with a neuropathy of the vestibular nerves. Of the 2 patients who had abnormal caloric responses without having peripheral neuropathies, 1 had a temperature-sensitive auditory neuropathy associated with a

demyelinating disorder of the auditory nerve. The other subject had an isolated auditory neuropathy, and a younger sibling of the subject had an auditory neuropathy with normal vestibular test results. The reports point towards a variability in the extent of the neuropathic lesion involving the vestibular nerve in subjects with AN associated with peripheral neuropathy as well.

The study by Starr, Michalewski, Zeng, Fujikawa-Brooks, Linthicum, Kim, Winnier, & Keats (2003) on a family with hearing loss of ANSD type associated with peripheral neuropathy was one of the pioneering studies which revealed the histopathological changes that occurred in the vestibular nerves, thereby enabling a correlation between the anatomical change that has occurred and the obtained clinical findings. Two of the family members assessed had absence of eye movements and no symptoms of vertigo or dizziness when tested by caloric stimulation of the labyrinths. The pathological findings suggested that the damage was related to the reduced overall vestibular nerve population between the receptor organ and the ganglion within the internal auditory meatus. Additionally, the vestibular nerve was found to have a beaded appearance suggesting incomplete remyelination. Also, fragmentation of the myelin layer with gaps nearly equal to the diameter of the nerve fibre was found along with the distortion of the nerve structure Such changes to the structure of the vestibular nerve could explain the absence of responses on caloric stimulation. Findings of beading along the distal portion of the vestibular nerve in the absence of such an extensive beading along the proximal portion, suggested that the pathology may be restricted to the distal portion of the nerve rather than the central portion. Thus, the central oculomotor pathways may not have undergone such changes. This correlates with the reports of normal functioning of subjects with ANSD on saccades, gaze and optokinetic tests (Starr *et al*., 2003; Abdel-

Nasser, Elkhayat, Khalil & Mahmoud, 2006; Sheykholeslami *et al*., 2000; Sheykholeslami, Schmerber, Kermany & Kaga., 2005)

A subsequent study by Sheykholeslami et al., (2005) revealed the absence of the involvement of the superior vestibular nerve and its end organ, the semi circular canal, in one subject with isolated ANSD. In the subject, caloric stimulation elicited a normal response in the presence of normal functioning on other central and peripheral ENG tests. Thus, these studies suggest that in ANSD patients who do not present with peripheral neuropathy, the vestibular system status also demonstrates a range of variability.

Review of the literature revealed some further reports on the association of vestibular neuropathies in cases of ANSD. This association seems to be independent of the presence or absence of associated neuropathic diseases. One such study on a large population of individuals with ANSD was conducted in 2006 by Abdel-Nasser, Elkhayat, Khalil & Mahmoud. They assessed 50 individuals with ANSD with a series of tests to assess the vestibular functioning. Bithermal caloric irrigation revealed that 30% patients of ANSD subjects had bilaterally reduced caloric response while 14% had bilaterally absent caloric response. In totality, 44% of ANSD subjects had bilateral extensive peripheral vestibular lesion as evidenced by the absence of responses to bilateral caloric stimulation. Of the 50 individuals assessed, only 18% complained of dizziness and other vestibular symptoms. ANSD subjects also showed absence of spontaneous, gaze evoked, positional and positioning nystagmus. Oculomotor test revealed normal Saccade velocity, accuracy and latency. Eye tracking and optokinetic tests were normal. Taken together, it can be inferred that the central vestibular connections are normal in such individuals with ANSD while the peripheral nerve functioning is affected.

Certain types of degenerative peripheral neuropathies are associated with neuropathy of the vestibular nerves as well. One such condition is neurosarcoidosis,

wherein subjects are found to have inflammatory demyelinating neuropathic changes of the vestibular, auditory, and facial nerves and a concomitant degeneration of the vestibular and cochlear sensory structures. The audiological profile of such subjects fit the criteria established for ANSD. Caloric stimulation fails to elicit nystagmus responses in such subjects indicating bilateral vestibular dysfunction. (Babin, Liu, Aschenbrener, 1984; Von Brevern, Lempert, Bronstein, Kocen, 1997). Frohman, Tusa, Mark, Cornblath (1996) described a patient with inflammatory demyelinating polyneuropathy with fluctuating findings of oscillopsia and ataxia. Bithermal calorics were abnormally reduced. These results provide evidence that vestibular dysfunction occurs in association with certain types of degenerative neuropathies involving the peripheral nerves.

Kaga (2009) reported that ice water caloric stimulation failed to elicit any response on electronystagmography (ENG) and VEMPs were also abolished in 5 of the ANSD subjects. These subjects were therefore categorized to have 'auditory-vestibular neuropathy'. Three other subjects performed normally on the vestibular evaluations and were thereby diagnosed to have 'auditory neuropathy only'.

Recently, Sharanya *et al.,* (2011) also reported 3 subjects diagnosed as having auditory neuropathy who underwent an extensive vestibular assessment consisting of clinical tests of stability (Romberg, Fukuda stepping test), cervical vestibular evoked myogenic potentials and a standard electronystagmography test battery. In the study, the entire subject population assessed showed hypofunctional caloric responses and absent VEMPs. Two out of the three subjects were asymptomatic of vestibular dysfunction. On the clinical tests of stability, two subjects showed deviations to the right, while one subject performed normally. The authors concluded from the study that individuals with auditory neuropathy may have associated abnormality of the superior and inferior vestibular nerve.

The authors also suggest that the subclinical manifestation of the vestibular neuropathy points to compensatory changes occurring over time.

2.5.1 ENG findings in children with ANSD.

Konradsson (1996) described the results of vestibular assessment carried out on 4 children with severe sensorineural hearing loss and normal otoacoustic emissions, Electrocochleography recordings. The children did not have any vestibular symptoms. ENG battery consisting of bithermal caloric tests as well as tests of pursuit and voluntary saccades and optokinetic nystagmus was administered. The recordings obtained in all the tests for the 4 subjects were similar to those obtained in normal individuals. The authors suggest that the subjects in the study may have had a pure ANSD affecting their auditory system without vestibular involvement. Akdogan , Selcuk, Ozcan, Dere (2008) assessed 3 individuals with ANSD in the age range of 4-5 yrs whose audiological profile yielded results typically as found in individuals with ANSD. Caloric responses were reported to be normal in all three individuals assessed. Based on their study, Fujikawa & Starr (2009) suggested that vestibular neuropathy in patients with auditory neuropathy was a late manifestation.

2.6 VEMP findings in individuals with ANSD

One of the earliest studies which employed the use of VEMP to obtain information on the status of the saccule and its innervations, the inferior vestibular nerve was Sheykholeslami et al's study in 2000. They assessed 3 individuals diagnosed to have ANSD in the absence of peripheral neuropathy. Rectified VEMP recordings were carried out for 500Hz air conducted tone stimuli. The VEMP responses obtained were abolished for all the subjects in both the ears suggestive of the involvement of the inferior vestibular nerve in addition to the auditory nerve in the subjects.

The extent of involvement of the inferior vestibular nerve mimics the variability seen in the auditory symptoms and findings in subjects with ANSD. The ensuing single case study by Sheykholeslami et al., 2005 wherein VEMP was carried out revealed normal VEMPs in the right ear and an absent VEMP response in the left ear. Those results, in conjunction with normal caloric responses in both ears led to the conclusive presence of a unilateral sacculo-collic neuropathy accompanying bilateral ANSD. of The authors noted that vestibular involvement could range from normal functioning to complete vestibular areflexia and involvement of only a single part of the vestibular apparatus, such as the sacculus and its innervations, the inferior vestibular nerve.

Absence of cervical VEMPs was reported in 16 out of the 20 ears of individuals with ANSD assessed (Kumar, Sinha, Singh, Bharti & Barman., 2007). Kumar et al. (2007) reported that either the VEMPs were absent or prolonged in latency and reduced in amplitude in 80% of the ears tested in the study. Kumar et al. (2007) also suggested that the term "acoustic neuropathy" be used to indicate those patients in whom only the acoustic nerve is affected and "vestibuloacoustic neuropathy" to label those patients who also show involvement of the vestibular system. The possible pathology resulting in the absence of VEMPs was attributed to the fact that the vestibular and cochlear branches are parts of the same fibre bundle system called the vestibulocochlear nerve, therefore making it likely that neuropathy in one branch of the nerve that is, the cochlear nerve, might extend to the other branch, the vestibular nerve.

A similar study, aimed at investigating the saccule and related neural pathways in ANSD was carried out by Sazgar, Yazdani, Rezazadeh & Yazdi., 2010. Eight patients (16 ears) with ANSD were tested for VEMPs. The obtained results were compared with a normal control groups. Participants in the study ranged in age from 21 to 45 years. VEMPs displayed normal responses in 3 ears and abnormal responses in all others,

including unrepeatable waves in 4 ears and absent VEMPs in nine ears. Apart from suggesting a dysfunction of the inferior vestibular nerve and its end organ saccule in ANSD, the study also highlighted the subclinical nature of the vestibular dysfunction. They suggested that vestibular symptoms reflect both the bilateral distribution of the disorder as well as the possible slow progression of vestibular neuropathy. In addition, the results demonstrated a centrally compensated decrease in the response of the vestibular end organs, which was associated with hearing loss (Sazgar et al., 2010)

The sole study dealing with cervical VEMP recordings in children with auditory neuropathy has been reported by Akdogan et al., 2007. They assessed 3 children in the age range of 4-5 years for sacculo-collic pathway paucity. The results revealed absence of repeatable VEMP responses in two out of the three subjects suggesting a sacculo-collic dysfunction in the two subjects. The obtained results, in conjunction with the presence of normal caloric responses in all 3 subjects led to the author's suggestion of the use of a comprehensive test battery involving both VEMP as well as ENG, in order to rehabilitate for the deficits at an early age.

To summarise, in individuals with auditory neuropathy it is likely that a neuropathic condition may involve the vestibular nerve also. Like the audiological findings in auditory neuropathy, vestibular findings also show a high variability. Also, in most of the cases with auditory neuropathy, pathology is restricted to the peripheral vestibular system rather than the central oculomotor system.

Chapter 3

METHOD

The study aimed at assessing the functioning of the peripheral and central vestibular pathways in individuals with auditory neuropathy and to report on the incidence of vestibular abnormality in such subjects. Additionally, it aimed at correlating the vestibular findings with the audiological profile obtained in subjects with auditory neuropathy spectrum disorder (ANSD).

3.1 Participants

Data was collected from a total of number of 52 participants. The participants were assigned to one of the two groups

- First group comprised of 26 individuals, 11 males and 15 females in the age range of 18 to 28years (mean =24.2yrs) with normal hearing sensitivity.
- Second Group comprised of 26 individuals, 10 males and 16 females in the age range of 13 to 42 years (mean = 21.8yrs) with ANSD.

For the ease of reading the first group will be defined as Normal Hearing individuals and second group will be defined as Individuals with ANSD throughout the report.

3.1.1 Subject Selection Criterion

3.1.1.1 Individuals with ANSD (Second Group)

- All the subjects were diagnosed to have bilateral ANSD based on the criteria of normal outer hair cell function as evidenced by the preservation of OAEs and cochlear microphonics; abnormal auditory brainstem evoked potentials beginning with wave I of the ABR; poor speech identification; and absent acoustic reflexes to ipsilateral and contralateral tones (Starr etl.,1996).

- The subjects were diagnosed to have sensorineural hearing loss.
- The subjects had UCL greater than 105dB HL for speech.
- They exhibited "A" type tympanograms with absent reflexes.
- No history or presence of middle ear pathology.
- Neurological examination indicated the absence of space occupying lesion.
- They did not present with a history of intake of vestibulotoxic drugs
- The subjects did not complain of any other illness prior to the testing.

3.1.1.2 Normal Hearing Individuals

- Subjects were diagnosed to have hearing sensitivity within normal limits in both ears (pure tone average of 500Hz, 1 kHz and 2 kHz less than ≤15 dB HL).
- The subjects had UCL greater than 105dB HL for speech
- They had "A" type tympanograms with reflexes present bilaterally.
- No history or presence of middle ear pathology.
- Neurological examination indicated the absence of space occupying lesion or significant neurological problems.
- The subjects did not have a history or present with vestibular complaints such as vertigo, giddiness, nausea, blurring of vision.
- Did not present with a history of intake of vestibulotoxic drugs
- The subjects did not complain of any other illness prior to the testing.

3.2 Test Environment

Testing was carried out in a sound treated room with ambient noise level within specified limits as per ANSI S3.1 (1991).

3.3 Instrumentation

- A calibrated two channel diagnostic audiometer, Madsen Orbiter 922 with TDH 39 headphones encased in MX 41AR ear cushion was used to obtain air-conduction thresholds and perform speech audiometry. Bone conduction testing was done using Radio ear B-71 BC vibrator.
- A Calibrated Grason Stadler Inc. - Tympstar middle ear analyzer (v 2.0) was used to assess the middle ear status and rule out middle ear pathology.
- ILO 292 V-6 was used for recording of otoacoustic emissions.
- Intelligent Hearing System (IHS version 4.3.02, with ER-3A Insert ear phone) was utilized for recording of auditory brainstem responses and vestibular evoked myogenic potentials.
- In order to carry out the electronystagmography test battery, RMS ENG instrument was used.

3.4 Procedure

The subjects underwent extensive audiological and vestibular evaluations consisting of the following.

3.4.1 Pure tone audiometry

Air conduction and bone conduction thresholds for all the subjects were established using the modified Hughson and Westlake procedure (Carhart and Jerger, 1959).Thresholds were obtained at octave intervals between 250 Hz to 8000Hz for air conduction and between 250 Hz to 4000 Hz for bone conduction.

3.4.2 Speech audiometry

Speech identification scores were assessed with using speech material developed by Vandana (1998) at an intensity of 40dB over the speech recognition threshold levels. A total of 25 speech stimuli were presented and were awarded 4% for every correct response.

3.4.3 Uncomfortable level (UCL)

Speech was presented through the head phones at different intensities using the ascending method to determine the uncomfortable loudness level of the subjects. The hearing level at which the subjects considered the speech material to be uncomfortably loud was taken to be the UCL for speech.

