

MASTERS DEGREE IN COMMUNICATION PATHOLOGY 2015

The impact of vestibular neurectomy via the retro sigmoid
approach on VEMPs in adults with Menière's Disease

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ABSTRACT

BACKGROUND:

The recent development of the ocular vestibular evoked myogenic potential (oVEMP) test protocol in addition to the cervical vestibular myogenic potential (cVEMP), can provide clinicians information about the functioning of the otolith end organs and their enervating pathways. The utilization of cVEMPs and oVEMPs together may also provide feedback on the success of the surgical attempt to preserve the cochlear fibres during vestibular neurectomy (VN), highlighting the need for including both oVEMPs and cVEMPs in Menière's Disease (MD) subjects post VN.

OBJECTIVES:

To describe the impact of VN via the retro sigmoid approach on cVEMPs and oVEMPs in subjects with MD.

METHODS:

This study compared cVEMP and oVEMP responses of 15 subjects with and without MD and 14 subjects with MD who received a VN. The AAO-HNS (1995) classification was used as diagnostic criteria for MD.

RESULTS:

cVEMP and oVEMP responses were absent on the side of the surgery, in all subjects with MD who had undergone VN.

CONCLUSION:

Following VN, cVEMPs and oVEMPs were found to be absent.

Key words: Menière's Disease, vestibular neurectomy, cVEMP, oVEMP, retro sigmoid.

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ABBREVIATIONS

air-conduction (AC)

air-conduction sound (ACS)

American Academy of Otolaryngology, Head and Neck Surgery (AAO-HNS)

asymmetry ratio (AR)

auditory brainstem response (ABR)

bone-conducted vibration (BCV)

cerebrospinal fluid (CSF)

cervical Vestibular Evoked Myogenic Potentials (cVEMP)

Ear Nose and Throat (ENT)

Ear Nose and Throat Surgeons (ENT's)

electrocochleography (EcochG)

Electromyography (EMG)

female (F)

horizontal visual subjective perception (HVS)

intensive care unit (ICU)

interquartile range (IQR)

male (M)

Ménière's disease (MD)

normal (N)

ocular Vestibular Evoked Myogenic Potentials (oVEMP)

standard deviation (SD)

sternocleidomastoid (SCM)

United States of America (USA)

video nystagmography (VNG)

vertical visual subjective perception (VVS)

Vestibular Evoked Myogenic Potential (VEMP)

Vestibular neurectomy (VN)

Vestibulo-ocular reflex (VOR)

vibration-induced nystagmus (VIN)

Video Head Impulse Testing (vHIT)

years (y)

INTRODUCTION AND RATIONALE

1.1. Introduction to Ménière's Disease

Prosper Ménière first described the condition now known as Ménière's disease (MD) in 1861, but at the time, he described these episodes of dizziness, fluctuating hearing loss and ringing in the ears as "glaucoma of the inner ear" (Sajjadi & Paparella, 2008) naming the condition "Ménière Syndrome" (Albera, Canale, Parandero, Ducati & Lanotte, 2011). Lustig and Lulwani (1997) credit Ménière's discovery as possible due to a number of technical and scientific advances in the late 1800's, combined with a keen intellectual mind. However they note that it took the medical world a further 70 years of scientific debate to accept that vertiginous disorders were caused by pathologic process in the inner ear.

MD is one of the most debated diseases in otology and the classic triad of symptoms are vertigo, tinnitus and low frequency hearing loss. The individual will report intermittent episodes of vertigo lasting hours in duration, fluctuating hearing loss that is most pronounced during an attack, tinnitus and a subjective sensation of aural fullness on the side of the affected ear (Van der Heyden & Handelsman, 2012). Although most researchers agree on this triad symptom complex, a definite etiology and treatment is still elusive (Borghi, Brandolini, Ferri, Modugno, Pirodda & Raimondi, 2010). MD is a chronic illness that continues to affect thousands of individuals both physically and emotionally, every year world-wide (Sajjadi & Paparella, 2008).

1.2. Epidemiology of MD

MD has been described as the third most common type of otologic dizziness diagnosed in balance clinics (Hain, 2015). The difficulty in clearly diagnosing patients leads to a corresponding difficulty in determining the incidence of the disease.

There appears to be quite a variable range of incidence of MD reported in the literature (Hain, 2015) with considerable disagreement between reports. Hain

(2015) proposed that this disagreement may be due to the basis of diagnosis and he called MD a “committee disease” where the diagnosis is based on the symptoms reported, as opposed to objective diagnostic criteria. In fact, the diagnosis is often only made in retrospect of symptom complaint and disease progression. In their study, Alexander and Harris (2010) commented that the differences in reported incidence and prevalence of MD might vary widely due to methodological differences between studies, changes in the diagnostic criteria for MD over time, as well as inherent differences in the populations studied. Schessel, Minor and Nedzelski (1998) reviewed differing reports of incidence and found significant differences across countries (157 MD patients per 100 000 in England, 46 MD patients per 100 000 in Sweden and 7.5 MD patients per 100 000 in France). Although González, González, Trinidad, Ibáñez, Pinilla, Martínez Ruiz-Coello, Rodríguez Valiente and López-Cortijo reported the incidence of MD in the United States of America (USA) as 100 per 100 000 in their study published in 2010, a more recent report by Albera, Canale, Parandero, Ducati and Lanotte in 2011 found that the prevalence of MD ranges between 17 – 46 per 100 000 of the population (50 - 500 cases) depending on the study. Harris and Alexander (2010) published a report where they reviewed data from medical and pharmaceutical claims in the USA over a three-year period from 2005 – 2007. Although the statistics are specific to the USA and drawn from a population of “commercially insured” individuals, they found the prevalence of MD to be 190 in 100 000 with a female:male ratio of 1.89:1. No reported figures could be found for South Africa.

Despite these figures, 2% of people living in the USA believe they have symptoms that would indicate a diagnosis of MD (Hain, 2015). These people either have the disease, and it has not been formally diagnosed, or they have symptoms suggestive of MD that are actually attributable to another condition.

Most research indicated that symptoms begin in the 4th and 5th decade of life (González, González, Trinidad, Ibáñez, Pinilla, Martínez Ruiz-Coello, Rodríguez Valiente & López-Cortijo, 2010), with Harris and Alexander (2010)

confirming that the incidence of MD increases with age, ranging from 9 per 100 000 under the age of 18, increasing to 440 per 100 000 for individuals 65 years and older.

The literature reported a strong family history in patients diagnosed with MD, with some reports stating that as many as 20% of family members report similar symptoms (Sajjadi & Paparella, 2008). Although there appears to be a paucity of literature regarding racial predisposition to MD (Hain, 2015), Sajjadi and Paparella (2008) report a higher incidence of MD in white people of European descent as compared to black people of African descent.

Many patients with unilateral MD may fear development of the disease in the contralateral ear (Hain, 2015). There was huge variance in the literature regarding the frequency of development of bilateral disease – ranging from 5% (Hain, 2015) to 23% (House, Doherty, Fisher, Derebery & Berliner, 2006) to 50% (Sajjadi & Paparella, 2008) and this remains a realistic concern for patients, particularly when considering ablative treatment options.

1.3. Pathophysiology of MD

The etiology of MD has been the subject of much debate in the literature (Rauch, 2010) and today MD is known as an idiopathic disorder of the inner ear (Paparella, 1984). MD is associated with the dilation of the scala media, with subsequent bulging of Reissner's membrane into the scala vestibuli (Gibson, 2010). Eventually small tears or cracks may be formed in the membrane leading to mixing of the endolymph and perilymph. This mixing of the ions of the two fluids in the inner ear causes a temporary toxic effect resulting in damage to the hair cells (Gibson, 2010). This process is thought to lead to the recurrent acute vertigo and fluctuating sensorineural hearing loss with tinnitus associated with MD (Albera, Canale, Papandero, Ducati & Lanotte, 2011; AAO-HNS, 1995; Barany Society, 2014). MD may also be referred to as primary idiopathic endolymphatic hydrops (Perez, Ducati, Garbossa, Benech, Fontanella, Canale & Albera, 2005), which infers that the endolymphatic spaces of the labyrinth are dilated leading to the afore-

mentioned symptoms. The prevailing definition of MD as a condition caused by endolymphatic hydrops, was historically confirmed on classic pathologic post-mortem examinations (Hallpike & Cairns, 1938) and in current times with extensive temporal bone studies (Merchant, Adams & Nadol, 2005) and Magnetic Resonance Imaging (MRI) findings (Nakashima, Naganawa, Sugiura, Teranishi, Sone, Hayashi, Nakata, Katayama & Ishida, 2007). These studies both confirmed the presence of endolymphatic hydrops in at least one ear in patients diagnosed with MD. However, conflicting research has found that not all MD patients have endolymphatic hydrops, with 6% of patient's presenting with endolymphatic hydrops on autopsy having no history of Meniere's associated symptoms (Rauch, Merchant & Thediner, 1989). This has led researchers to question the generally accepted idea that MD and endolymphatic hydrops are *always* associated (Hain, 2015). Recent studies suggest that MD results from a combination of the endolymphatic hydrops or increased pressure in the scala media *combined* with genetic factors (Rauch, 2010), infection (Gacek, 2009), vasculopathy (Rauch, 2010), diet (Smith, Sankar & Pfeleiderer, 2005), allergies (Sajjadi & Paparella, 2008), trauma (Rauch, 2010), autonomic, endocrine and auto-immune diseases (Greco, Gallo, Fusconi, Marinelli, Macri & de Vincentiis 2012). Once the pressure in the scala media stabilizes, symptoms are drastically if not totally reduced, but over the course of many years hearing and vestibular function will gradually decrease (Sajjadi & Paparella, 2008).

1.4. Diagnosis and Differential Diagnosis of MD

The most widely accepted classification for diagnosing Meniere's is that of the American Academy of Otolaryngology, Head and Neck Surgery (AAO-HNS) (Syed & Aldren, 2012), and there are four possible classifications as summarized in Table 1.

Table 1. Diagnostic criteria of MD by the American academy of otolaryngology-head and neck surgery (AAO-HNS)

| | |
|--------------------------------------|---|
| 1. Certain Ménière's disease | <ul style="list-style-type: none"> •Definite MD •Histopathological confirmation. |
| 2. Definite Ménière's disease | <ul style="list-style-type: none"> •Two or more definitive spontaneous episodes of vertigo 20 minutes or longer •Audiometrically documented hearing loss on at least one occasion •Tinnitus or aural fullness in the treated ear •Other causes excluded |
| 3. Probable Ménière's disease | <ul style="list-style-type: none"> •One definitive episode of vertigo •Audiometrically documented hearing loss on at least one occasion •Tinnitus or aural fullness in the treated ear •Other causes excluded |
| 4. Possible Ménière's disease | <ul style="list-style-type: none"> •Episodic vertigo of the Ménière type without documented hearing loss, or fluctuating or fixed sensorineural hearing loss, with disequilibrium but without definitive episodes •Other causes excluded |

The consensus criteria for a definition of *definite MD* was further upgraded at the Barany Society meeting in 2014 (Lopez-Escamez et al, 2015) as follows: Two or more spontaneous episodes of vertigo, each lasting 20 minutes to 12 hours; audiometrically documented low-to-medium-frequency sensorineural hearing loss in one ear, defining the affected ear on at least one occasion before, during or after one of the episodes of vertigo; fluctuating aural symptoms (hearing, tinnitus or fullness) in the affected ear; not better accounted for by another vestibular diagnosis.

At the same meeting in 2014, the Barany Society further upgraded the definition for *possible MD* to: Two or more episodes of vertigo or dizziness, each lasting 20 minutes to 24 hours; fluctuating aural symptoms (hearing, tinnitus or fullness) in the affected ear; not better accounted for by another vestibular diagnosis.

As seen from these diagnostic criteria, the diagnosis of MD remains a clinical decision based primarily on a detailed case history and a complete physical examination of the patient by a qualified and registered ENT surgeon and the physician will need to be familiar with the presentation of the symptoms in order to make an informed differential diagnosis (Sajjadi & Paparella, 2008). As such, these symptoms are discussed in more detail below.

Most patients with MD will initially present with a reverse-slope low frequency sensorineural *hearing loss* or an inverted type audiogram with a peak at approximately 2 kHz (Abou-Bieh & Kombar, 2009) that over time and with many fluctuations, may stabilize into a flat sensorineural hearing loss (Sajjadi & Paparella, 2008). A small conductive component to the hearing loss may be present initially in some patients (Arts, Kileny & Telian, 1997), which may confuse the diagnosis and be mistaken for eustachian tube dysfunction at the outset of the disease. Many Ear Nose and Throat Surgeons (ENT's) will request serial audiograms in order to document the fluctuation of the sensorineural hearing loss (Paperella, 1991).

As part of the diagnostic process, some ENT's will make use of the glycerol dehydration test. Zhao, Zhu and Liu (2005) found that in the early stages of the disease, 83% of patients showed a sensitivity to the glycerol dehydration test, leading Vassilou, Vlastarakos, Maragoudakis, Candiloros and Nikolopoulos (2011) to report a high sensitivity of this test combined with repeat audiometry 90 minutes and again 3 hours after ingestion of 100g of 95% glycerol combined with an equal amount of water. The test is considered positive and can aid in the diagnosis of MD, if there is an improvement of pure tone thresholds of 10dB or more in at least two frequencies and of speech discrimination scores of at least 10%. They also reported a possible improvement in postural control, which was observed in as many as 70% of patients during attacks in the early stages of MD.

The *tinnitus* associated with MD is often described by patients as a low-pitched roar or buzz (Barber, 1983) with 79% of patients in another study

describing the tinnitus as a white noise (Oliveira, Bezerra & Araújo, 1998). The tinnitus may be continuous or intermittent but is usually reported as increasing in loudness with the onset of an attack, subsiding after an attack and leaving the patient with a feeling of relief (Naudé, 2006).

Usually the most distressing complaint reported by the MD patient is that of repeated attacks of incapacitating *vertigo* separated by intervals of complete freedom from dizziness of any kind. Naudé (2006) demonstrated that vertigo was the most debilitating symptom in MD. The vertigo that is typical of MD may occur at any time, unrelated to position or activity and may even waken the patient from sleep (Paparella, 1991). Schessel, Minor and Nedzelski (1998) stated that it is important for the clinician to document the duration and frequency of individual attacks of vertigo, the effects of head movement and associated aural symptoms and concomitant ear disease when making the diagnosis of MD.

Essential tests that help guide the clinician in making the appropriate diagnosis include a full audiometric assessment and video nystagmography (VNG) with bithermal caloric evaluation. Dobie, Snyder and Donaldson (1982) considered the most important finding from vestibular testing to be a unilateral vestibular hypofunction as seen on the bithermal caloric test. However up to 50% of MD patients may present with a normal caloric test and VNG even with a history of severe and incapacitating vertigo (de Sousa, Piza & da Costa, 2002). Additional vestibular tests may include electrocochleography (EcochG), vestibular evoked myogenic potentials (VEMP) and Video Head Impulse Testing (vHIT).

In all unilateral cases, magnetic resonance imaging (MRI) of the brain including views of the internal auditory canal with and without contrast is often included in order to exclude any retrocochlear pathology that may present with similar symptoms (Sajjadi & Paparella, 2008). The same authors also proposed that all patients with a case history including the symptomatology suggestive of MD have routine haematological testing to rule out the more common causes of vertigo and ill feeling.

The differential diagnosis of MD includes otosclerosis (the cochlea variant may manifest vestibular symptoms in 25 – 30% of patients), acute vestibular labyrinthitis or neuronitis and vestibular migraine (Hain, 2015). Clinicians will also need to differentiate MD from other pathologies that can cause tinnitus including otologic conditions such as presbycusis and noise-induced hearing loss, metabolic disorders such as hypo- or hyperthyroidism or vitamin deficiencies, neurologic problems such as head trauma, multiple sclerosis or stroke, drugs and psychological factors such as anxiety or stress (Vassilou, Vlastarakos, Maragoudakis, Candiloros & Nikolopoulos, 2011). Therefore it is clear that a multidisciplinary team approach is necessary in order to differentiate between MD and other disorders with similar symptom complexes. This process may include auditory and vestibular assessments, appropriate imaging, blood and urine analysis in order to distinguish between MD and those disorders listed in Table 2 (Lopez-Escamez et al, 2015).

Table 2. Differential diagnosis of MD

| |
|---|
| Autosomal dominant sensorineural hearing loss type 9 (DFNA9) caused by COCH gene |
| Autosomal dominant sensorineural hearing loss type 6/14 (DFNA6/14) caused by WSF1 gene Autoimmune inner ear disease |
| Cerebrovascular disease (stroke/TIA in the vertebrobasiliar system/bleeding) |
| Cogan's syndrome. Some cases may have recurrences. |
| Endolymphatic sac tumor Meningiomas and other masses of the cerebellopontine angle |
| Neuroborreliosis |
| Otosyphilis |
| Susac syndrome |
| Third window syndromes (Perilymph fistula, canal dehiscence, enlarged vestibular aqueduct) |
| Vestibular migraine |
| Vestibular paroxysmia (neurovascular compression syndrome) |
| Vestibular schwannoma |
| Vogt-Koyanagi-Harada syndrome |

1.5. Treatment and management options for MD

Over the past 160 years a variety of medical and surgical treatments have been proposed for MD and as yet there is still no definitive cure (Borghi, Brandolini, Ferri, Modugno, Pirodda & Raimondi, 2010). Treatment options vary considerably from palliative care to surgery, however around 85% of patients (Walton & Axon, 2012) will be helped by a combination of lifestyle changes, dietary modifications (such as reducing caffeine, chocolate, alcohol and salt intake), medical (pharmacological) therapy as well as psychological counselling and support (Sajjadi & Paparella, 2008).