3.4.4. Immittance Evaluation

Tympanometry measurements were carried out using a probe tone frequency of 226 Hz at 85dB SPL. Reflex eliciting tone of 500, 1000, 2000, and 4000 Hz were presented ipsilaterally and contralaterally to measure reflex thresholds.

3.4.5 Transient Evoked Otoacoustic emissions (TEOAEs)

TEOAEs were recorded using non linear clicks presented at 80dBpeSPL. Responses to 260 sweeps were averaged to obtain the TEOAE response. Amplitude of the response as well as the noise level was measured and amplitude to noise ratio of 6dBSPL or more with a reproducibility of 80% or more was the criterion used to quantify the presence of a response (Glattke, Pafitis, Cummiskey and Herrer., 1995)

3.4.6 Auditory Brainstem Responses (ABRs)

Subjects were instructed to sit comfortably on a reclining chair and to relax during the testing. They were instructed to close their eyes during testing to avoid any artifacts. ABRs were recorded on the IHS system using an electrode montage of forehead (CZ) to the ipsilateral mastoid (test ear) and ground to contralateral mastoid (non-test ear). The amplifier band pass was set at 100–3000 Hz. Alternating polarity click stimuli (100μsec)

were presented monaurally at a rate of 11.1 Hz at 90 dBnHL. Averaged responses to1500 clicks were collected in 2 runs.

3.4.7 Vestibular evaluations

3.4.7.1 Case History and Administration of Maryland Dizziness Questionnaire.

A Detailed clinical history was obtained regarding the nature, frequency, and triggering mechanism of the vertiginous attacks. Information was also obtained regarding the existence of associated visual, neurological conditions along with pertinent medical history. Additionally, a part of the dizziness questionnaire developed by Maryland hearing and balance centre was administered. The questionnaire consists of 5 sections; only the 2nd section which pertained to the symptoms of dizziness was administered.

3.4.7.2 Cervical vestibular -evoked myogenic potentials (cVEMPs).

cVEMPs were recorded for all the subjects by averaging the acoustically evoked electromyogram of the sternocleidomastoid (SCM) muscle. The subjects were seated in an upright position and were instructed to turn their heads to the side opposite to the test ear to activate the SCM unilaterally. To control for movement related artifacts, subjects were instructed to not move their head and neck during the cVEMP recording. Visual feedback system available in the instrument was utilized during the recording in order to ensure that the subjects monitored the tonic EMG activity of the SCM and maintained it between 100% to 200 %(50μv to 100μv) to obtain optimum responses. Before placing the electrodes, the sites were cleaned using the skin preparation paste and silver chloride electrodes were placed with ten-20 conduction paste designed to increase conductivity. The electrode impedance was checked to ensure that the absolute impedance of each electrode site was within 5kohms and the interelctrode impedance was within 2kohms. The non-inverting electrode was placed at the midpoint of the SCM of the side being

evaluated and the inverting electrode was the sternoclavicular junction, with the forehead serving as the site for the ground electrode.

The responses were filtered from 30 Hz to 1500 Hz. Analysis time was kept at 70msec and a total of 100 stimuli with a repetition rate of 5.1/sec were presented at 95 dBnHL intensity in alternating polarity. Waveforms produced in response to tone burst stimuli were recorded twice to ensure reliability.

3.4.7.3 Electronystagmography (ENG).

The participants underwent an ENG test battery consisting of recordings of positional, positioning, gaze (30° lateral gaze) and caloric-induced nystagmus. Also, oculomotor system integrity was evaluated by means of saccadic and optokinetic test. The protocol followed while carrying out the ENG test is given un table 1.

3.4.7.3.1 Pre-procedural instructions.

The subjects were instructed in advance to avoid eating for at least four hours before the test, avoid consuming alcohol for 48 hours preceding the test. They were also advised to discontinue taking sedatives, hypnotics, antihistaminic, antivertigo medication medications for 48hrs prior to evaluations. The external ear canal was examined for wax, discharge, infection, perforation of the tympanic membrane.

3.4.7.3.2 Stimuli.

RMS ENG System which generates stimuli locked to the acquisition of the responses was utilized. The computerized system allowed for use of light-emitting diodes on a light bar placed at a distance of 1 meter away from the participant at the eye level. Saccadic and Gaze testing required target lights at specified distances of 10°and 30°in each direction from the centre. Optokinetic testing was conducted with a stream of red lights moving from an eccentric position towards the centre at the slow speed setting of the instrument. Caloric testing was carried out with 30ml of warm (44°) and cool (30°) water.

3.4.7.3.3 Preparation of the subject.

The electrode sites were cleaned with a skin preparation agent to remove grime so as to ensure good skin-electrode contact. Ten-20 conduction paste was then used and the electrodes were firmly applied to the respective sites. A single channel recording of horizontal eye movements was obtained by placing the non-invertng electrode to the skin of the temples 1.5-2cm lateral to the outer canthi of the right eye and the inverting electrode 1.5-2cm lateral to the outer canthi of the left eye. The ground electrode was placed on the forehead.

3.4.7.3.4 Calibration of the equipment.

Electrical calibration of the instrument was carried out before evaluating the subjects in order to translate the amplitude of the eye to microvolts. The subjects were seated facing a light bar and were instructed to follow the lights on the light bar as accurately as possible while keeping their head still. Randomly generated targets appeared on the light bar for 1 to 4 seconds within a range of 10° from centre before changing its position. The input sensitivity of the instrument was then adjusted in such a way that every 10^{o} of eye movement which corresponded to 10 mm movement of the recording paper generated a corneoretinal potential of 200μvolts in 1 sec. Thus, 1mm of needle deflection was equal to 20μvolts. Therefore, for a beat to be labelled as nystagmus, it must have amplitude of more than 1mm. The filter settings were such that responses were band passed between 0.01 to 30Hz.

3.4.7.3.5. Tests Carried out in ENG

3.4.7.3.5.1 Saccade test. The subjects were seated facing a light bar and were instructed to follow the lights on the light bar while keeping their head still. Randomly generated targets appeared on the light bar within a range of 10° towards the left and the right from the centre. The subjects were instructed to follow the lighted dots as accurately

as possible without moving the head. The saccade test is a central test used to assess the integrity of the oculomotor system.

3.4.7.3.5.2 Gaze test. For gaze testing, the subjects were instructed to look straight ahead and fixate on computer generated targets on the light bar. Fixation was maintained for approximately 30 seconds in centre gaze and for the same duration in eccentric gaze (30° to the left or right).

3.4.7.3.5.3 Optokinetic tracking Test. To assess the central optokinetic system, the subjects were instructed to track the red lighted dots across a light bar, which moved centre ward from an eccentric position of 30° (left/right). Recordings of the tracking were obtained for 30 secs for leftward as well as rightward movement.

3.4.7.3.5.4 Positional test. The purpose of positional testing is to assess the functioning of the otolith organs. During the test procedure, the subjects were made to go through four different static head and body positions and recordings were obtained for 30 secs in each of the positions. The positions included sitting, supine, supine with head turned to lateral right and lateral left.

3.4.7.3.5.4 Positioning test. The positioning test is administered to earmark a diagnosis of Benign positional paroxysmal vertigo. The subjects were seated on the examination table and recordings were performed for 30secs with the eyes closed. The subjects were then assisted in turning their heads towards the test ear 45° away from the midline and 20° extended backward while the clinician provided support to the participant's neck and back. Maintaining the same position, the participants were assisted briskly to a supine position with the head hanging to the right. They were left in this position for a period of 30 seconds while eye movements were recorded. The subjects were again brought back to sitting position and were observed for nystagmus for about 30

seconds. The manoeuvre was then repeated for the head hanging position with the head turned towards the opposite side.

3.4.7.3.5.5 Caloric testing. The subject was made to lie supine on the table and the head end of the table was elevated to 30° above the horizontal. Caloric stimulation was provided through monaural open loop water irrigation of the external ear canal at temperatures of 30°C and 44°C for duration of 30 seconds per incident. 20ml of fluid was measured out in a syringe and was irrigated over a period of 30secs. The returning liquid was collected in a dish placed under the subject's ear. The order followed to irrigate the ear canal was Right ear warm (RW) followed by Left ear warm (LW) and Right ear cool (RC) followed by Left ear cool (LC). Immediately after irrigation recording was started and were made for approximately 2 minutes while the subjects were given simple mathematical calculations or were asked to answer simple questions as a mental diversion task. Time gap of approximately 5 minutes (ANSI, 1999) were given between the irrigations, so as to avoid effect of preceding irrigation on the later. A gap of 8 minutes was given between the cool and warm conditions. Cumulative frequency was calculated by manual marking of obtained nystagmus recordings. Table-2 shows the protocol used for recording of the ENG

Table 3.1

Recording protocol for Electronystagmography

Parameters	ENG
Band-pass filter	.01 Hz to 30 Hz
Notch	On
Gain	Gain of the incoming signal adjusted in such a way that 10 mm deflection of recording pen represents 200 μv of corneoretinal potentials
No. of channels	1
Electrode placement	Noninverting electrode (+): Outer canthus of the right eye Inverting electrode (–): Outer canthus of the left eye Ground electrode: Forehead

3. 8 Analysis

Analysis of cVEMP

The absolute latency of p13and n23 responses and amplitude of p13-n23 complex was noted for the two groups of participants.

Inter-ear amplitude asymmetry was calculated for p13-n23 complex by using the following formula-

$$\frac{[\text{Right ear amplitude - Left ear amplitude}]}{[\text{Right ear amplitude + Left ear amplitude}]} \times 100$$

Analysis of ENG

Saccade test: The obtained recordings were analysed with respect to their morphology as well as symmetry to the directions.

Gaze test: It was analysed based on

1. Presence or absence of nystagmus in the gaze centre position
2. Presence of right beating nystagmus in the right lateral position with no nystagmus in the left lateral position of gaze and vice versa
3. Presence of direction changing or direction fixed nystagmus within any of the gaze conditions.

i.e. presence or absence of spontaneous nystagmus (centre gaze); presence, absence, or exacerbation of nystagmus with addition of off-centre gaze tasks.

Optokinetic test: The results obtained for the two directions i.e. rightward to centre and leftward to centre were analysed based on their symmetry and equality of the obtained responses as well as its morphology. For a given speed of stimulus, the intensity of the right beating nystagmus recorded was compared to the left beating nystagmus.

Positioning test: The analysis of the recordings of the positional tests were based on the presence or absence of nystagmus, and if present, on their direction.

Positional test: the recordings obtained in the positional test, in its various positions were analysed for the presence of nystagmus and their direction (direction fixed or direction changing)

Caloric test: The cumulative frequency was chosen as the parameter to be represented on the butterfly chart .The response waves obtained in the 4 conditions

were analysed and the cumulative frequency was calculated. In order to calculate it, the recordings were divided into 10sec intervals. The 3 adjacent intervals having the most number of nystagmus beats, as determined by manual calculations in each 10sec interval, was considered. Thus, the cumulative frequency represented the total number of beats present over a 30sec period. This was done for the normal as well as the experimental group. The data of the normal group was utilized to determine the normative range of the claussen butterfly chart for the 4 conditions. The obtained frequencies for the 4 recordings in the control group were then plotted on the butterfly chart established for the normal's. The measured cumulative frequency for the clinical group was then measure and plotted on the obtained butterfly chart obtained from the control group.

Statistical Analysis

The statistical analyses carried out were-

- Descriptive statistics for the determination of mean, standard deviation and range of absolute measures of p13, n23 latency and p13-n23 complex amplitude.
- Determination of range of nystagmus beats for the 4 caloric recordings.
- Chi-square test to find out the association between the configuration of hearing loss and the caloric response pattern and presence /absence of cVEMP responses.

Chapter 4

RESULTS and DISCUSSION

The present study was undertaken as an attempt at determining the incidence of vestibular dysfunction in individuals diagnosed to have auditory neuropathy. This involved assessing the functioning of the vestibular system, peripheral as well as central, in individuals with auditory neuropathy in comparison to normal hearing individuals. The study also aimed at correlating the vestibular findings with audiometric findings such as type and configuration of loss.

In order to achieve the abovementioned aims, relevant data obtained from the two groups containing 26 individuals with normal hearing and auditory neuropathy was subjected to measures of descriptive statistics and correlations using SPSS (Statistical package for social sciences).

4.1 Vestibular test findings in the control group

4.1.1 Cervical vestibular evoked myogenic potentials- cVEMP

Recording of rectified cVEMP was possible in all the subjects who formed the control group. The following parameters of the obtained responses were analysed- latency of p13, n23; amplitude of the p13-n23 complex and the resulting amplitude asymmetry between the two years. Bilateral cVEMP recordings for one participant in the control group in response to the 500Hz tone burst stimuli presented at 99 dB nHL is shown in figure 4.1.