The different treatment options as researched in the literature are discussed in more detail below. As a means of introduction and possible treatment algorithm, Figure 1 depicts a flow diagram as proposed by Telian and Wiet (2008) for the treatment and available management options for MD.

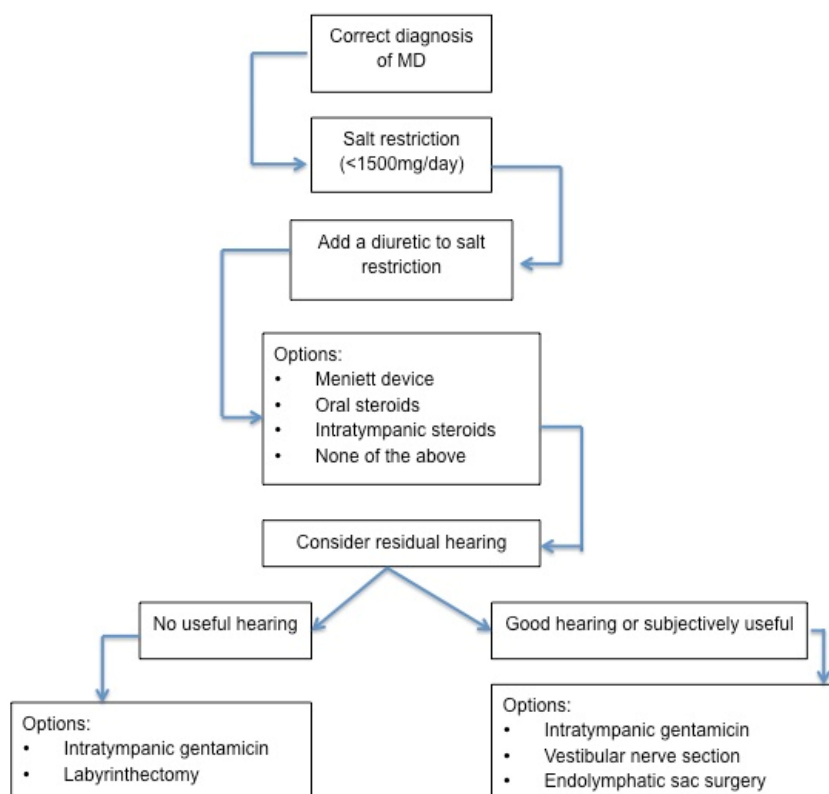


Figure 1. Management of Meniere’s disease (Telian and Wiet, 2008)

The literature showed a strong association between seasonal allergies and the diagnosis of MD, illustrating that simple lifestyle changes and allergy avoidance may improve the quality of life for many MD patients (Derebery & Valenzuela, 1992). In 1997, Derebery showed that up to 62% of MD patients reported a reduction in the frequency and severity of vertigo attacks after starting immunotherapy for allergies.

Sajjadi and Paparella (2008) advocated investigating MD patients for food allergies as much as possible as many patients with the symptoms of MD react adversely to large quantities of caffeine, alcohol, chocolate and salt. Non-invasive therapies and procedures for the treatment of MD may therefore also include life style and dietary changes (Smith, Sankar & Pfeleiderer, 2005), such as eliminating caffeine and changing to decaffeinated drinks, minimizing the patient's intake of chocolate, avoiding alcohol and tobacco products, and reducing salt intake to between 1500 and 2000mg per day (Telian & Wiet, 2008).

Previous research has shown that many people respond to long-term treatment with oral medications such as diuretics (Smith, Sankar & Pfeleiderer, 2005) or Betahistine (Lacour, Van de Heyning, Novotny & Tighilet, 2007), as these drugs appear to reduce the frequency of Menière's attacks. Diuretics may be ototoxic as well as have a possible side effect of loss of potassium (hypokalemia) and it has been suggested that clinicians should monitor blood levels if prescribing these drugs (Sajjadi & Paparella, 2008). A noted benefit of using diuretics and/or Betahistine is that they do not interfere with achieving central vestibular compensation (Borghi, Brandolini, Ferri, Modugno, Pirodda & Raimondi, 2010).

In between vertigo attacks, vestibular rehabilitation exercises (to help retrain the brain to process balance information correctly) may play a role in the management of MD. These exercises play an important role in promoting adaptation to decreased vestibular input (Clendaniel & Tucci, 1997). Vestibular rehabilitation therapy (VRT) can be quite successful in helping patients prevent the significant sequelae of vestibular loss and dizziness. In

particular it can play a significant role in preventing falls (Sajjadi & Paparella, 2008).

Although oral medications such as drugs for motion-sickness or anti-nausea medications may lessen the severity of the symptoms during an attack, it should be noted that anticholinergics also affect vestibular compensation, producing a reversible overcompensation if administered after vestibular compensation has been achieved subsequent to a vestibular imbalance (Zee, 1988).

Depending on the severity of the hearing loss and the stage of the disease (i.e. whether the hearing loss has started to stabilize), amplification in the form of a hearing aid (to improve the loss of hearing) may be recommended and form part of the treatment process (Smith, Sankar & Pfeleiderer, 2005). The use of amplification and sound stimulation in the form of a hearing aid has also been shown to be effective as part of a tinnitus treatment protocol (Searchfield, Kaur & Martin, 2010).

Intratympanic therapies are obviously more invasive than oral medical therapies, but aim to deliver the treatment drug of choice directly to the inner ear via the tympanic cavity and in so doing optimize the inner ear dosage and reduce the risk of developing systemic side effects (Walton & Axon, 2012). Lloyd (2012) comments that delivery of drugs to the inner ear is challenging: variable penetration due to the blood-inner ear barrier as well as the risk of significant side effects such as acute labyrinthine failure and loss of the drug down the eustachian tube.

At present there are two main groups of drugs used to treat MD intratympanically (Walton & Axon, 2012): aminoglycoside antibiotics and steroids. Aminoglycoside antibiotics, particularly gentamicin, are commonly used to treat MD due to the fact that one of its common side effects is ototoxicity. Gentamicin is predominantly vestibulotoxic and less likely to result in hearing loss than other drugs in this class. The effectiveness of intratympanic gentamicin in completely resolving vertigo symptoms in MD

varies from 27% to 100% depending on the study (Walton & Axon, 2012). The main risk in using intratympanic gentamicin as a treatment for vertigo in MD is a possible side effect of increased sensorineural hearing loss as well as residual sensation of disequilibrium which is often reported by patients (Sajjadi & Paparella, 2008). The administration of intratympanic gentamicin may also be referred to as a chemical labyrinthectomy, and can be used with caution in patients with useable hearing. Many studies suggest that a partial ablation can reduce the risk of hearing loss to approximately 20% (Carey, 2004).

Intratympanic steroid injections have become popular as a means of controlling vestibular symptoms in MD as they have the potential advantage over gentamicin of not being inherently ototoxic (Lloyd, 2012). Garduno-Anaya et al (2005) found that 82% of their subjects with MD achieved complete control of their vestibular symptoms with the use of intratympanic steroids as opposed to 57% in the placebo group. Their finding also correlated with most other studies in suggesting that both hearing and tinnitus are neither positively nor negatively affected by this treatment method (Lloyd, 2012).

It remains unclear as to why some patients do not respond to intratympanic therapies. Suggested theories include adhesions or round window thickening (Crane, Minor, Della Santina & Carey, 2005). Surgical management then becomes necessary in the presence of on-going and disabling vertigo.

There are several surgical options available and a few factors must be taken into consideration. The choice depends on: degree of useable hearing, the severity of the attacks, and the condition of the contralateral ear (Ghossaini & Wazen, 2006).

Patients with both intractable vertigo and residual hearing benefit from treatment options with the least impact on cochlear function. These include grommet insertion combined with the Meniett® device (which may improve

symptoms of vertigo, tinnitus and aural pressure) and endolymphatic sac surgery.

Insertion of the Meniett® device is a more recent treatment option for patients with MD and intractable vertigo. It uses the introduction of positive pressure through a pulse-generator into the ear. Researchers comparing the efficacy of the Meniett® device to a placebo found a significant reduction in the frequency and intensity of reported vertigo, tinnitus and aural pressure in the experimental group with no significant side effects (Densert & Sass, 2001). However others have found the long-term efficacy of the device to be poor (Boudewyns et al, 2005).

ELS shunt surgery (also known as endolymphatic sac enhancement) as initially proposed by Portmann (1927) approximately 90 years ago, involves the wide decompression of the ELS via exposure of the posterior fossa dura both superiorly into the retrofacial air cells and inferiorly towards the jugular bulb. The sac is incised and a silastic tube is inserted to maintain decompression of the endolymphatic sac (Walton & Axon, 2012). Researchers claimed a vertigo cure rate of approximately 70% and a reduction in vertigo rate of around 90% (Huang, 2002; Paparella, 2002). However, detractors of this technique reported an equal success rate with placebo surgery (Thomsen, Bretlau, Tos & Johnsen, 1981). Endolymphatic sac surgery was considered to be a conservative choice of surgical management, nonetheless it was still seen as a very controversial surgical choice in the literature, and has a very small risk of harming residual hearing (Walton & Axon, 2012).

1.6. Vestibular Neurectomy

According to Sajjadi and Paparella (2008), effective management of MD through dietary control and medical treatment including the intermittent use of oral steroids and middle-ear perfusion with steroids or gentamicin has substantially reduced the number of patients with intractable vertigo requiring vestibular neurectomy (VN). In addition, they also comment that at most

otological centres, this procedure is performed far less at present than it was in the mid-1980s.

VN should be considered in patients where there is residual hearing (Walton & Axon, 2012). VNs are done to relieve vertigo, but also to preserve residual hearing if present. The vestibular portion of the eighth cranial nerve is cut in such a manner that the hearing portion of the nerve is preserved (Ghossaini & Wazen, 2006). With this surgery, the vertigo is addressed, because the afferent vestibular information from the nerve is no longer transmitted to the brain (see Figure 2 for an illustration of this procedure).

VN was initially made popular by Dandy in the mid 1900's (Sajjadi & Paparella, 2008) but was modified by House in 1961 when he introduced the middle-fossa approach (House, 1961). This technique was further modified to include inferior VN for improved vertigo control (Glassock, Kveton & Christiansen, 1984). Silverstein and Norrell (1980) were the first to describe a retro labyrinthine approach for VN in the treatment protocol for MD, but this technique was once again modified to the retro sigmoid/internal auditory canal approach in 1985 (Silverstein, Norrell & Smouha, 1987).

The retro sigmoid approach as described by Silverstein and Rosenberg (1996) and illustrated in Figure 2, is the most commonly used procedure today, because of its ease of use and shortened surgical time (Teufert & Doherty, 2010). A 3cm retro sigmoid craniotomy is performed, removing the posterior wall of the internal auditory canal to the singular canal, therefore gaining access to the cochleovestibular nerve. Delineation of the vestibulocochlear plane in the posterior fossa is critical to ensure that only the vestibular portion of the nerve is severed (Ghossaini & Wazen, 2006). This produces a complete denervation of the vestibular labyrinth and preserves the patient's hearing (Silverstein and Rosenberg, 1996). Silverstein, Norrell and Haberkamp (1987) considered the retrosigmoid VN to be an important improvement in the evolution of VN for the treatment of vertigo.

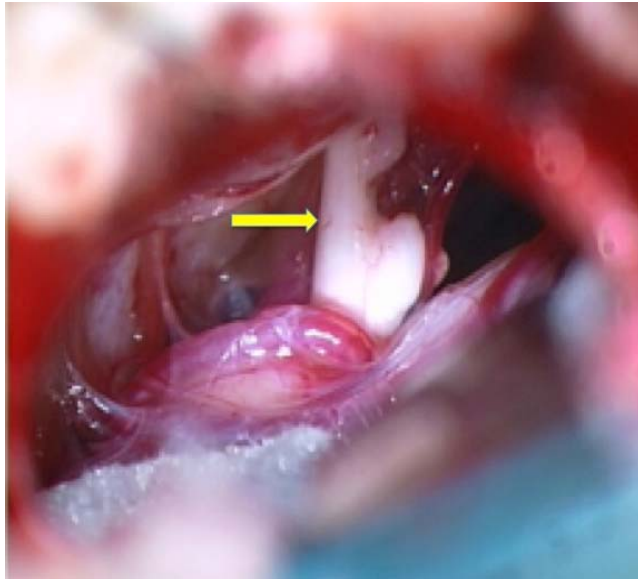


Figure 2. Left sided vestibular neurectomy in a subject with MD. A portion of the nerve is removed to prevent any possible spontaneous reanimation. At this point the cochlear fibres run in the inferior (left in this picture) part of the nerve and are separate from the vestibular fibres (picture courtesy of Dr L Hofmeyr).

Silverstein and Jackson (2002) cite a vertigo cure rate of 85% and substantial improvement in a further 7% of cases. Hearing was preserved in 76% of subjects, with only 20% of subjects showing a slight change in hearing levels as compared to pre-surgery thresholds, and only up to 4% of subjects showing significant hearing loss. Potential complications included hearing loss, facial nerve paralysis, cerebrospinal fluid leaks and headaches. Surgical complications of VN via the retro sigmoid approach are rare (Ghossaini & Wazen, 2006).

To this end, in severe cases, and in those where stable balance is essential for one's occupation, such as an airline pilot, VN is the surgical treatment option of choice in order to minimize the vestibular symptoms experienced by the patient (Walton & Axon, 2012).

Two separate studies, one by Leveque, Seidermann, Tran, Langagne, Ulmer and Chays (2010), and another more recent publication by Angeli, Telischi

and Eshraghi (2014), have identified that many subjects continue to report episodes of recurrent vertigo or constant disequilibrium post VN, although two previous studies found that the episodes of vertigo or imbalance are usually of reduced intensity and frequency as compared to pre-surgery (Perez, Ducati, Garbossa, Benech, Fontanella, Canale & Albera, 2005; Aw, Magnussen, Todd, McCormack & Halmagyi, 2006). Several possible causes of this have been proposed, including incomplete vestibular nerve section, neuroma formation, poor central compensation, vestibular dysfunction in the contralateral ear, nerve regeneration and the possibility of non-otologic vertigo such as vestibular migraine (Leveque, Seidermann, Tran, Langagne, Ulmer & Chays, 2010).

Previous literature has attempted to evaluate the efficacy of VN in treating the vestibular component of MD and in doing so, researchers have utilised tests such as calorics (Leveque, Seidermann, Tran, Langagne, Ulmer & Chays, 2010; Perez, Ducati, Garbossa, Benech, Fontanella, Canale & Albera, 2005), vHIT (Leveque, Seidermann, Tran, Langagne, Ulmer & Chays, 2010) and (cervical) vestibular evoked myogenic potentials (Leveque, Seidermann, Tran, Langagne, Ulmer & Chays, 2010; Angeli, Telischi & Eshraghi, 2014).

The study by Leveque and colleagues (2010), attempted to evaluate a wide range of frequencies in order to extend the testing to each vestibular organ. They therefore included calorics and vibration-induced nystagmus (VIN) tests using VNG recording, vertical and horizontal visual subjective perception (VVS and HVS), vHIT and VEMP. It should be noted that only cervical VEMPs were utilized in their study. Post-operative results of their study can be summarized as follows: all of the subjects (n=24) had absent caloric responses post surgery (23 of the 24 demonstrated a caloric response prior to surgery); while all subjects exhibited a strong VIN response to 30, 60 and 100Hz stimulation, the VIN response at 30Hz was lower than that of 60 and 100Hz for all subjects; vHIT results revealed an absence of VOR for horizontal, anterior and posterior canal stimulation in 23 out of the 24 subjects on the operated side; VVS and HVS results consistently deviated toward the operated side. It should be noted that these authors were unable to compare

pre and post operative data as the only vestibular testing that all subjects had undergone prior to surgery was bithermal calorics. Of the 24 subjects studied, only one reported experiencing any recurrence of a vertigo crisis since the surgery. The researchers concluded that their study proves that VN can provide a complete deafferentation.

In contrast to the afore-mentioned study which looked at a broad range of frequencies when evaluating the post operative vestibular functioning of VN subjects, the study by Perez and colleagues (2005), only considered calorics in their vestibular examination. They also looked at post-operative hearing status, finding that of the 12 subjects studied, 10 out of the 12 had no change in their hearing status with 2 subjects presenting with improved hearing thresholds. All of their subjects had present calorics pre-surgery and absent calorics on the operated side post surgery with no change in the caloric status of the healthy (contra-lesional) ear.

Angeli, Telischi and Eshraghi (2014) were the first researchers to have published a study comparing cervical VEMP (cVEMP) results before and after VN. The surgical team used the middle fossa approach in performing the VN. They studied five subjects who underwent the surgery between 2002 and 2011; three with present cVEMPs pre-operatively remained present post-operatively. One subject with absent cVEMPs pre-surgery was not retested post surgery. The fifth subject never had pre-operative cervical cVEMPs performed and did not appear to be tested post-operatively. Changes in latency or amplitudes were not reported upon. They concluded that their surgical approach was effective for achieving vertigo control as well as for preserving function of the inferior vestibular nerve. They did not utilise any other vestibular testing in their study such as oVEMPs to test superior vestibular nerve integrity.

1.7. Vestibular Evoked Myogenic Potentials

Many of the routine vestibular tests previously available in our clinics assess the functioning of the horizontal canal and superior vestibular nerve while they

fail to evaluate the four remaining vestibular organs and the inferior vestibular nerve (Akin & Murnane, 2001). Recent research has focused on developing assessment tools, which look at all three semi-circular canals as well as the otolith organs themselves.