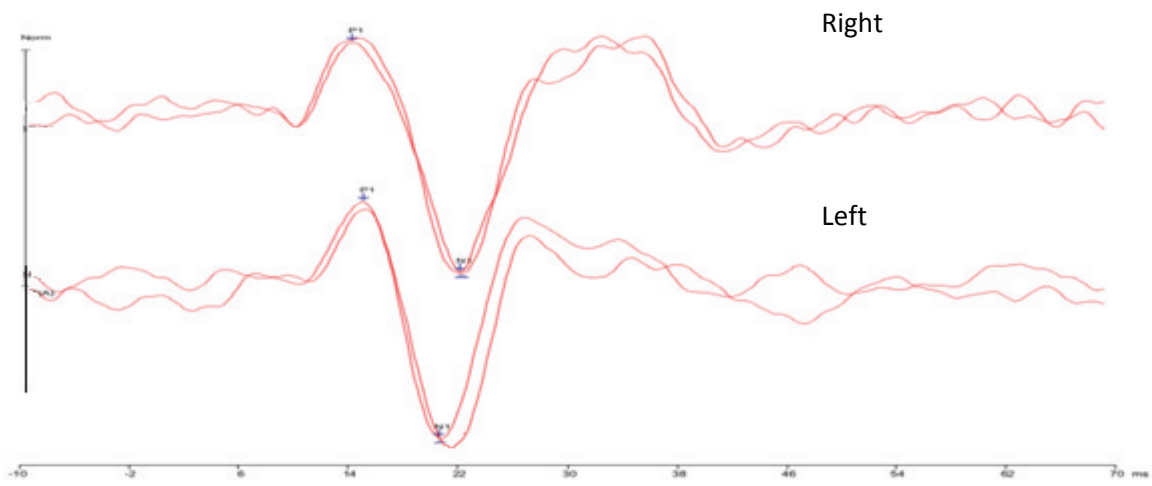

Figure 4.1 : cVEMPs response of one control group participant

Descriptive analysis of the obtained data was done to determine the mean and standard deviation (SD) of the latency as well as amplitude complex of the p13, n23 responses. The obtained results is as shown in table 4.1

Table 4.1

Mean, standard deviation (SD) values and range of latency and amplitude measures of cVEMPs in control group

Parameters	Mean	Standard deviation	Range
P13 latency (msec)	15.33	1.17	13.60 - 17.60
N23 latency (msec)	22.33	1.98	18.80 - 27.20
Amplitude of p13-n23 complex (µv)	44.10	18.71	19.73 - 88.60
p13- n23 complex inter-ear amplitude Asymmetry (%)	15.06	9.23	3.41 - 34.60

The results obtained from the preset study suggest that the percentage of occurrence of cVEMP in individuals with normal hearing sensitivity and no episodes of vestibular dysfunction is 100%. Sheykholeslami, Murofushi, Kermany, & Kaga (2000) also measured air conducted VEMPs in individuals with normal hearing sensitivity and reported of its presence in all the subjects assessed. Kerdsiri, Thongyai, Chongvisal, Atipas, & Imviriyakul (2010) also reported of 100% occurrence of cVEMPs in the 40 normal hearing individuals assessed by them. Unlike in the current study, a lesser percentage of occurrences of cVEMPs in normal hearing individuals 86% were reported by Isaradisaikul, Navacharoen, Hanprasertpong & Kangsanarak (2012). The difference in percentage of occurrence can be attributed to the stimulus intensity parameters not being intense enough. The stimulus intensity used in the study was 120 dBSPL, which is less than that used in the current study (125dBSPL). Additionally, the mean ± standard deviation of the threshold was reported to be 100–115.1 ± 4.6 dBSPL, which again suggests that perhaps the lowered stimulus intensity may have caused the lowered incidence. However, at the vestibular clinic at AIISH, using parameters similar to the current study, Saravanan (2012) also reported of 100% occurrence of cVEMP in normal hearing subjects.

The latency of the p13 and n23 obtained in the current study were 15.33ms (±1.17) & 22.33 ms (±1.98) respectively. The obtained values are similar to those obtained in other studies such as by Isaradisaikul et al. (2012) who reported of latencies of p13 and n23 being 15.99 (± 2 .04) , 23.08 (± 1 .50) ms respectively. Wu, Shiao, Yang, & Lee (2007) assessed 22 individuals with normal hearing sensitivity and stated that the p13 and n23 peaks occurred at 14.83 (± 0 . 8 1) & 22.54 (± 1 . 30) in the subjects tested. Saravanan (2012) obtained latencies similar to that obtained in the current study with p13 occurring at 15.10± 1.24 ms and n23 at 22.45 ms ± 2.05.

The p13-n23 complex amplitude obtained in the control group was 44.10 ± 18.71 µv. The amplitude measure obtained is not in agreement with the scores obtained in other studies, such as by Welgampola and Colebatch (2001) in whose subject's complex amplitude measures were recorded to be 72.5± 46.8 µv. Such a difference could be attributed to differences in the population size, with Welgampola and Colebatch (2001) having recruited nearly 70 subjects as well as differences in the instrumentation in the two studies. Saravana (2012) who used the same instrument as was used in this study obtained amplitude values of 40.39µv (±12.66) which is almost similar to that obtained in the current study.

4.1.2 Electronystagmography test battery

4.1.2.1 Peripheral sub-tests.

4.1.2.1.1 Positional test.

In the positional test, out of the 26 subjects assessed, only 3 subjects had nystagmus tracings. Of the recordings in the 3 positions assessed, nystagmus was recorded in either a single position or two, but never at all three positions. The number of nystagmus beats recorded was a maximum of 19 beats during 30 sec duration in all the 3 subjects. The subjects did not complain of any perception of dizziness or vertigo like characteristics during the testing process. Figure 4.2 is a tracing of the recording obtained during positional testing in one subject belonging to the control group.

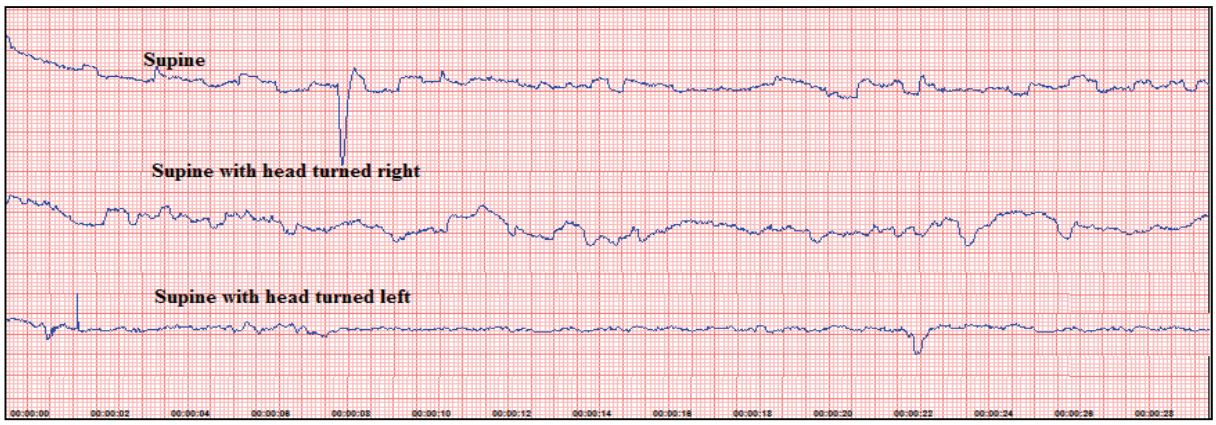

Figure 4.2. Tracing of response obtained in 1 subject from the control group for the positional test. The figure shows absence of nystagmus beats.

4.1.2.1.2 Positioning test.

5 of 26 subjects were found to have nystagmus beats in the recordings obtained on carrying out the Dix Hallpike test. Out of the 4 positions that the recording was carried out in, resulting nystagmus beats were evident in not more than 3 positions. The presence of the nystagmus beats were in less than 3 of the 4 positions that recordings were carried out at. The maximum number of nystagmus beats recorded was 19 in 30 sec analysis duration in all the 3 subjects. The subjects did not complain of any perception of dizziness or vertigo like characteristics during the testing process. Tracing for positioning test is shown in figure 4.3.

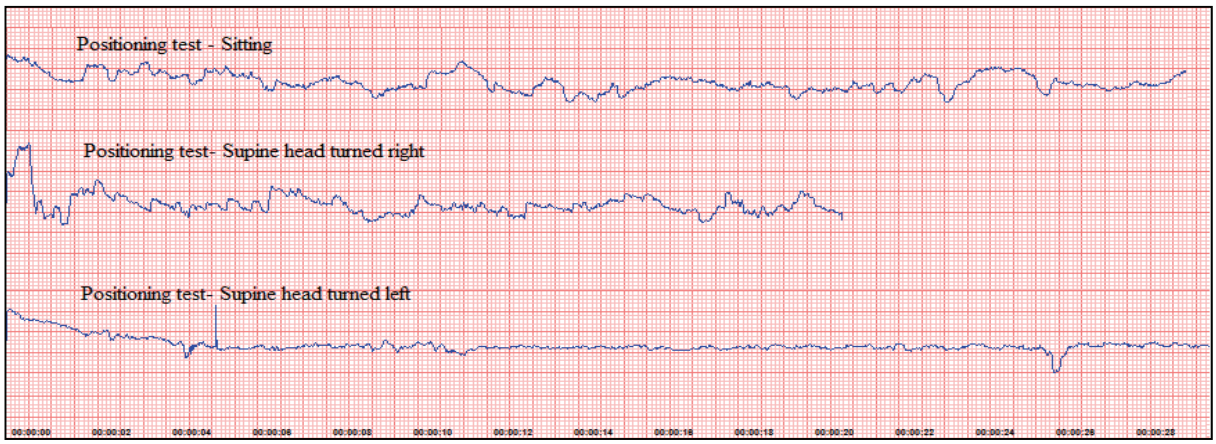

Figure 4.3. Tracing of 1 participant from the control group for the positioning test. The figure shows absence of nystagmus beats

Most of the studies reported in literature have interpreted the results of the positional and positioning test based on the intensity of the nystagmus beats and have arrived at a criteria of 6°/ sec. That is, the presence of nystagmic beats, geotropic or ageotropic; persistent or intermittent with intensity greater than 6°/ sec is considered as cause for indication of possible dysfunction along the vestibular system (Barber & Wright, 1973). Since the instrument used in the current study was incapable of calculating the intensity, the number of beats obtained per second in the 26 subjects is taken to be the normative criteria for the two tests.

In the positional test, nystagmus beats were observed in 11.53% of the control group. The observed beats were intermittent and geotropic in the 3 subjects with a maximum of 19 beats / 30 second occurring in less than 2 of the 3 positions. In the positioning test, 19.23% of the control group exhibited geotropic nystagmus, with number of beats not exceeding 19 per 30 second. Previous reports indicate that 82% of healthy individuals experience nystagmus during positional testing (Barber and Wright, 1973; Barber and Stockwell, 1976). This high percentage could be due to the methodology used in Barber and Wright's (1973) study, wherein a computerized chair was used, as well as the parameter assessed, which was intensity .

4.1.2.1.3 ***Caloric test.***

Evaluation of the responses obtained to bithermal caloric stimulation in all the subjects carried out yielded cumulative frequencies for the 4 stimulations. The range of the cumulative frequency was then determined for each of the conditions, taking into consideration the two stimulation temperate (warm and cold) and the two stimulation sites (right ear, left ear). The range of the cumulative frequency, measured by taking the highest and the lowest number of nystagmus beats, is illustrated in the table below. The obtained range of cumulative frequency from the 26 subjects was then used to derive the butterfly

chart against which analysis of the obtained nystagmus for the experimental group was carried out.

Table – 4.2

Range of culmination frequency (beats/30 seconds) for the 4 caloric stimulation in the control group

Stimulation temperature	Cumulative frequency (beats/ 30 sec)
Right warm	20-59
Right cold	20-70
Left warm	21-58
Left cold	22-64

Figure 4.4 is a tracing of the waveforms from the 4 stimulations considered for calculation of the cumulative frequency in one subject from the control group. Figure 4.5 is the resulting butterfly chart for the same subject.

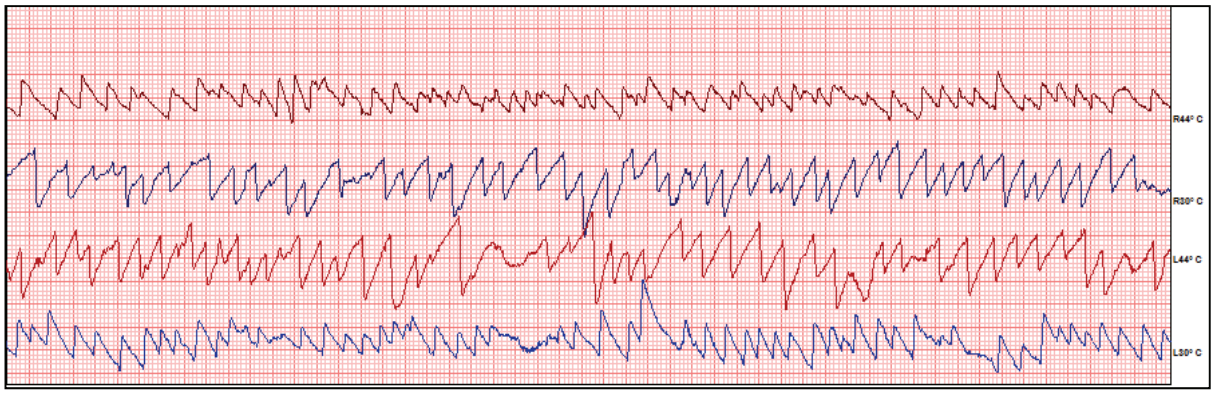

Figure 4.4. Tracing of one subject obtained in caloric testing. Figure 4.4 shows the presence of nystagmus beats in all the four recordings.

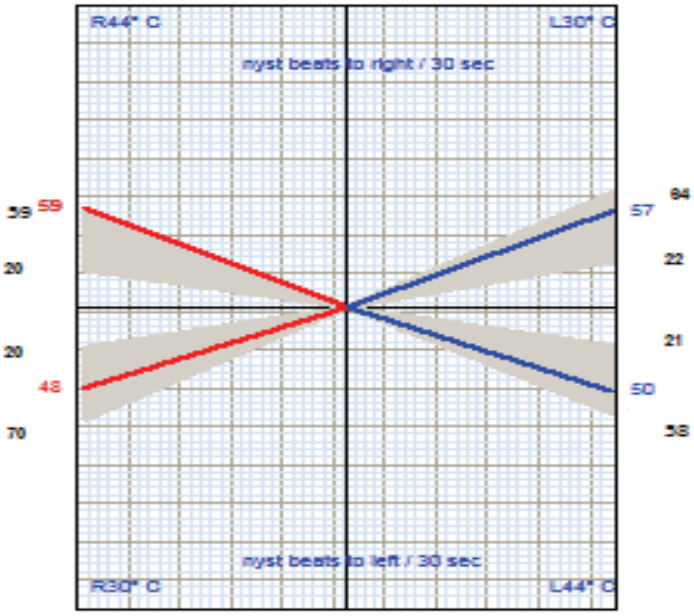

Figure 4.5. Butterfly chart of one subject from the control group. Butterfly chart shows a normal pattern.

The range of nystagmus beats obtained in the current study varies marginally from that reported by Kirtane in 1979. The ranges for the RW, RC, LW, LC stimulations obtained were 22-59; 23-63; 24-67; 27-68 respectively. Additionally, it was reported that stimulation of the left ear yielded more number of nystagmus beats than did the right, this was not evident in the current study. The obtained differences could be attributed to the smaller population size considered here as well, as compared to the 105 subjects used in the previous study mentioned. Additionally, factors such as the mode of irrigation as well as the instrument utilized may have resulted in the variations in this study as compared to Kirtane (1979). While the current study utilized the syringing method to introduce the fluid, the abovementioned study incorporated the use of a 3 mm diameter catheter introduced deep into the external auditory meatus. On the other hand, Saravanan (2012) reported values similar to that obtained in the current study in his study carried out at the vestibular clinic at the All India institute of speech and hearing. The

values obtained for the RW, RC, LW, LC stimulations were 22- 59; 21- 51; 20-70; 22-64 respectively.

4.1.2.2 Central sub-test.

4.1.2.2.1 Saccade test.

In all the individuals assessed, the recordings of the saccade test revealed responses with appropriate latency morphology to the stimulation. There were no instances of hypermetric or hypometric saccades and the recordings were free of ocular flutter. There was no gross asymmetry in the observed responses. This is in line with the results for the saccade test described by Kirtane (2009) who reported that normal individuals stop precisely at the target each time without evidences of overshooting or undershooting. Tracing obtained in one subject from the control group is shown in figure 4.6

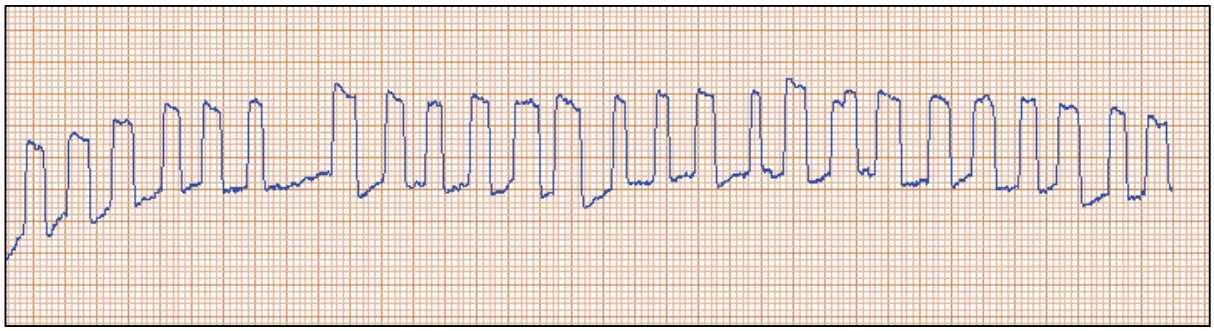

Figure 4.6 Tracing of response to saccade test in one subject from the control group

4.1.2.2.2 Gaze test.

The responses obtained upon carrying out the gaze test in three direction – centre, left lateral (30°), right lateral (30°) were visually analysed. The recordings indicated the absence of spontaneous nystagmus (centre gaze) as well as absence of nystagmus beats in the off-centre gaze tasks which are designed to stress the system. Similar findings in normal subjects have been reported by Kirtane (2009), and Barin (2011) wherein the authors suggested that the absence of nystagmus in the left or right 30° lateral position is

considered to be normal. The obtained tracing to the three instances of the gaze test in one subject is shown in fig 4.7

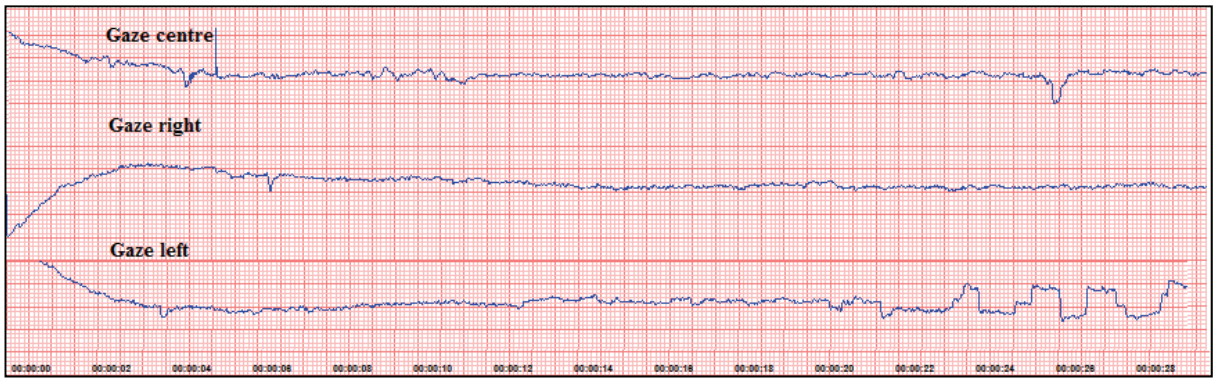

Figure 4.7. Tracing of one participant in the control group for centre, right and left gaze position. Figure shows absence of any nystagmus beats.

4.1.2.2.3 Optokinetic test.

In the optokinetic task, analysis of the recordings revealed that all the subjects were found to have symmetrical responses for visual targets moving from the lateral-30° (right, left) position to the midline (0°). This is in agreement with the response findings described by Kirtane (2009) in normal subjects. The figure 4.8 below illustrates the symmetry of obtained responses of one subject to optokinetic stimulation in one subject.

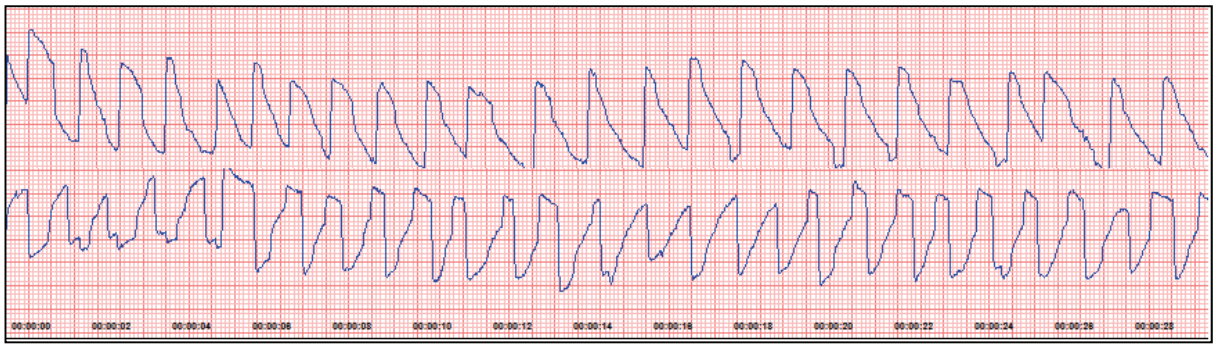

Figure 4.8. Tracing of one participant in the control group for optokinetic stimulation (Right to centre and left to centre)

4.2 Vestibular findings in experimental group

The experimental group consisting of 26 individuals with ANSD were subjected to the vestibular test battery described previously. Of the 26 individuals, 2 of the subjects were diagnosed to have peripheral neuropathy in addition to neuropathic involvement of the VIII cranial nerve. The duration of auditory symptoms in the subjects ranged from congenital conditions to as recent as 2-3 months prior to diagnosis. The results of the auditory test battery, based on which the subjects were diagnosed to have ANSD is provided in table 4.3.

Table 4.3

Findings of auditory test battery in subjects with ANSD

Sl.No	Age(years) /Gender	Duration of auditory Symptoms	Ear	Air conduction thresholds (dB HL)					SIS (%)	Immittance/ Reflexes	OAE	ABR
				250Hz	500 Hz	1KHz	2 KHz	4 KHz				
1	21/M	11 ½ years	R	40	30	15	20	5	56	Ad/NR	+	-
			L	30	25	25	15	15	48	Ad/NR	+	-
2	19/M	6years	R	65	70	65	45	30	0	A/NR	+	-
			L	45	55	55	30	15	0	Ad/NR	+	-
3	22/F	6 months	R	50	35	45	45	45	0	As/NR	+	-
			L	35	40	40	40	35	0	A/NR	+	-
4	20/M	2 years	R	70	60	65	55	60	32	A/NR	+	-
			L	40	50	55	40	35	44	A/NR	+	-
5	20/M	7 years	R	90	75	70	70	75	72	A/NR	+	-
			L	65	50	50	30	30	84	A/NR	+	-
6	22/F	?congenital	R	90	110	110nr	110nr	110nr	CNT	As/NR	+	-
			L	80	105	105	110	105	CNT	As/NR	+	-
7	38/F	1 years	R	25	30	25	25	20	88	A/NR	+	-
			L	35	30	30	40	30	84	A/NR	+	-
8	17/F	1 years	R	45	45	20	15	20	94	A/NR	+	-
			L	60	60	40	30	20	84	A/NR	+	-
9	13/F	?congenital	R	60	70	80	85	80	CNT	As/NR	+	-
			L	80	90	85	95	80	CNT	As/NR	+	-
10	18/M	2-3 months	R	40	30	20	10	5	88	A/NR	+	-
			L	30	35	20	5	10	92	A/NR	+	-
11	19/F	8 years	R	70	75	70	80	85	40	A/NR	+	-
			L	50	50	65	65	65	44	A/NR	+	-
12#	27/F	R- 5 years L- 2-3 months	R	60	65	50	50	45	68	A/NR	+	-
			L	45	40	15	15	15	92	D/NR	+	-

13#	20/M	5 years	R	50	70	40	10	10	24	A/NR	+	-
			L	60	50	55	10	40	12	A/NR	+	-
14	32/M	2 years	R	60	60	15	15	15	88	As/NR	+	-
			L	75	65	55	50	50	60	As/NR	+	-
15	42/F	20 years	R	70	50	35	25	25	84	A/NR	+	-
			L	70	45	30	30	30	32	A/NR	+	-
16	21/M	3 years	R	30	20	20	35	40	88	Ad/NR	+	-
			L	30	25	30	35	35	100	A/NR	+	-
17	27/F	$1^{1/2}$ years	R	15	15	10	20	10	24	A/NR	+	-
			L	70	70	65	55	35	16	A/NR	+	-
18	15/F	2 years	R	50	50	55	45	50	CNT	As/NR	+	-
			L	45	50	50	40	40	CNT	As/NR	+	-
19	25/M	4 years	R	60	60	65	55	60	36	As/NR	+	-
			L	65	50	55	40	35	24	As/NR	+	-
20	19/F	6 years	R	75	80	85	65	70	CNT	As/NR	+	-
			L	75	75	75	60	30	CNT	As/NR	+	-
21	14/F	2 years	R	80	70	75	70	65	0	A/NR	+	-
			L	75	70	60	50	45	0	As/NR	+	-
22	15/F	4-5 years	R	75	55	45	25	30	72	As/NR	+	-
			L	25	40	25	30	40	84	A/NR	+	-
23	25/F	3 years	R	45	50	60	50	30	CNT	A/NR	+	-
			L	60	60	60	50	50	CNT	A/NR	+	-
24	15/F	4 years	R	50	45	35	40	40	68	A/NR	+	-
			L	55	55	45	40	25	64	A/NR	+	-
25	45/M	20 years	R	30	25	20	20	15	64	A/NR	+	-
			L	20	15	15	10	5	72	A/NR	+	-
26	16/M	5 months	R	45	35	30	25	15	76	A/NR	+	-
			L	10	10	5	15	10	84	A/NR	+	-

'#'- Subjects with associated peripheral neuropathy; nr- no response; CNT – could not be tested; A, As, Ad, D – Immittance patterns; NR- No reflexes; '+' OAEs present; '-' ABR Absent.

4.2.1 cVEMP results

cVEMP recording was carried out on all 26 subjects belonging to the ANSD group. The recordings were carried out in rectified mode for 25 of the 26 participants. 1 subject was unable to attain and maintain the necessary SCM muscle tension in order to carry out the recording in the rectified mode, to cater to this; assessment of the sacculo-collic pathway function was carried out in the unrectified setting. In the aggregate of 52 ears assessed, 50 cVEMP recordings did not contain replicable p13, n23 responses. In the remaining 2 ears, replicable cVEMP peaks found. Amongst the 2, one recording had p13, n23 latencies and p13-n23 complex amplitude measures which correlated with the normative data obtained from the control group. The second replicable cVEMP recording obtained had normal latencies of p13 as well n23, but the p13-n23 complex amplitude measured fell outside the normal range calculated, in particular, the lower amplitude limit. Thus, 96.15% (50 ears) of the ANSD population assessed showed an absence of cVEMP responses indicating a highly probable dysfunction along the sacculo-collic pathway and/or its innervating organ, the saccule. 1.9% (1 ear) of the subject group had a normal sacculo-collic pathway / saccule functioning unilaterally. The remaining 1.9% (1 ear) had abnormal n13-p23 amplitude complex indicating a possible dysfunction along the sacculo-collic pathway and an asymmetry in the function between the left and the right pathways and/or innervating organ, the saccule. The predominant pattern of cVEMPs recorded from ANSD individuals (absent response) is shown in figure 4.9

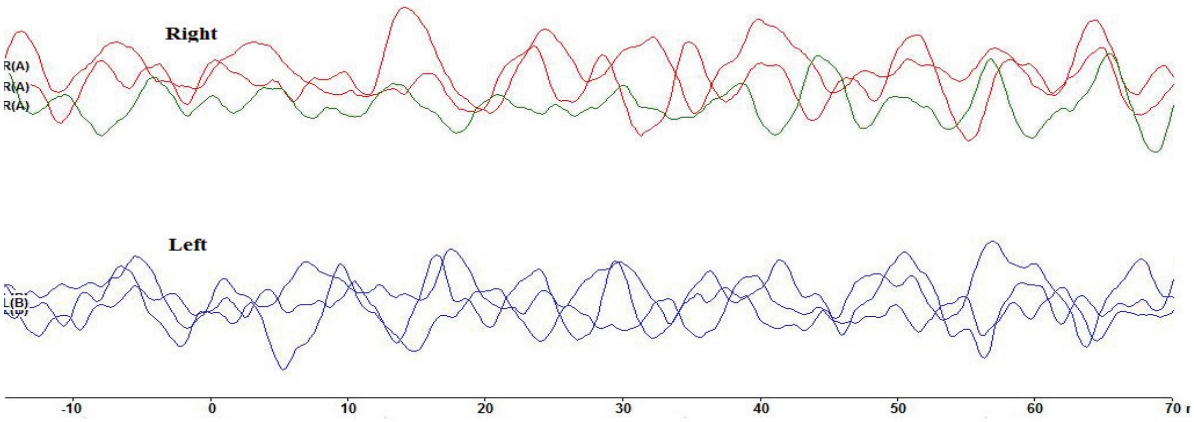

Figure 4.9 Absent cVEMP response to 500Hz toneburst at 95dBnHL in one subject with ANSD

A total of 98.05% of the subject population showed evidence of abnormal cVEMP responses inclusive of 50 ears with absent waveforms (96.15%) and 1 ear with low amplitude waveforms (1.9%). The obtained absence of responses could possibly be indicative of a dysfunction along the inferior vestibular nerve and/or its end organ the sacculus (Murofushi , Curthoys, & Gilchrist, 1996). Similar responses were obtained by Sazgar, Yazdani, Rezazadeh and Yazdi (2010) and Kumar, Sinha, Singh, Bharti and Barman(2007). Sazgar et al. (2010) demonstrated the absence of responses in 81.25 of the subject population assessed, while Kumar et al., reported of similar prevalence rates of 80%. The prevalence of dysfunction of the sacculo-collic pathway and/or its innervating structure in the current study is relatively higher than those previously reported. This could be due to the larger subject population assessed in the present study, with the former studies having assessed 16 and 20 ears respectively. Additionally, variability in the extent of the involvement of the pathway has also been noted. The degree of involvement ranges from normal functioning of the sacculo-collic pathway and the saccule to partial involvement in the form of unilateral dysfunction to complete areflexia. Complete absence of cVEMP responses in all the 6 ears assessed was reported by Sheykholeslami, Kaga, Murofushi, and Hughes (2000). On the

other hand, the study conducted by Sheykholeslami, Schmerber, Kermany and Kagain (2005), on a single subject with ANSD indicated normal functioning of the right pathway and absence of measurable response along the left pathway.