In humans, the otolith organs (the utricle and saccule) are sensitive to horizontal and vertical linear movement respectively. Researchers have previously noted that in some lower vertebrates such as fish and amphibians, the saccule functions as the end organ of hearing (Popper, Platt & Saidal, 1982). With evolutionary development, the saccule has been replaced by the cochlea in mammals, but researchers have found some neurophysiological evidence that the mammalian saccule remains responsive to sound (Akin & Murnane, 2001). Reactions to sound stimulation at frequencies and levels within the range of hearing of humans, have been shown in the squirrel monkey (Young, Fernandez & Goldberg, 1977), the cat (McCue & Guinan, 1994) and the guinea pig (Murofushi, Curthoys, Topple, Colebatch & Halmagyi, 1995).

Since the otolith organs are sensitive to linear acceleration, researchers have attempted to deliver linear accelerations to the patient's head while measuring the responses to that stimulus. However most of the stimulation methods used, such as centrifuges and tilt chairs, while excellent research tools, remain unviable for the clinic setting. Recent research has found that 500 Hz bone conducted vibration (BCV) of the head and (in many) 500 Hz air conduction sound (ACS) cause a series of linear accelerations at the mastoids therefore rendering BCV as a clinically feasible otolithic stimulus (MacDougall, McGarvie, Halmagyi, Curthoys & Weber, 2013).

Previous researchers were able to demonstrate that the saccule is the origin of a short latency myogenic potential generated by the electromyography (EMG) of neck muscles and that the amplitude of the response depended on the stimulus level (Townsend & Cody, 1971). Although the evoked response could be replicated by other researchers, the specificity of the saccule as the origin of the response was only accepted as recently as 1992, when

Colebatch and Halmagyi demonstrated that the VEMP response (when recorded from a site over the sternocleidomastoid muscle as opposed to earlier research which recorded from the inion) disappeared following unilateral VN and that the response was preserved in subjects with severe sensorineural hearing loss and normal vestibular functioning (Akin and Murnane, 2001). Colebatch and Halmagyi initially referred to the response as “click-evoked vestibulo-collic responses”, whilst other researchers have since coined the term “vestibular evoked myogenic potentials” as they are muscular potentials evoked by stimulation of the vestibular end organ (Zhou & Cox, 2004).

Although clinically, practitioners used ACS to perform VEMP studies, continued use of 500 Hz BCV in research studies found that this stimulus activates both the utricule and saccule. In an effort to develop separate tests of utricular and saccular function, Curthoys et al (2010) proposed that due to the fact that these two sense organs have rather different neural pathways, there is a very strong projection of utricular afferents to the oculomotor system, whereas the saccular projections to the oculomotor system are weak. Conversely saccular projections to cervical spinal regions are strong. Therefore Curthoys et al (2010) proposed that the ocular vestibular evoked myogenic potential (oVEMP) with the first trough around 10 msec and labeled n10, predominantly tests *utricular* function and that the cervical vestibular evoked myogenic potential (cVEMP) with the first peak at around 13 msec and the following trough at around 23 msec labelled p13-n23, predominantly tests *saccular* function. Although the responses appear to be stronger using a 500 Hz Fz stimulus for both tests, there is also excellent evidence that ACS is effective.

In their article, Zhou and Cox (2004) summarize the reasons cVEMPs are suitable for clinical use as follows: Firstly the response is repeatable and consistent. Despite variations in amplitude, the latency is relatively stable. Secondly, VEMP testing may be more specific than other tests in locating site of lesion. Results may reveal abnormal function of the saccule and/or the inferior vestibular nerve. Thirdly, VEMPs could potentially be a sensitive test

and may be able to detect minor changes in the function of the vestibular system specific to the otolith organs and their central pathways. Fourth, VEMPs are relatively easy to perform. Most current equipment that is capable of recording the auditory brainstem responses (ABR) can be adapted to record VEMPs. Unlike VNG, which may take 1–2 hrs to complete an evaluation, VEMP testing takes less than 1 hr. Furthermore, the testing does not induce discomfort, and most people can tolerate the procedure with ease, involving minimal cooperation.

With the recent discovery of oVEMPs, we can add a fifth point with respect to this new test: oVEMPs may reveal abnormal function of the utricle and/or the inferior vestibular nerve (Piker et al, 2011).

Therefore with the advent of cVEMP in 1992 (Colebatch & Halmagyi, 1992) and more recently the oVEMP in 2005 (Piker et al, 2011), we now have accessible diagnostic techniques available to researchers and clinicians, which provide information regarding the functioning of the otolith end organs and their enervating pathways.

To summarize, the cVEMP is an inhibitory response measured at the tonically contracted ipsilateral sternocleidomastoid muscle (SCM) in response to loud sounds, bone vibration and galvanic stimuli. As stated previously, it is thought that this response is part of the vestibulo-collic reflex that originates in the saccule, continues up through the inferior vestibular nerve to the vestibular nuclei, the vestibulospinal tract and the ipsilateral sternocleidomastoid muscle (Brantberg & Mathiesen, 2004). As such we can infer functional status of the saccule and inferior vestibular nerve (Piker, Jacobson, Burkard, McCaslin & Hood, 2013). Normal cVEMP responses are characterized by a biphasic (positive–negative) wave. In many studies, the peaks and troughs are labeled with the mean latency in milliseconds preceded by the lowercase letters “p” (for positive) or “n” (for negative), as proposed by Yoshie and Okudaira (1969) to distinguish them from neurally generated evoked potentials. The first positive - negative complex is often labeled as p13–n23 (Figure 3) due to the normative latency values (Zhou and Cox, 2004).

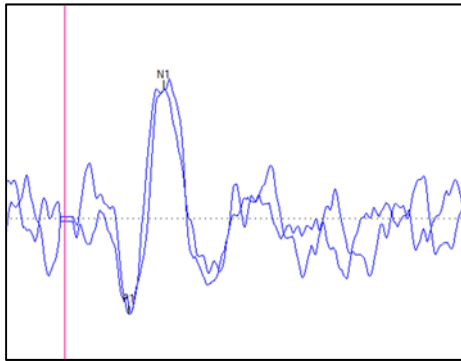


Figure 3. A normal cVEMP p13-n23 response

The oVEMP is an excitatory response recorded with electrodes placed inferiorly on the contralateral eye with the subject looking up. An identical test stimulus is used as for the cVEMP (Piker et al, 2011). In this protocol it is thought that the response is initiated in the utricle and travels via the VOR to the inferior oblique muscles via the superior vestibular nerve. We can therefore make inferences to utricular status and superior vestibular nerve function (Piker et al, 2011). In Figure 4 below, a simple schematic diagram of the cVEMP and oVEMP pathways is depicted as described by Curthoys et al (2013).

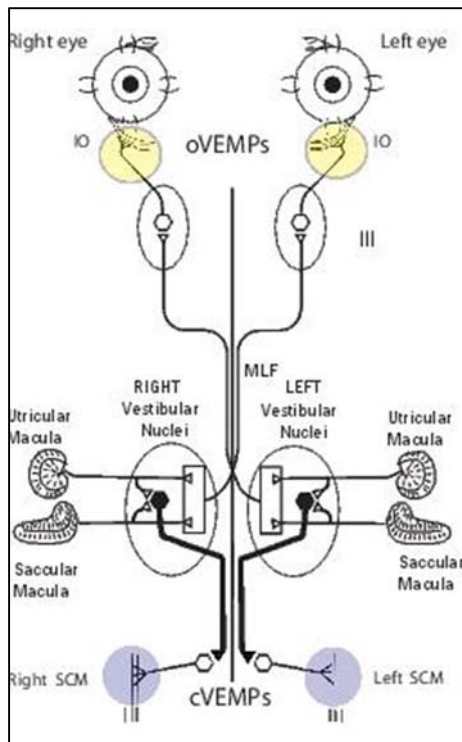


Figure 4. Schematic diagram of the cVEMP and oVEMP pathways (Curthoys et al, 2013)

The oVEMP consists of a series of negative and positive peaks, most often beginning with a negative peak with latency of about 10 msec (n10 or N1), followed by a positive trough with latency around 15 msec (P1) (Rosengren, Welgampola and Colebatch, 2009). Below is a graph (Figure 5) depicting a normal oVEMP response.

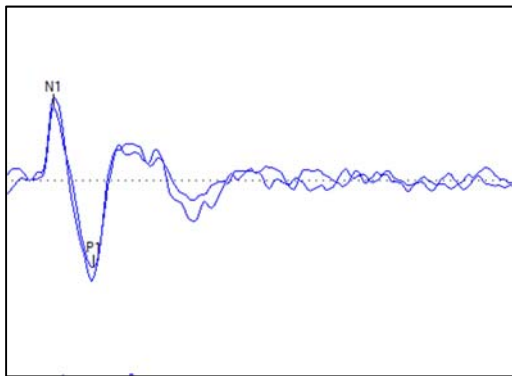


Figure 5. A normal oVEMP n10 response

1.8. VEMP in MD

Early studies evaluating cVEMP results in MD, found that approximately 40% of subjects with unilateral MD had abnormal VEMPs (Morufushi, Matsuzaki & Shimizu, 2000) while another study by De Waele, Tran Ba Huy, Diard, Freyss and Vidal (1999) reported that 54% of subjects with MD showed an absence of VEMPs on the affected side. In MD, cVEMP amplitudes are often absent or reduced (Morufushi, Matsuzaki & Shimizu, 2000), a finding attributed to a saccular hydrops (Zuniga, Janky, Schubert & Carey, 2012). In assessing the stages of MD with cVEMPs, Young and Huang (2003) found that there are significant amplitude changes, with an increase in amplitude often found in the early stages of MD. The more recent research has looked at the effect of stimulus frequency on the VEMP response and has found a shift in the dominant response frequency from 500Hz to 1kHz in MD which may be utilised as a diagnostic finding (Rauch, Zhou, Kujawa, Guinan & Hermann, 2004).