Such a deterioration of the sacculo-collic pathways functioning in individuals with ANSD has been hypothesized to occur due the commonalities shared by the auditory and the vestibular systems. There are similarities in cochlear and vestibular hair cell ultra structures in addition to the common arterial blood supply to the cochlea and vestibular end organs (Sazgar et al., 2010). As reported by Murofushi , Curthoys, and Gilchrist(1996), the absence of cVEMP responses indicates towards a pathology in either the saccule or its innervations, the inferior vestibular nerve, but Starr, Michalewski, Zeng, Fujikawa-Brooks, Linthicum, Kim, Winnier, and Keats (2003) in their cadaver study on subjects with ANSD reported that the sensory epithelium of the vestibular organs appeared to be normal. This could possibly eliminate the saccule as the site of dysfunction. Thus, the obtained findings could point towards the presence of the demyelination /axonal degeneration or a combination of both pathological conditions in the inferior vestibular nerve (Sheykholeslami et al., 2000; 2005).

Neuropathic involvement of the vestibular nerve was also noted by Starr et al. 2003 wherein beading of the nerve, along with fragmentation of myelin sheath was noted. Further, it was reported that the number of nerve fibres between the vestibular receptors and the vestibular ganglion was noted, this being in line with the reports of axonal degeneration. Demyelination results in the disruption of production as well as propagation of action potentials by the inferior vestibular nerve. This occurs due to a reduction in membrane resistance due to which the action potential does not spread very far before requiring regeneration (Starr, Picton, & Kim, 2001). This in turn leads to a reduction in conduction velocity. Besides that, a conduction block may also result in due to the absence ion channels in the unmyelinated region resulting in the inability to transfer the impulse to the subsequent

node of ranvier and therefore the conduction block. Axonal neuropathies are on the other hand characterized by maintenance of conduction velocity but reduction in the amplitude of the resulting action potential (Starr, Picton, & Kim, 2001). This translates to the inability of the neural pathway, i.e. the sacculo-collic pathway to generate an appropriate amount of potential necessary for response collection or the presence of a replicable response with reduced amplitude.

4.2.2 Electronystagmography test battery

4.2.2.1 Peripheral sub-tests.

4.2.2.1.1 Positional test.

In the positional test, out of the 26 subjects assessed, 4 subjects (15.38%) had nystagmus tracings. Of the recordings in the 3 positions assessed, nystagmus was recorded in 2 positions for all the subjects. The number of nystagmus beats recorded was below 19 per 30 sec duration in 2 subjects. The other 2 subjects (7.69% of the individuals) had 20 nystagmus beats in one position each, out of the two positions that nystagmus beats were observed in. The direction of the nystagmus recording was geotropic in one subject and was right beating in the other subject, recorded in the supine position. The number of beats recorded was 20 and 22 respectively in the two subjects. Throughout the testing process, the subjects did not complain of any perception of dizziness or vertigo like characteristics. Tracing for positional test depicting the response obtained in most of the subjects, absence of any beats, is shown in figure 4.10.

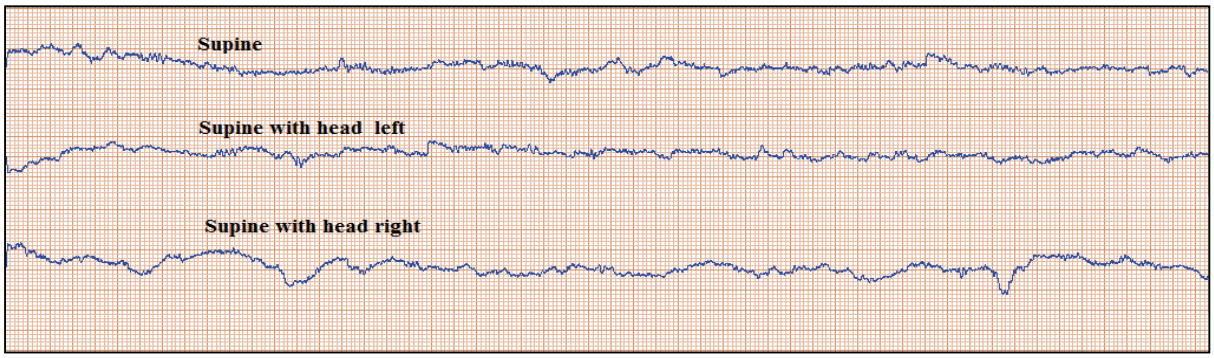

Figure 4.10 Tracing of positional test result in one subject from the experimental group.

Figure shows absence of nystagmus beats in the recording.

4.2.2.1.2 Positioning test.

In the Dix hallpike test, 8 subjects were found to have recognizable nystagmus beats. That is, 30.76% of the ANSD groups were found to have nystagmus recordings while assisted too the Dix hallpike positions. The number of positions that the nystagmus beats were observed in varied from 1 to all the 4 positions that the subjects were assisted to. Of the 8 subjects, significant number of beats was found in only 3 subjects (11.53% of individuals in the ANSD group), in one position each. The direction of the beats was geotropic in two of the subjects and was right beating in the sitting position that followed the supine head right position in the third subject. The number of beats ranged from 20 to 23 in the three subjects. The remaining 18 subjects did not present with any instances of nystagmic beats. None of the subjects, including those with significant number of nystagmus findings, complained of any perception of dizziness or vertigo like characteristics during the testing process. Tracing of one subject for positioning test is shown in figure 4.11.

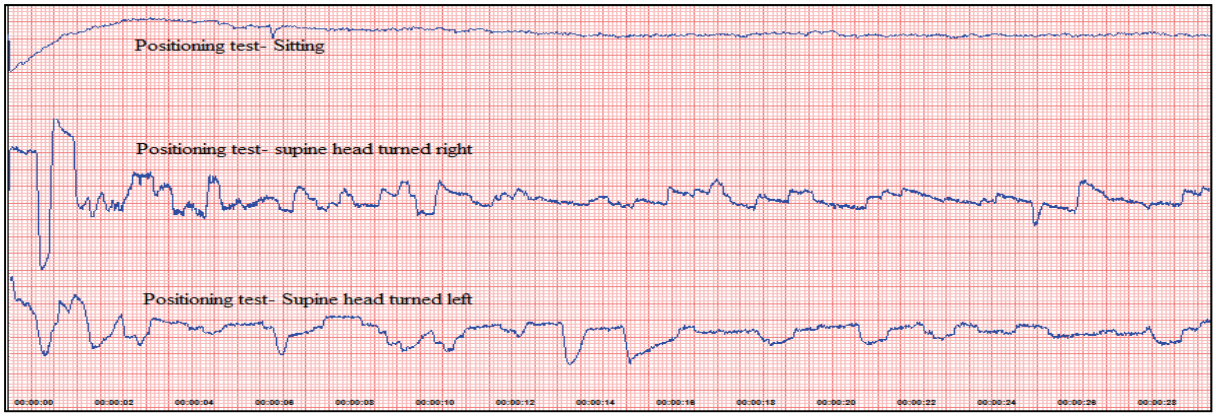

Figure 4.11 Tracing of peripheral subtest- positioning test in one subject with ANSD. Few nystagmus beats can be observed only in the second tracing.

4.2.2.1.3 Caloric test.

Caloric testing was carried out on 26 subjects diagnosed to have ANSD. The obtained 4 (RW, RC, LW, LC) recordings were analysed for geotropic or ageotropic nystagmus. The obtained results, when plotted against the normative data established revealed 3 patterns of

responses, hypoactive responses, hyperactive responses and responses within the normal limits. The most significant response was that of hypoactivity, with 86.53% (45 ears) of the individuals assessed presenting with it. A smaller percentage of the population, 5.76% (3 ears) showed responses that were outside the upper limit of the recording range and were therefore classified as having hyperactive responses. 7.69% (4 ears) of the ANSD group had responses that fell well within the normative range obtained for the control group. The 13.46% of the subjects who did display the presence of nystagmus beats on stimulation exhibited nystagmus responses that were consistent with that expected for the side as well as temperature of stimulation.

Taking into consideration the configuration of the vestibular dysfunction, it was estimated that bilateral hypofunction was the most common finding with 76.92% of the subject populace or rather, 20 individuals demonstrating bilateral hypofunctional dysfunction. 19.23% (5 subjects) of the individuals were found to have asymmetrical dysfunction in the caloric responses of which, 4 subjects (15.38%) has hypofunctional responses in one ear and responses within the normal range in the other ear. The 5th subject proven to have asymmetrical responses, had hypofunctional responses in one ear and hyperfunctional responses in the other ear. The remaining 1 subject (3.84%) from the ANSD group had bilateral hyperfunctional recordings. Ocular flutter was evident in the response tracings of 3 subjects in the ANSD group. Of the 3 subjects, one subject was diagnosed to have associated neuropathic condition of other peripheral nerves in addition to the VIII cranial nerve. The response tracing obtained by the ANSD group, ranging from hypofunctional to hyperfunctional have been represented in figure 4.12. Additionally, butterfly charts obtained for all the subjects with ANSD is depicted in figure 4.13a, 4.13b, 4.13c, and 4.13d.

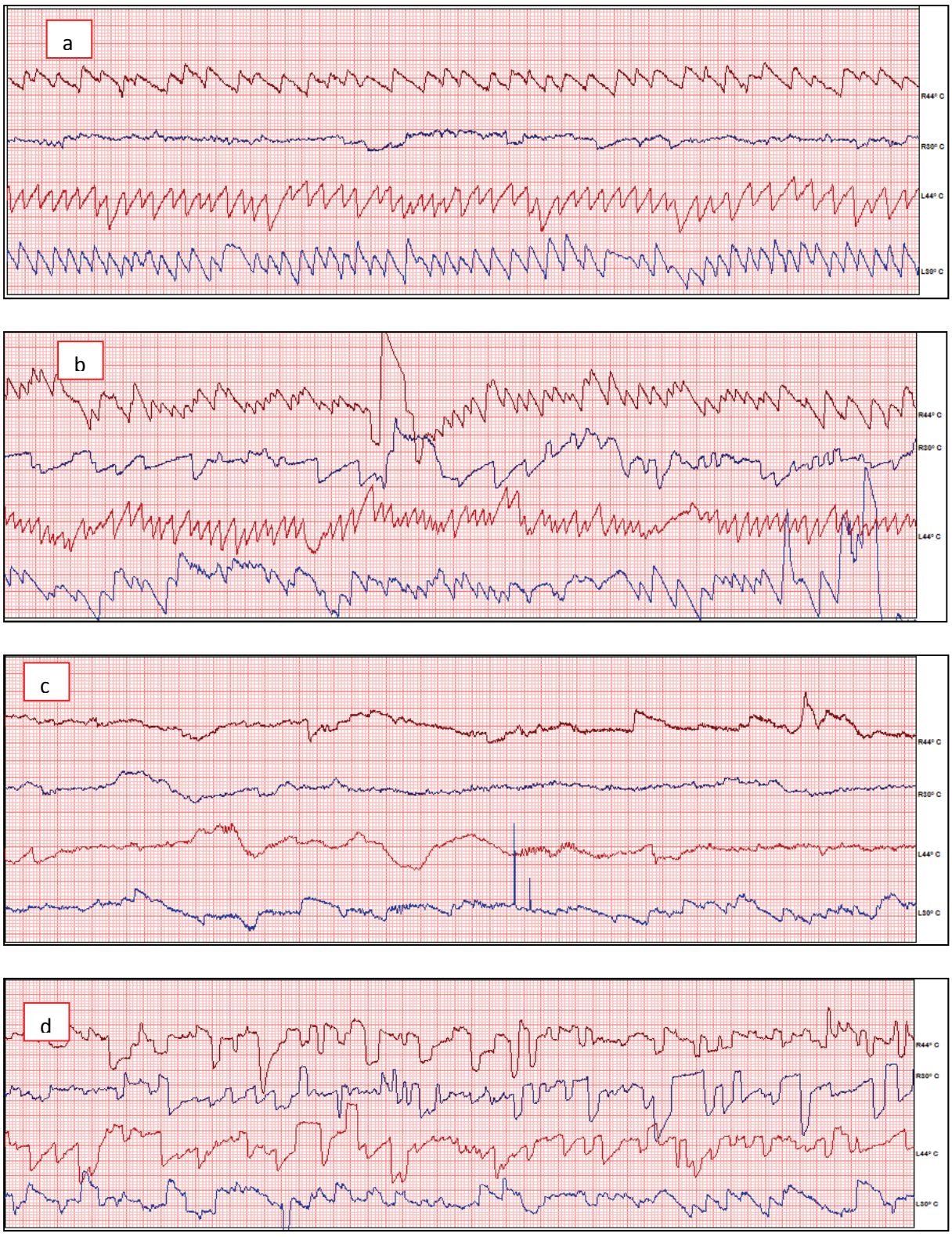

Figure 4.12. Tracings of subjects with a. Normal responses b. hyperfunctional, c. hypofunctional and d. ocular flutter.

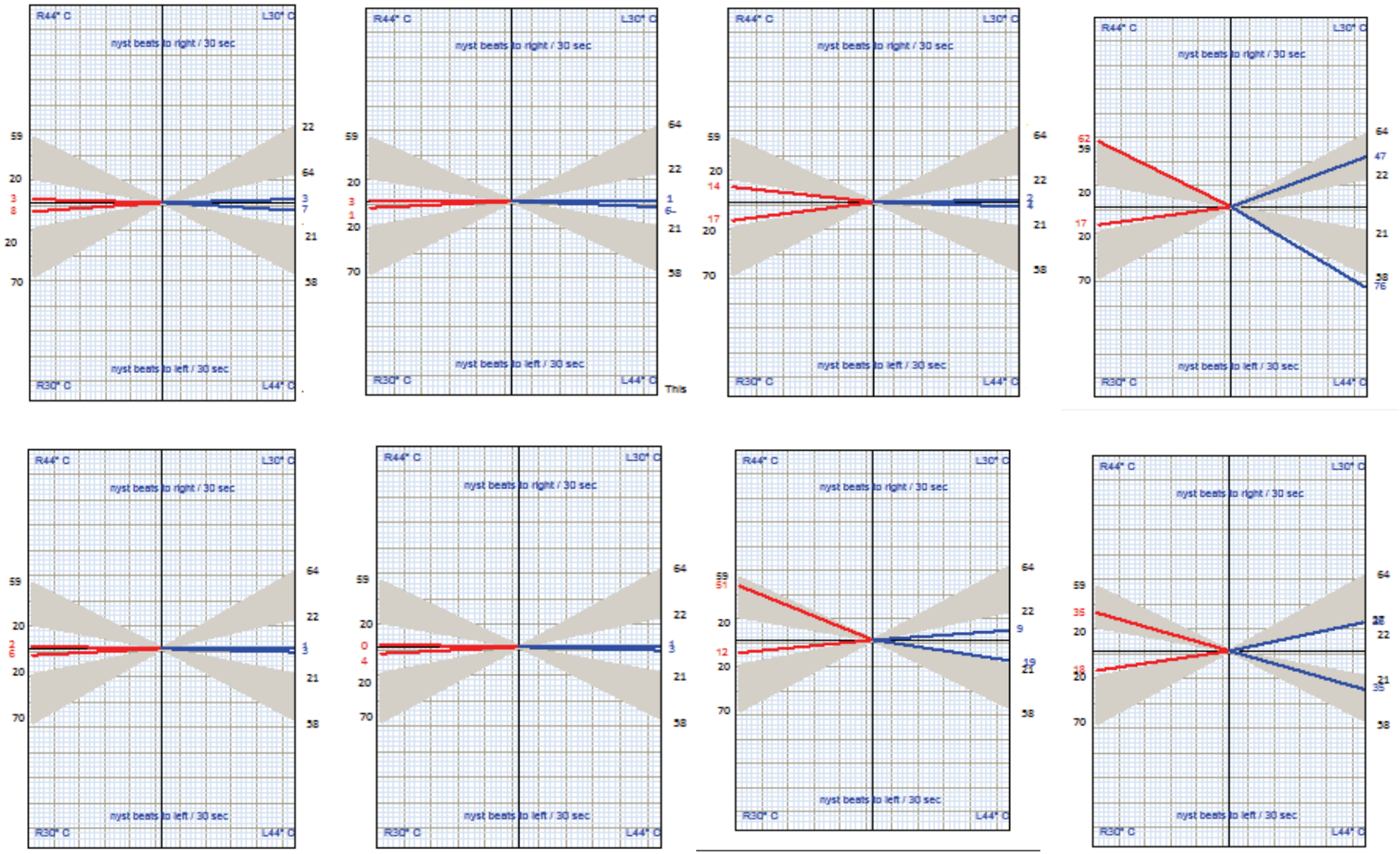

Figure 4.13a. Butterfly charts of 8 subjects from the experimental group.

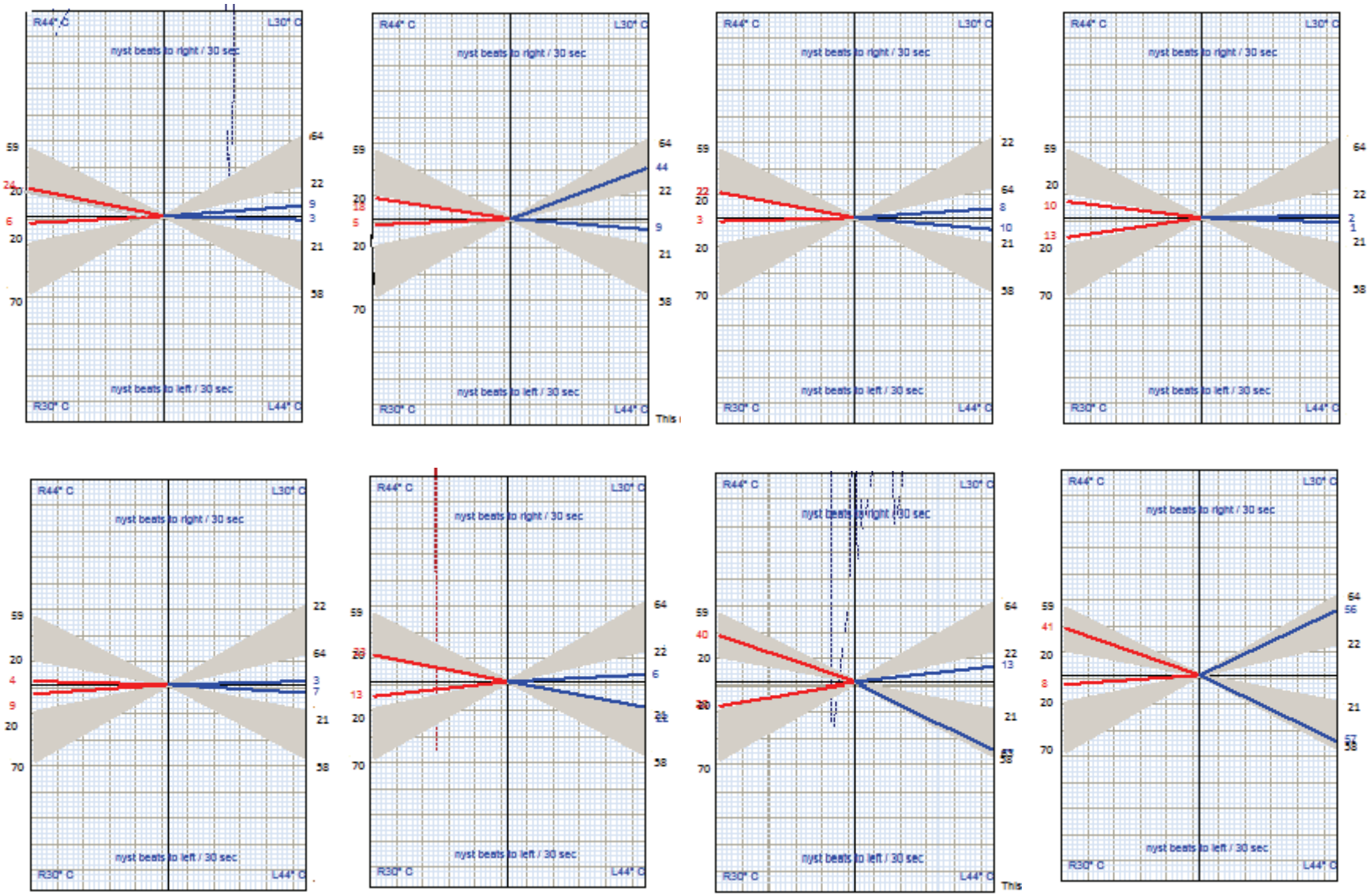

Figure 4.13b. Butterfly charts of next 8 subjects with ANSD

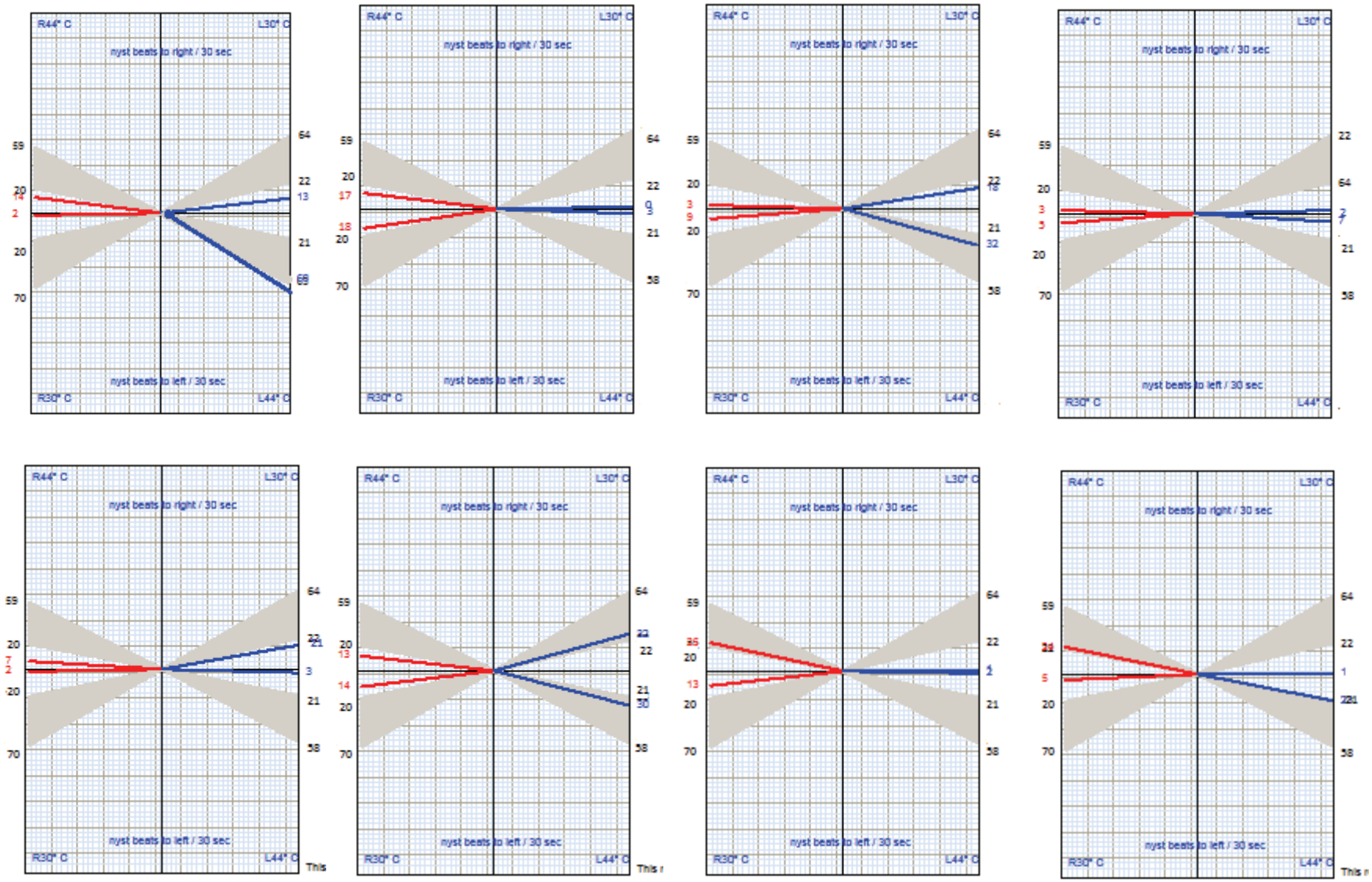

Figure 4.13c. Butterfly charts of 8 subjects with ANSD

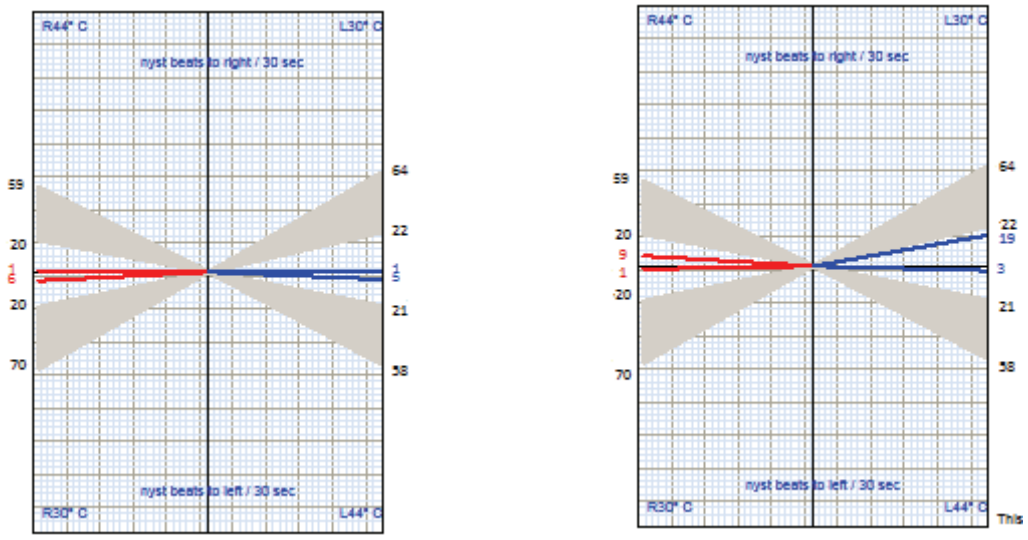

Figure 4.13d. Butterfly chart of 2 individuals from the experimental group

4.2.2.2 Central sub-test's.

4.2.2.2.1 Saccade test.

23 of the 26 subjects were able to follow the instructions for the saccade test and perform normally responses with appropriate latency and morphology to the stimulation. The recordings of 3 subjects were found to have ocular flutter in their responses. Ocular flutter is characterized by intermittent rapid bursts of horizontal oscillations without an intersaccadic interval. Amongst the 3, one subject had associated peripheral neuropathy. Apart from those, there were no instances of hypermetric or hypometric saccades in the data analysed. There was no gross asymmetry in the rest of the observed responses. The typical response obtained during the saccade test is shown in figure 4.14

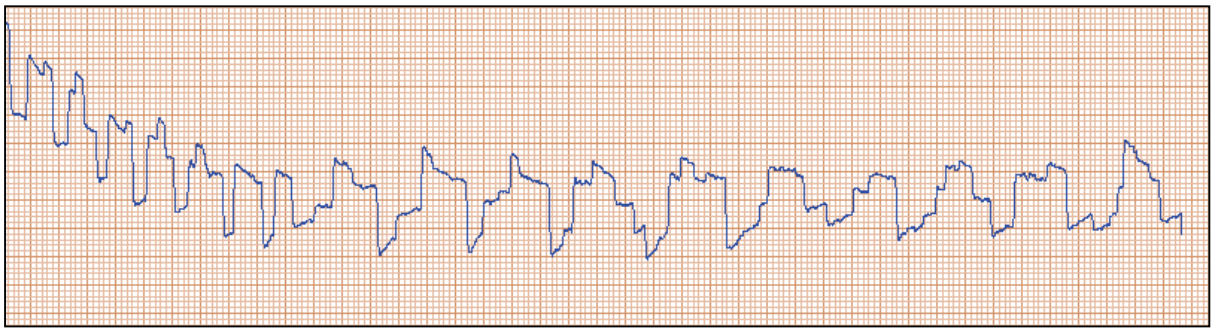

Figure 4.14 Response obtained on saccade test in subject with ANSD shows abnormal response.