In an effort to establish the vestibular evoked-potential profile of MD, Young and Huang (2003) studied air-conducted (AC) sound and bone-conducted vibration (BCV) evoked responses in 77 subjects and 35 controls. They found that definite MD is characterized by an evoked-potential profile that affects both sound- and vibration-evoked cVEMPs and oVEMPs, with a significantly higher prevalence of abnormalities to AC-stimuli. In addition, they reported that sixty percent of the subjects studied demonstrated abnormalities to one or both AC VEMPs, with a similar prevalence of AC oVEMP and AC cVEMP abnormalities but a significantly higher proportion of absent responses for AC oVEMPs. Many studies evaluating the VEMP findings in MD have confirmed the findings of Rauch, Zhou, Kujawa, Guinan and Hermann (2004) where they found that “Ménière’s ears display alterations in vestibular evoked myogenic potentials threshold and tuning”, with Winters, Campschroer, Grolman and Klis (2011) finding that the best stimulus frequency for tone burst oVEMPs was 1000Hz.

In 2012, Zuniga, Jankey, Schubert and Carey found that the N1 latency of oVEMPs was significantly longer in MD as compared to controls also finding that the amplitudes of recorded oVEMPs were smaller in MD when compared to controls. This correlated with other studies (Winters, Campschroer, Grolman & Klis, 2011) which found that in general, patients with MD showed lower amplitudes and higher thresholds for oVEMPs as compared to normal subjects.

1.9. Problem statement and Rationale

Current knowledge assumes that if cVEMPs are not recorded post VN as reported by Welgampola, Rosengren, Halmagyi and Colebatch (2003) and later confirmed by Leveque and colleagues (2010), this is due to the resection of the inferior vestibular nerve (Brantberg & Mathiesen, 2004). With the advent of the oVEMP technique, which is now available routinely in a clinical setting, we are able to infer the functional status not only of the utricle but also of the superior vestibular nerve (Piker et al, 2011). This branch of the cochleovestibular nerve should be fully resected together with the inferior

vestibular nerve in a successful VN surgery when applied for the treatment of MD. As yet, there are no reports describing oVEMPs subsequent to VN using the retro sigmoid approach in MD. The availability of both of these types of vestibular evoked potentials might provide a new way to evaluate the success of the retro sigmoid surgical approach to de-afferent both the inferior and superior divisions of the cochleovestibular nerve. The two, together, may also provide feedback on the success of the surgical attempt to preserve the cochlear fibres during the VN procedure, therefore highlighting the need for including both cVEMPs and oVEMPs in MD subjects post VN and thus providing the impetus for the aim of this current study.

2. METHODOLOGY

2.1. Main Aim

The main aim of this study was to describe the amplitude and latency characteristics of cVEMP and oVEMP responses in adults with MD who underwent VN via the retro sigmoid approach and to compare the results with VEMP responses obtained from subjects diagnosed with MD as well as a group of subjects without MD and no history of vestibular symptoms.

2.2. Research Design

This is a quantitative research study, produced through the recording of cVEMPs and oVEMPs responses in the three groups of subjects with several sets of numerical data.

Studies aimed at quantifying relationships can either be descriptive or comparative. A descriptive design attempts to describe and explain conditions of the present to describe a phenomenon, while a comparative research design attempts to explore cause and affect relationships where causes already exist and cannot be manipulated (Carroll, 2012).

The research design in this study was predominately descriptive with results from post-operative VEMP measurements being compared to two control groups – the first consisting of normal subjects matched for age and gender, with no history of vestibular symptoms and no current vestibular involvement, and the second consisting of age matched subjects with MD.

2.3. Ethical Considerations

The Faculty of Humanities' Research and Ethics Committee at the University of Pretoria approved this study for ethical clearance. The letter of ethical clearance and approval from the Committee is included as Appendix A.

Any medical research faces ethical issues. The four principles (Salkind, 2006) that must be discussed when facing these ethical dilemmas are respect for autonomy, beneficence, non-maleficence and justice.

2.3.1. Respect for autonomy

As with all medical research, individual privacy, anonymity and confidentiality needs to be maintained (Mouton, 2001). Research subjects were allocated an identifying code where necessary for data processing. Only this code was used in data analysis or reporting. This was clearly explained in the informed consent letter.

a) Informed consent

Each prospective research subject was asked to sign a letter of informed consent (Appendix B). This was both an ethical and legal requirement. According to Moodley (2011), truly informed consent is a process and may be unavoidably time consuming. All research subjects must have the competence (legal judgement) and capacity (clinical judgement) to give informed consent (Mkhize, 2006).

According to Oliver (2010), informed consent is a primary ethical principle and involves three main components: the participants should fully comprehend the research procedure; they should give free and willing consent for participation and should be free to withdraw from the research at any point in time. Subsequently, the present study aimed to acquire written informed consent from each participant by signing the appropriate form (attached as Appendix B). Each participant signed this form after they had read a letter explaining the goal of the study and what would be expected of them (see Appendix C). In addition, the letter clearly stated that participation was completely voluntary and that participants could withdraw from the study at any time. The letter also assured participants of confidentiality. A verbal explanation of the study and testing process was provided prior to the onset of the testing process.

The researcher verbally discussed the informed consent letter with all prospective participants and the competent research subjects were “able to communicate a choice, understand the information given to him/her, appreciate the medical consequences, reason about treatment options” (Moodley, 2011).

b) Confidentiality

Medical confidentiality is a crucial part of maintaining a research subject’s autonomy whereby the researcher(s) implicitly or explicitly promise(s) their participants that all information provided by them will be kept confidential (Moodley, 2011).

The following steps were taken to ensure non-disclosure of information and subject confidentiality:

- No personal information linking the subject to the study was documented or utilized.
- The files of research subjects were not removed from the ENT practice.
- The coding process ensured subject confidentiality.
- All information gained in the study was treated as confidential.
- Storing data on a computer package with a secret user password ensured the security of research records (Neuman, 1997).

2.3.2. Beneficence and non-maleficence

“Beneficence refers to doing good and the active promotion of goodness, kindness and charity” (Beauchamp & Childress, 2001). Medical practise is firmly rooted in the principle of *primum non nocere* – first do no harm. Avoiding or minimizing harm to patients is a fundamental obligation of all practitioners (Moodley et al, 2011). This is the principle of non-maleficence.

The potential inconvenience of participating in the study (the time and effort required to complete the questionnaires and to participate in the hearing and

vestibular testing) was indicated in the letter of consent. The letter also explained that the information gathered should provide useful data to audiologists, ENT Surgeons as well as Neurosurgeons in South Africa and abroad by publication of results upon completion of the study. Participants were also offered a summary of the results upon completion of the study as well as reports on their current hearing and vestibular status. There were no incentives or rewards (financial or other) offered for the participation in the study.

2.3.3. Distributive justice

The effect of potential inequality between the researcher and research participants was limited by the fact that all subjects were of a similar cultural/linguistic background as the researcher.

2.4. Sample Population and subject selection criteria

Typical case sampling was used to recruit the MD and MD with VN subjects from an ENT's private practice. These subjects were initially approached by the treating physicians for consent to participate within the study before being approached by the researcher. The subjects in the normal (N) group were recruited via convenience sampling.

A total of 44 subjects participated in the study: 14 subjects diagnosed with MD according to the AAO-HNS (1995) classification by a board-certified ENT and who had undergone selective VN (group name = MD + VN), 15 subjects diagnosed with MD only (group name = MD) and 15 age and gender matched subjects (with respect to the MD + VN group) with no history of vestibular symptoms and no current vestibular involvement were evaluated for participation in the study (group name = N). Subjects were matched for age as much as possible across the three groups evaluated as, even though previous research has indicated the effects of age on the VEMP response (Piker, Jacobson, Burkard, McCaslin & Hood, 2013), this age group could not

be eliminated from the study due to the purposive sample population used for the MD + VN group.

Of the 20 eligible MD subjects who had the VN via the retro sigmoid approach surgery performed, 2 were since deceased, one subject refused participation in the study and 3 live in locations too far away for participation in the study. The 14 remaining subjects were very amenable to participating in the research. Their surgeries were performed over a period from 2009 to 2013 by the same surgical team as described above. All of the subjects, including the two comparative groups, were tested over a four month period from June – September 2014. The age and gender characteristics of the subjects (as at the time of testing) are described in Table 3. The mean interval between the date of surgery and the date of testing was 34 months (with a range of 6 to 65 months). Nine of the subjects underwent a left VN, while five underwent a VN on the right side.