4.2.2.2.2 Gaze test.

Analysis of the obtained responses for the gaze test carried out in three direction: centre, left lateral (30°), right lateral (30°) indicated the absence of spontaneous nystagmus (centre gaze) as well as absence of nystagmus beats in the off-centre gaze tasks which are designed to stress the system in 23 subjects. As previously mentioned, 3 of the 26 subjects were found to have ocular flutter in the responses, which were manifested by additional oscillations in the three positions tested for. These random oscillations were unlike

nystagmus in that they were not characterized by slow and fast phases. Tracing without flutter obtained in the ANSD group is shown in figure 4.15.

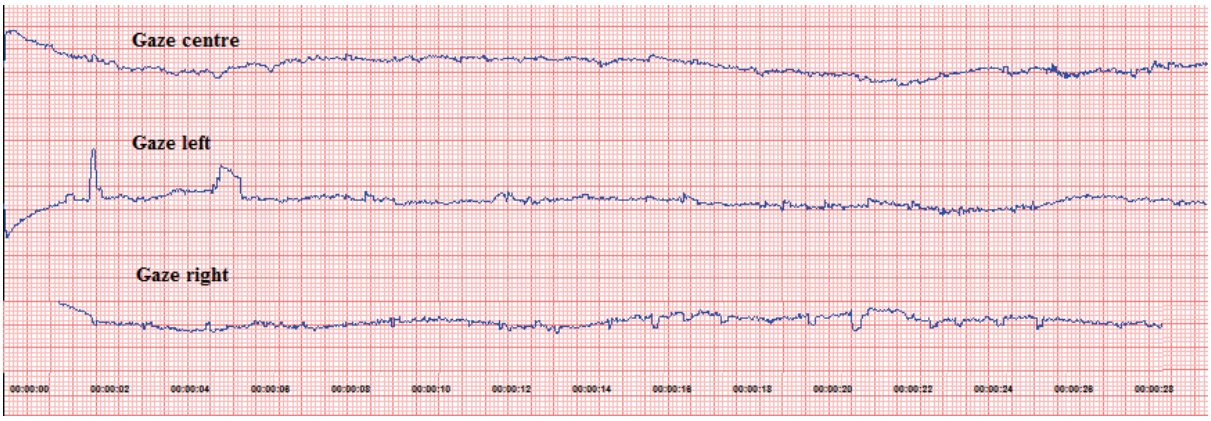

Figure 4.15 Response obtained on the gaze test (30° lateral as well as at 0°) in one subject with ANSD. Graph shows absence of gaze evoked nystagmus in all the tracings.

4.2.2.2.3 Optokinetic test.

In the optokinetic task, analysis of the recordings revealed that all the subjects with no associated peripheral neuropathy were found to have symmetrical responses for visual targets moving from the lateral-30° (right, left) position to the midline (0°). The two subjects with associated peripheral neuropathy demonstrated asymmetry in the optokinetic responses, with the morphology of the response deteriorating in the recording of one direction over the other as well as with time. Additionally, the ocular flutter exhibited by one of the subjects with peripheral neuropathy further resulted in disruptions in the optokinetic tracings. The figure below illustrates the symmetry of obtained responses of one subject as well as the asymmetry seen in the subject with peripheral neuropathy in addition to ANSD.

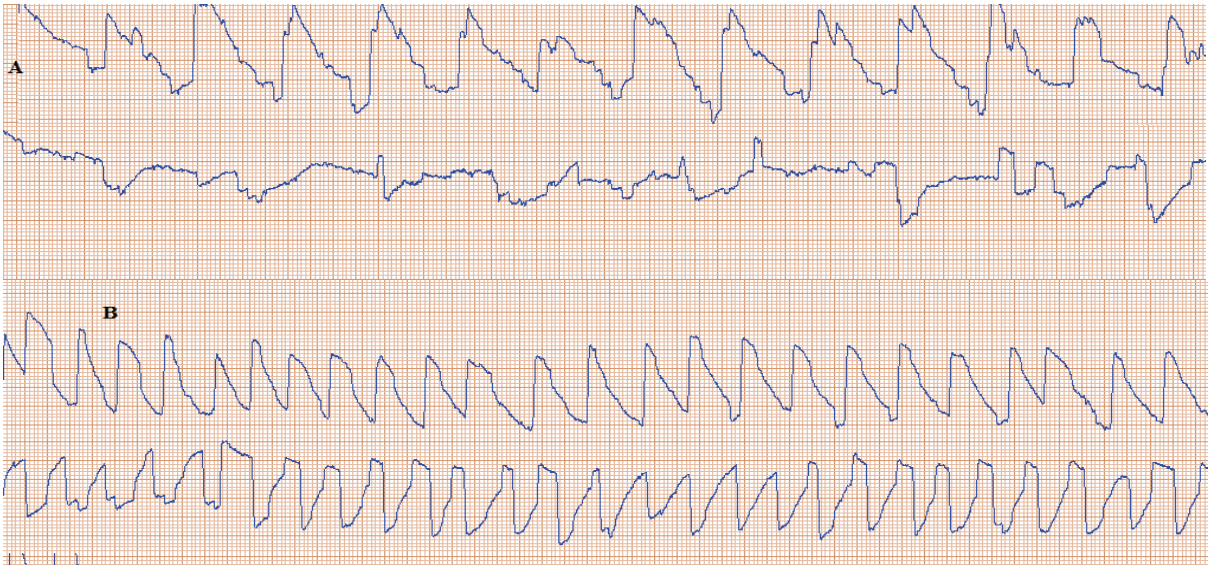

Figure 4.16 Optokinetic response (A) asymmetrical response seen in a subject with associated peripheral neuropathy (B) symmetrical response in subject with VIII nerve neuropathy alone.

Caloric assessment yielded the most prevalent response to be hypoactivity with 86.53% (45 ears) exhibiting it. Responses within the established normal range were found in 7.69% (4 ears) of the subjects and the least common response displayed was hyperactivity with 5.76% (3 ears). The absence of any measurable nystagmus beats is indicative of a predominantly peripheral pathology, in particular, of the superior vestibular nerve and its innervating organ, the posterior semi-circular canal (SCC) (Kirtane, 2009). Similar absence of response upon caloric stimulation in 2 subjects with ANSD was reported by Kaga, Nakamura, Shinogami, Tsuzuku, Yamada, and Shindo (1996). Based on the absence of any other significant finding in the rest of the vestibular test battery, the authors attributed the dysfunction to exist along the vestibular organs or the brainstem. Kaga (2009) reported that ice water caloric stimulation failed to elicit any response on electronystagmography in 5 ANSD subjects. These subjects were therefore categorized to have 'auditory-vestibular neuropathy' indicating the possible involvement of the superior vestibular nerve and/or the posterior SCC. Three other subjects performed normally on the vestibular evaluations and

were thereby diagnosed to have 'auditory neuropathy only'. Nasser, Elkhayat, Khalil and Mahmoud (2006) subjected 50 individuals with ANSD to a series of tests to assess the vestibular functioning. 44% of the subjects had bilateral extensive peripheral vestibular lesion as evidenced by the absence of responses to bilateral caloric stimulation. Over the years, other similar reports have been published and such studies have attributed the hypoactive findings to neuropathic involvement of the vestibular nerve (Sinha, Barman, Rajeshwari, Singh & Sharanya 2012; Kaga, 2009; Nasser at al., 2006; Shaykholeslami et al., 2000; Von Brevern, Lempert, Bronstein, & Kocen, 1997).

Anatomical evidence of the neuropathic condition affecting the vestibular nerve has been reported of by Starr, Michalewski, Zeng, Fujikawa-Brooks, Linthicum, Kim, Winnier, & Keats (2003). The authors, based on their study of a family with ANSD, reported that the vestibular nerve itself had structural changes that were not found in the normal control group. The overall vestibular nerve population between the receptor organ and the ganglion within the internal auditory meatus was noted to be reduced (Starr et al., 2003). In the ANSD individuals who were found to have vestibular involvement, both the auditory as well as the vestibular nerve had an irregular beaded appearance (Starr et al., 2003). Additionally, fragmentation of the myelin layer with gaps nearly equal to the diameter of the nerve fibre was reported along with the distortion of the nerve structure (Starr et al., 2003). Such changes in the structure of the vestibular nerve could explain the findings of absent caloric responses obtained in the current study.

In the experimental group, in addition to hypoactive responses, hyperactive as well as normal responses were seen in 3 ears and 4 ears out of the 52 ears. This indicates a degree of variability within the population. Studies in literature have also reported of subjects with ANSD exhibiting normal caloric responses (Nasser et al., 2006; Fujikawa & Starr, 2000; Kaga, 2009; Starr et al., 1996).

It was also observed that, the prevalence of positional and positioning nystagmus was higher in the experimental group than in the control group. While only 11.53% & 19.23% of the control group exhibited positioning and positional nystagmus respectively, 15.38% & 30.76% of the experimental group were found to have nystagmus beats on the positioning and positional test. Amongst those, 2 out of 4 subjects in the positioning and 5 out of 8 subjects in the positional test had less than 19 beats per seconds therefore falling within the established normative range. Although the other 2 subjects (in the positioning test) and 3 subjects (in the positional test) did present with marginally more number of beats, they were intermittent and geotropic not persisting in more than one position out of all the positions assisted to. In the positioning test, the presence of nystagmus in one position alone is considered clinically insignificant or a normal variant (Kirtane, 2009). According to Kirtane (2009), the presence of positional nystagmus is considered as a non specific evidence of vestibular dysfunction with little or no localizing value. Additionally, he states that the positional nystagmus may not be arising from the vestibular receptors, but rather from proprioceptive impulses from the neck region. In subjects with ANSD, Sheykholeslami et al. (2000) reported the absence of any significant finding on the positioning and positional test in their 3 subjects. Nasser et al. (2006) also reported of the absence of positional and positioning evoked nystagmus in their subjects with ANSD with and without concomitant peripheral neuropathy.

Apart from the cases exhibiting ocular flutter, all the subjects with ANSD alone have performed normally on the oculomotor tests, i.e the saccade, Gaze and optokinetic tests. Only the two subjects with associated peripheral neuropathy, one of whom had ocular flutter, exhibited disturbances in the optokinetic test, possibly indicative of the beginning of central involvement of the optokinetic system Reports on normal functioning on the central oculomotor tests as has been reported in the current study in subjects with ANSD alone have

been reported by Fujikawa and Starr (2000) in their ANSD subject population. Sheykholeslami et al. (2000, 2005) in both their studies noted that Saccades, smooth pursuit eye movements and optokinetic nystagmus were normal in the 3 subjects initially tested by them, as well as in their single subject in the proceeding study. Such a finding is indicative of an intact central oculomotor system tract and its normal functioning in individuals with ANSD. This is in agreement with the findings of Starr et al. (2003) who reported that the distal portion of the vestibular nerve was found to have a beaded appearance compared to the proximal portion, suggesting pathology restricted to the distal portion of the nerve rather than the central portion of the nerve. Thus it can be hypothesized that the neuropathy may be restricted to the Schwann cells and not the oligodendroglial cells. Thus, these central occulomotor pathways which are central pathway and are myelinated by the oligodendroglial cells may not undergo such changes, and hence a normal finding on these test.

4.3 Association between symptoms exhibited by the individuals and test findings

The table below shows the relation between the symptoms reported of by the individuals correlated with the caloric, and cVEMPs findings. Section II of the Maryland dizziness questionnaire which assesses the prevalence of relevant symptoms has been utilized.

Table 4.4

Association between symptoms and caloric and cVEMPs test findings

Sl.No	Symptoms	Number of subjects presenting with the symptoms	Abnormal rate in caloric test (%)	Abnormal and/or absent cVEMPs- ear wise (%)
1	Light headedness/swimming sensation in the head	4	100	100
2	Blackouts/Loss of consciousness	1	100	100
3	Tendency to fall	0	-	-
4	Object spinning/ turning around you	4	78.5	100
5	Sensation that you are turning or spinning inside	6	100	91.66
6	Loss of balance while walking	7	100	92.8
7	Headache	9	94.4	94.4
8	Pressure in the head	0	-	-
9	Nausea/ vomiting	5	100	90

42.3% (11 subjects) of the ANSD population did not present with any vestibular complaints on the dizziness questionnaire developed by the Maryland hearing centre. The remaining 57.6% (15 subjects) did present with at least one of the symptoms described in the questionnaire. Thus, with respect to the presence of vestibular complaints, the ANSD group

may be divided into those who presented with complaints of vertigo (15 subjects) and those subjects who remained asymptomatic of vestibular dysfunction.