Table 3. Description of subjects

| Factor | MD + VN | MD only | N |
|-------------------------|----------------|-----------------|----------------|
| Number of subjects | 14 | 15 | 15 |
| Age range (y) (min-max) | 40-71 | 43-71 | 40-72 |
| Mean age \pm SD (y) | 58.2 \pm 8.3 | 59.4 \pm 11.9 | 58.1 \pm 8.6 |
| Gender (F:M) | 4:10 | 9:6 | 5:10 |

MD= Menière’s Disease; VN = Vestibular Neurectomy; N = normal (no MD and no vestibular symptoms); SD = standard deviation; y = years; F = Female; M = Male

2.5. Data collection procedures

Once subjects agreed to participate in the study after reading the cover letter (Appendix C) and signing the informed consent form (Appendix B), testing commenced.

A data collection sheet (Appendix D) was compiled in order to organize the impedance and pure tone results used for subject inclusion as well as the

cVEMP and oVEMP latency, amplitude and asymmetry ratio results in tabular form for ease of comparison and analysis.

2.5.1. Surgical procedures

All surgeries were performed by the same surgical team, using the same surgical procedure as described by Silverstein and Rosenberg (1996). All of the subjects were operated on, under general anaesthesia without muscle relaxant. Preoperative antibiotics and cortico steroids were administered and the subject placed in the side lying position. A mayfield head clamp was placed to secure the head. After a linear skin incision, a craniotomy was performed posterior to the sigmoid sinus and inferior to the transvers sinus. The dura mater of the posterior cranial fossa was incised and reflected to anterior. Gentle retraction of the cerebellar hemisphere was performed and Leila retractor placed to gain access to the cerebellopontine angle. After identifying the cochleovestibular nerve and the facial nerve, the cochleovestibular nerve was divided in its length to separate the cochlea and vestibular fibre tracts. Intra operative auditory brainstem response (ABR) (using the Interacoustics Eclipse AEP system) and facial nerve monitoring (using a Neurosign® Motor Nerve Monitor) were utilized in all cases in order to ensure preservation of the cochlea and facial nerves. Delineation of the vestibulocochlear plane in the posterior fossa is critical to ensure that only the vestibular portion of the nerve was severed (Ghossain & Wazen, 2006) (see Figure 1). The facial nerve was confirmed with the facial nerve stimulator (Neurostim® from Visionmedical) before the vestibular fibre tract was cut and a segment removed to avoid possible future reanastomosis. Bleeding was controlled and after removing the Leila retractor, the dura mater of the posterior fossa was closed. Hitching sutures were placed to minimise hematoma formation. After covering the craniotomy with a titanium mesh plate the surgical wound and skin were meticulously closed in layers. The subjects were kept awake in the intensive care unit (ICU) overnight, for observation and discharged after 4 days in the surgical ward.

2.5.2. Otologic and audiological examinations

Before any diagnostic test was conducted, an otoscopic examination using a Heine 2000 diagnostic otoscope was performed in order to visually inspect the external canal for any debris, cerumen or foreign bodies that may occlude the external auditory meatus and to identify any possible perforations of the tympanic membranes. If foreign bodies were present and/or impacted cerumen was present ear canal management was performed.

Y-226 Hz tympanometry was performed using the Interacoustics Titan Diagnostic oto-admittance meter. Once again, disposable tips were used and hand washing with hand sterilizer was employed between subjects.

All subjects in the study had to present with a type A tympanogram (Jerger, 1970) and no significant air-bone gaps (< 10 dB HL) in order to exclude any post-surgery subjects presenting with a conductive hearing component due to bone debris post VN (Teixido & Wiet, 1992).

Pure tone (air and bone conduction) audiometry was performed in a sound-isolated booth using the Madsen Itera II Diagnostic Audiometer. The audiometer had been calibrated in January 2014 (testing occurred from May – July 2014) and daily functional inspection, performance checks, and bio-acoustic measurements were conducted in order to verify the equipment's performance prior to use. Air conduction thresholds were obtained using E-A-R Tone insert earphones, which were matched and calibrated to the audiometer. Disposable insert earphone tips were used and discarded after each test was completed. The researcher washed her hands in between subjects, using hand sterilizer as an additional precaution. Pure tone thresholds were obtained using the 10 down – 5 up bracketing technique as suggested by the ASHA guidelines for obtaining pure-tone thresholds (2005).

2.5.3. Vestibular Examinations

Before initiating the formal vestibular examinations, the researcher enquired about each subject's current vestibular symptoms at the time of participation i.e. each subject was asked the question: Are you currently experiencing any vertigo or dizziness?

2.5.3.1. cVEMP protocol

All of the research subjects were tested in a semi-recumbent position and were asked to turn their heads away from the test stimulus during the procedure. This facilitated a unilateral tensing of the sternocleidomastoid (SCM) muscle and allowed for minimal strain on the neck muscles – a concern for many in the test population. Standard electrode placement was used as described in the literature (Welgampola & Colebatch, 2005). cVEMP waveforms and electromyography (EMG) activity were recorded using a commercial GN Otometrics system, the ChartR 200, with self-adhesive single use ICS® electrodes. Single use ICS® differential electrodes were placed symmetrically on the midpoint of each SCM muscle of the side being stimulated – with the superior electrode positioned as the non-inverting electrode for recording the response and the inferior electrode for monitoring the EMG activity. The inverting electrode was placed on the sterno-clavicular junction with the ground electrode on the forehead. Impedances were checked and accepted if below 5 kOhm. The response was elicited using a 500Hz tone burst at 95dBnHL through E3A 300 ohm insert earphones. Stimuli were delivered monaurally and testing was paused after 100 tracings were obtained within the test parameters. Due to EMG monitoring only responses with surface activity of between 65 and 75µV were accepted as a response. EMG monitoring allowed equal muscle contraction between the two sides to avoid side-to-side differences due to inadequate muscle activation. In addition, the use of the monitor allowed for a visual feedback system in order to achieve constant and adequate muscle tension. Adequate rest breaks as per each individual subject's needs were given in order to

avoid muscle strain and/or fatigue. This data collection process was repeated twice and the results were added together and then averaged for analysis.

A positive cVEMP response was identified as a biphasic waveform with an initial positive polarity (P1) and a subsequent negativity (N1) within a post stimulus period of 30 msec. The absolute latencies of P1 and N1 were determined as the time in msec between $t = 0$ msec and the maximal peaks of P1 and N1, respectively. Inter-peak amplitude covered the amplitude span between P1 and N1, where both peaks were expressed in microvolts (μV) relative to the baseline. The relative parameter asymmetry ratio (AR) was determined by calculating the inter-aural peak-to-peak amplitude difference divided by the sum of the peak to peak amplitude of both ears of each subject. Parameters considered in the analysis included the latencies (msec) of P1 and N1, the inter-peak amplitudes (μV) thereof, as well as the AR's (%) between ears if considered significant at greater than 35% (Welgampola and Colebatch, 2001).

2.5.3.2. oVEMP protocol

Test subjects were kept in the semi-recumbent testing position as above. This was done for two reasons. Firstly, by keeping the head in a common position and having a marking on the ceiling it is easy to achieve a constant eye position across test subjects. In addition, this position appears to reduce the pulling on the skin by the electrodes as experienced by the elderly, in particular, in a seated position. Standard electrode placement was used as described in the literature (Piker et al, 2011). The oVEMP waveforms were recorded using a commercial GN Otometrics system with self-adhesive ICS® electrodes. The non-inverting electrodes were placed just below the eye with the inverting electrodes 2cm below the non-inverting counterpart. The ground electrode was placed on the chin. As the oVEMP is an excitatory response there is no need to monitor the EMG activity or to take this into consideration when analysing the results. Impedances were checked and accepted if below 5 kOhm. The contralateral response was elicited using a 500Hz tone burst at 97dBnHL through insert earphones. Stimuli were delivered monaurally and

testing was paused after 100 tracings were obtained within the test parameters. Adequate rest breaks were given as per each individual subject's needs. A positive oVEMP response was identified as a biphasic waveform with an initial negative polarity (N1) and a subsequent positivity (P1) within a post stimulus period of 20 msec. Parameters considered in the analysis included the latencies of N1 and P1, the amplitudes thereof, as well as the asymmetry ratios (%) between ears if considered significant as for cVEMP at greater than 35% (Welgampola & Colebatch, 2001). Once again, the two responses recorded were added together and averaged for analysis purposes.

In order to ensure infection control was maintained, the researcher sterilized her hands between subjects. The electrode sites were sterilized and scrubbed in preparation for electrode placement. Disposable insert earphones were utilized and discarded after each subject was tested.