Considering the group of 15 subjects who were noted to experience symptoms possibly indicative of vestibular dysfunction/vertigo, the most common symptom was headache's accompanying the episodes of vertigo or occurring by itself with 9 of the 15 subjects presenting with it. Loss of balance was also commonly reported with 7 subjects (46.6% of the symptom presenting group) reporting it. Regarding the description of the vertigo attack, a larger percentage of the population, 6 individuals, reported of a subjective sensation of spinning of self or tuning over an objective sensation of spinning or perception of objects around them spinning (4 subjects, 26.6%). Nausea or vomiting was also reported regarding by 5 subjects (33.3%) as was a sensation of light-headedness (4 individuals). Uncommon amongst the symptoms was backing out, with only 1(6.6%) of the 15 subjects accounting for it. Based on the questionnaire, it can be noted that the episodes of vertigo experienced were never severe enough or of a sudden nature to cause a fall and were never accompanied by a pressure in the head. Nasser et al. (2006) reported the incidence of a portion of the symptoms in their 50 subjects diagnosed with ANSD. Other audio-vestibular symptoms reported included headache and dizziness in 13 (26%) and 9 (18%) respectively. A significantly smaller percentage of occurrence than in the current study could be due to the smaller population size of the current study. Sheykholeslami et al. (2000) reported of 3 subjects with ANSD all of whom complained of vestibular dysfunction manifested in the form of instability and disturbances in gait while walking. Fujikawa and Starr (2000) on the other hand reported that none of their 14 subjects with ANSD reported of any vestibular symptoms such as dizziness or instability or unsteadiness that worsens with darkness.

In the present study, 42.3% of the subject population did not report of any vestibular symptoms inspite of extensive vestibular dysfunction. Vestibular functioning in such subjects

with auditory neuropathy in fact has not been widely reported predominantly due to its asymptomatic nature. The absence of concomitant vestibular symptoms has been hypothesized by many authors to be due to the bilateral distribution of the disorder and the slow progression of vestibular neuropathy (Sazgar, Yazdani, Rezazadeh, & Yazdi, 2010; Kumar et al., 2007). Central compensation that occurs in case of asymmetric inputs, via the proprioceptive and visual systems would further account for the subclinical nature of the disorder.

In addition to it, the diameter of the vestibular nerve fibres has been found to be slightly larger than that of the auditory nerve fibres (Starr et al., 2003). It is well reported that the conduction of action potentials is slower in smaller diameter neurons than their larger counterparts. Thus, demeyelination, although affecting both the neurons to the same extent, would result in further slowing of the already slow conduction capacity of the smaller diameter nerve, consequently affecting its performance to a greater extent as compared to a larger diameter neuron. Therefore, the presence of a pathological condition such as demyelination affects to a larger extent the physiologic functioning and conduction properties of the smaller diameter fibres (i.e. the auditory fibres) over the larger diameter fibres (the vestibular nerve fibres). It can thus be hypothesized that the overt manifestation as well as progression of the auditory deficits would be earlier and greater than that of the vestibular, therefore providing more opportunities for compensation to occur for the vestibular symptoms

Most of the subjects who did complain of vestibular symptoms were also identified as having vestibular dysfunction based on caloric and cVEMP results. Apart from symptoms of objective spinning and headache, all the subjects presenting with the remainder 5 symptoms were found to have abnormal results in the caloric test. 78.5% of the subjects complaining of headaches and 94.4% of the individuals perceiving objective spinning were found to have

hypofunction or hyperfunction on the caloric test. All the subjects who indicated of the presence of light-headedness, blackouts and objective spinning sensation were found to have abnormalities in the cVEMP recordings obtained. The remaining symptoms were found to have correlating abnormalities in cVEMP ranging from 90% to 94.4% amongst those complaining of nausea and headaches respectively.

4.4 Association between the configuration of hearing loss, degree of loss and caloric test and cVEMP

Chi-square analysis was carried out in order to determine if there was a significant association between the parameters of audiometric configuration, the caloric response obtained and the cVEMP response. The audiometric configuration considered were flat pattern (≤ 20dB difference between the thresholds at 250 and 4000Hz), rising pattern (≥ 20dB difference between the thresholds at 250 and 4000Hz, with poorer thresholds at the low frequencies), peaked pattern (peak at a single frequency with worsening of thresholds at immediately adjacent frequencies) and sloping pattern (≥ 20dB difference between the thresholds at 250 and 4000Hz, with thresholds worsening at the higher frequencies). Of the 52 ears assessed, the most prevalent pattern of audiogram was the flat type with 46.15% (24 ears) exhibiting such a configuration. Following that, rising patter of audiogram was found in 34.61% (18 ears) of the group and peaked and sloping were exhibited by 13.46 (7 ears) and 5.76% (3 ears) of the experimental group. Goodman's classification (1965) was utilized to classify the degree of hearing loss of the 26 individuals with ANSD. The categories considered were normal hearing, minimal, mild, moderate, moderately severe, severe and profound hearing loss. The most prevalent degree of loss amongst the ANSD group was mild and moderate degree's, with 13(25%) and 12 (23.07%) ears respectively exhibiting it. The caloric responses were considered earwise and were categorized under the following

categories, normal, hypofunctional and hyperfunctional). cVEMP responses were considered to be either present or absent.

Chi square analysis was used to calculate if a significant interaction was present between the 3 parameters; in particular, to see if an association between the audiometric configuration and the vestibular test results (Caloric responses and cVEMP responses). The statistical analysis revealed that there was no significant correlation between the audiometric configuration and the caloric response, the audiometric configuration and cVEMP responses and no statistically significant correlation between the caloric response and the cVEMP response in the ANSD subject population. Table 4.5 describes the correlation between the three parameters and the chi square values obtained

Table 4.5

Association between configuration of loss, caloric responses and cVEMP responses

Test		Caloric responses				cVEMP responses		
		Hypo function	**Hyper function**	**Normal**	**Total**	**Present**	**Absent**	**Total**
Audiometric configuration	Rising	15	1	2	18	1	17	18
	Flat	20	2	2	24	1	23	24
	peaked	7	0	0	7	0	7	7
	sloping	3	0	0	3	0	3	3
	Total	45	3	4	52	2	50	52
	p value*	**.90**				**.90**		
Caloric responses	Hypofunction					1	44	45
	Hyperfunction					0	3	3
	Normal					1	3	4
	Total					2	50	52
	p value*					**.07**		

*chi square test

In a similar manner, the vestibular test results data and the degree of hearing loss data of individuals with ANSD was subjected to chi square analysis in order to determine if any

association between them existed. The statistical test revealed the absence of any significant association between the degree of hearing loss and the caloric as well as cVEMP result as has been depicted in table 4.6

Table 4.6

Association between degree of hearing loss, caloric responses and cVEMP responses

Test		**Caloric response**				**cVEMP response**		
		Hypofunction	**Hyperfunction**	**Normal**	**Total**	**Present**	**Absent**	**Total**
Degree of hearing loss	Normal	3	0	0	3	0	3	3
	minimal	7	0	0	7	0	7	7
	Mild	10	0	3	13	2	11	13
	Moderate	10	1	1	12	0	12	12
	Moderately severe	6	2	0	8	0	8	8
	Severe	7	0	0	7	0	7	7
	Profound	2	0	0	2	0	2	2
	Total	45	3	4	52	2	50	52
	P value*	**.30**				**.39**		

In summary, the current study reveals that most of the ANSD subjects assessed presented with absent cVEMP's, hypofunctional caloric responses and normal functioning on the central oculomotor tests as well as the positioning and positional tests. Additionally, variability in the response patterns were observed as well with few subjects exhibiting hyperfunctional or normal caloric responses as well as abnormal functioning on the oculomotor tests as well. While a part of the subjects did present with symptoms of dizziness, asymptomatic individuals were also seen which may be due to central compensation having occurred. The perception of most of the symptoms correlated well with the results of the vestibular tests. No significant correlations were observed between the audiometric findings of degree and configuration of hearing loss and the vestibular test results of cVEMPs and caloric responses.

Chapter 5

SUMMARY AND CONCLUSION

In the existing literature on the condition, ANSD is investigated as a solitary concern. The symptomatology, clinical findings and aetiology of the neuropathic condition are discussed usually in relation to one component of the VIIIth cranial nerve i.e. the cochlear branch. Forming an element of the same nerve bundle is the vestibular branch of the cranial nerve comprising of the superior and the inferior vestibular nerve. While the superior vestibular nerve innervates the horizontal, superior semicircular canal and the utricle, the inferior vestibular nerve innervates the posterior semicircular canal and the sacculus. It is likely that neuropathic conditions involving the auditory nerve may affect the vestibular nerve too (Akdogan, Selcuk, Ozcan & Dere., 2008). The prevalence of such vestibular dysfunction has not been widely reported for the reason that vestibular evaluations are not routinely carried out in ANSD subjects.

In order to study the effect of ANSD on the functioning of the vestibular system, 52 subjects were recruited to the study. The 52 participants were divided into two groups

1. The experimental group consisted of 26 individuals (10 males & 16 females) aged between 13 to 42 years diagnosed to have bilateral ANSD by means of a comprehensive audiological test battery. Included in the group were 2 individuals with associated peripheral neuropathy as well.
2. The control group consisted of 26 individuals (11 males & 15 females) as well aged between 18 to 28years with hearing sensitivity within normal limits in both ears and having no history or current complaints of vertigo or dizziness.

The individuals were subjected to detailed audiologic as well as vestibular test batteries. The vestibular tests consisted of the Maryland dizziness questionnaire, cVEMP recording as well as ENG recording. The recordings were analyzed in the following manner.

1. The interpretation of the findings of the Maryland dizziness questionnaire was based on the presence or absence of the symptoms listed.
2. In cVEMPs, latency of p13 & n23, amplitude of p13-n23 complex and inter-ear amplitude asymmetry was calculated for p13-n23 complex.
3. The obtained recordings for the saccade test were analysed with respect to their morphology as well as symmetry to the directions.
4. Presence or absence of gaze nystagmus and direction changing or direction fixed nystagmus within the 3 gaze condition.
5. Optokinetic test results were analyzed based on symmetry or equality of optokinetic responses between the 2 directions.
6. Interpretation of the positioning as well as positional test results was based on the presence or absence of nystagmus. If present, the number of nystagmus beats occurring in a 30 second period as well as its nature- direction fixed or direction changing.
7. For the caloric test, the cumulative frequency was calculated for each of the irrigation conditions and it was plotted on the Claussen's Butterfly chart for interpretation.

The obtained data was statistically analyzed. The following analyses were carried out to better understand the findings.

1. Descriptive statistics was done to find out the mean and standard deviation of P13 and n23 latency, amplitude of p13-n23 complex in cVEMPs and inter ear amplitude ratio in control group.
2. Descriptive analysis of symptoms and percentage of abnormal results in each test for the ANSD group

3. Chi-square test to find association between the configuration of hearing loss and caloric results and cVEMP test results in the ANSD group
4. Chi-square test to find the association between the degree of loss, caloric and cVEMPs test results in the experimental group.

The results of the study revealed that

1. In the ANSD group, cVEMP responses were absent on 50 (96.15%) of the 52 ears evaluated. Of the remaining 2 ears, 1 ear (1.9%) had abnormal cVEMP response, with the amplitude of the p13-n23 complex being lower than that observed in normal hearing individuals and 1 ear had normal cVEMP responses. Such an absence of response or asymmetry in responses is indicative of a dysfunction along the inferior vestibular pathway and/or its innervating organ, the sacculus.
2. In the caloric test, variable results were noted. The most prevalent response pattern was hypoactive, found in 45 ears (86.53%). Hyperactive response was exhibited by 3 ears (5.76%) and the remaining 7.69% (4 ears) of the population had responses which fell within the normal range of cumulative frequency for the side as well as temperature of stimulation.
3. In the positioning and positional tests, 15.38% & 30.76% of the experimental group were found to have nystagmus beats. This was higher than the 11.53% and 19.23% identified in the control group. Amongst those exhibiting nystagmus in the experimental group, 2 out of 4 subjects in the positioning and 5 out of 8 subjects in the positional test had less than 19 beats per seconds therefore falling within the established normative range. Although the other 2 subjects (in the positioning test) and 3 subjects (in the positional test) did present with marginally more number of beats, they were intermittent and geotropic, not persisting in more than one position out of all the positions assisted to.

4. 3 subjects in the experimental group exhibited ocular flutter. Of the 3, one subject had associated peripheral neuropathy.
5. On the oculomotor tests, 22 subjects, who were diagnosed to have neuropathic involvement of the VIII nerve alone, performed normally. 2 other subjects were found to have ocular flutter and therefore had recordings with marked disruptions. The remaining 2 subjects who were those with associated peripheral neuropathy performed normally on the saccade and gaze test, but had asymmetric responses on the optokinetic test.
6. On the Maryland dizziness questionnaire, 42.3% (11 subjects) of the ANSD population did not present with any vestibular complaints 57.6% (15 subjects) did present with at least one of the symptoms described.
7. Statistical analysis suggested no correlation between the degree of hearing loss and the vestibular test results i.e. caloric responses and cVEMPs.
8. Chi square test further signalled the absence of any correlation between the degree of loss and the vestibular test results of caloric and cVEMP responses as well

Conclusion

Accordingly, the results of the current study suggest that a large percentage of individuals with ANSD have accompanying vestibular dysfunction as well. It is therefore necessary to carry out vestibular evaluations in individuals diagnosed to have auditory neuropathy so as to further streamline the diagnosis as auditory neuropathy only' or 'auditory-vestibular neuropathy' as suggested by Kaga (2009). The importance of a precise diagnosis of the extent of the condition lies in its utility during planning of rehabilitation in order to ensure that the individuals have the benefit of a better quality of life. Thus, in order to detect concomitant symptomatic/asymptomatic vestibular dysfunction and plan for

effective management strategies, it is necessary to include vestibular assessment in the ANSD protocol.

Implications of the study

1. The study provides information regarding the possible vestibular pathways demonstrating dysfunction as well as the extent of vestibular system involvement in individuals with auditory neuropathy.
2. Appropriate and timely rehabilitation measures in individuals with auditory neuropathy can be implemented based on the results of the present study.

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