2.6. Data Analysis

The data gathered was quantitative in nature. It was collated and submitted for statistical analysis. All descriptive (means, standard deviations and percentages) and inferential statistics were performed using the commercially available statistical software package SPSS® for Windows, version 22. As the outcome of Kolmogorov-Smirnov test statistic showed that the collected VEMP response data were not normally distributed, non-parametric test statistics were used. An independent Kruskal-Wallis test statistic was used to evaluate the differences in mean latency, amplitude, and asymmetry values between the different groups. Post hoc testing was carried out using multiple individual Mann-Whitney U tests.

3. Results

This study described the cVEMP and oVEMP responses in adults with MD who underwent selective vestibular neurectomy via the retro sigmoid approach, in comparison to a group of MD subjects and a group of subjects without a history of vestibular symptoms.

Of the 14 subjects diagnosed with MD and who had undergone a VN via the retro sigmoid approach, 5 of them still reported that they experienced episodic periods of recurrent dizziness, while the other 9 remained symptom free.

cVEMPs

Table 4 summarizes the cVEMP responses for the 3 different groups. The results of the cVEMP analysis showed that all cVEMPs were absent on the side of the operated ear in the group of MD subjects who had undergone selective VN.

Table 4. Description of cVEMP findings

| Parameter | n | Mean | Median | SD | 95% CI for Mean | | IQR | Range |
|----------------------------|----|---------------|--------|-------|-----------------|-------|-------|--------|
| | | | | | Lower | Upper | | |
| Latency P1 (msec) | | | | | | | | |
| N | 15 | 16.35 | 15.84 | 1.71 | 15.40 | 17.29 | 1.83 | 7.17 |
| MD only | 15 | 15.19 | 15.92 | 0.86 | 15.19 | 16.35 | 1.17 | 3.00 |
| MD + VN | 14 | ALL ABSENT | | | | | | |
| Latency N1 (msec) | | | | | | | | |
| N | 15 | 24.41 | 24.17 | 2.35 | 23.11 | 25.71 | 3.42 | 7.75 |
| MD only | 15 | 23.57 | 24.27 | 2.38 | 21.97 | 25.17 | 4.36 | 6.75 |
| MD + VN | 14 | ALL ABSENT | | | | | | |
| Amplitude (uV) | | | | | | | | |
| N | 15 | 65.55 | 57.71 | 35.53 | 45.87 | 85.22 | 46.96 | 142.44 |
| MD only | 15 | 53.74 | 38.40 | 36.89 | 28.96 | 78.52 | 34.02 | 105.60 |
| MD + VN | 14 | ALL ABSENT | | | | | | |
| Asymmetry Ratio (%) | | | | | | | | |
| N | 15 | 13.06 | 10.73 | 9.38 | 7.86 | 18.25 | 17.80 | 26.20 |
| MD only | 15 | 44.39 | 56.74 | 24.24 | 28.11 | 60.67 | 49.29 | 64.61 |
| MD + VN | 14 | UTC | UTC | UTC | UTC | UTC | UTC | UTC |

n = number of subjects; SD = standard deviation; CI = confidence interval; IQR = Interquartile Range; N = Normal (no vestibular history); MD= Menière's Disease; VN = Vestibular Neurectomy; UTC = Unable to calculate

Latency

Table 4 contains the latency values of P1 and N1 for the different study groups. Statistical analysis of the average latencies of P1 and N1 in the different groups did not demonstrate any statistically significant differences (Table 4). The latency values of P1 in the N group ranged between 14.33 and 21.50 msec (mean = 16.35 ± 1.71 msec) and between 14.25 and 17.25 msec (mean = 15.19 ± 0.86 msec) for P1 in the MD group. The latencies for N1 ranged between 21.58 and 29.33 msec in the N group and between 20 and 26.75 msec for the MD group with similar means of 24.41 ± 2.35 msec and 23.57 ± 2.38 msec for the two groups ($p > 0.05$). Since all cVEMP responses for the MD + VN group were absent, no latency analysis on this group could be performed.

Amplitudes

Table 4 contains the amplitude values of P1 and N1 for the different study groups. Statistical analysis of the average amplitudes of P1 and N1 in the different groups did not demonstrate any statistically significant differences (Table 4). Although the mean amplitudes (Table 4) obtained for the group suffering from MD appeared to be smaller than those obtained for the N group, with mean values for inter-peak amplitudes for the MD group at 53.74 ± 36.89 uV as compared to 65.55 ± 35.53 uV for the N group, the variability is considerable across subjects as shown by the large standard deviations for the two groups. The interquartile ranges for the two groups were 34.02 and 46.96 respectively, with two outliers in the N group at 105.72 and 161.76uV and two in the MD group found at 120.16 and 126.10uV. Since all cVEMP responses for the MD + VN group were absent, no amplitude analysis on this group could be performed.

Asymmetry Ratio

Table 4 contains the AR values for the different study groups. A highly statistically significant difference ($p < 0.001$) between the AR's for the N and MD groups was found on the Kruskal-Wallis Test. The mean AR for the N group was found to be $13.06 \pm 9.38\%$ with all of the absolute values for the AR's below the 35% normative cut-off (Welgampola & Colebatch, 2001) correlating with the literature. 73% of the absolute values of AR's in the MD only group were considered significant with the mean at $44.39 \pm 24.24\%$ whilst the mean of the MD + VN group was unable to be calculated due to 14% of subjects having absent responses bilaterally and therefore an AR which could not be calculated. 86% of the subject's had a 100% AR which is considered significant in terms of the normative data.

oVEMPs

The results of the oVEMP analysis showed that 100% of oVEMPs were absent on the side of the operated ear in the MD + VN group. The descriptive

analyses of the oVEMP results obtained for the three groups in the study are summarized in Table 5 below.

Table 5. Description of oVEMP findings

| Parameter | n | Mean | Median | SD | 95% CI for Mean | | IQR | Range |
|----------------------------|----|------------|--------|-------|-----------------|-------|-------|-------|
| | | | | | Lower | Upper | | |
| Latency N1 (msec) | | | | | | | | |
| N | 15 | 10.73 | 10.58 | 0.68 | 10.34 | 11.10 | 1.08 | 2.58 |
| MD only | 15 | 10.77 | 10.73 | 0.92 | 10.15 | 11.38 | 0.59 | 3.42 |
| MD + VN | 14 | ALL ABSENT | | | | | | |
| Latency P1 (msec) | | | | | | | | |
| N | 15 | 15.39 | 15.37 | 1.40 | 14.62 | 16.17 | 1.54 | 6.16 |
| MD only | 15 | 15.36 | 15.54 | 1.90 | 14.08 | 16.63 | 2.50 | 7.55 |
| MD + VN | 14 | ALL ABSENT | | | | | | |
| Amplitude (uV) | | | | | | | | |
| N | 15 | 6.56 | 5.26 | 5.21 | 3.67 | 9.44 | 7.84 | 15.55 |
| MD only | 15 | 4.29 | 3.36 | 4.32 | 1.55 | 7.04 | 3.80 | 15.78 |
| MD + VN | 14 | ALL ABSENT | | | | | | |
| Asymmetry Ratio (%) | | | | | | | | |
| N | 15 | 12.02 | 11.82 | 9.17 | 6.93 | 17.10 | 12.07 | 33.78 |
| MD only | 15 | 35.67 | 32.87 | 27.70 | 17.06 | 54.28 | 39.72 | 85.50 |
| MD + VN | 14 | UTC | UTC | UTC | UTC | UTC | UTC | UTC |

n = number of subjects; SD = standard deviation; CI = confidence interval; IQR = Interquartile Range; N = Normal (no vestibular history); MD= Menière's Disease; VN = Vestibular Neurectomy; UTC = Unable to calculate

While none of the MD + VN group had any oVEMP responses, twelve out of fifteen subjects (80%) with MD only had absent responses too.

Latency

Table 5 contains the latency values of P1 and N1 for the different study groups. Statistical analysis of the average latencies of P1 and N1 in the different groups did not demonstrate any statistically significant differences (Table 5). There were no significant differences observed between the mean latencies of N1 and P1 in either of N or MD groups (Table 5) with the latency

values for N1 ranging between 9.42 and 12 msec (mean = 10.73 ± 0.68 msec) for the N group and between 9.13 and 12.54 msec (mean = 10.77 ± 0.92 msec) for the MD group. The latencies for P1 ranged between 11.46 and 17.63 msec for the N group and between 11.58 and 19.13 msec for the MD group, with means of 15.39 ± 1.40 msec and 15.36 ± 1.90 msec respectively. Since all oVEMP responses for the MD + VN group were absent, no latency analysis on this group could be performed.

Amplitude

Table 5 contains the latency values of N1 and P1 for the different study groups. Statistical analysis of the average latencies of N1 and P1 in the different groups did not demonstrate any statistically significant differences (Table 5) even though the mean inter-peak amplitudes obtained for the MD only group appeared to be smaller than those obtained for the N group, with mean values for inter-peak amplitudes for the MD group at 4.29 ± 4.32 uV as compared to 6.56 ± 5.21 uV for the N group.

Asymmetry Ratio

Table 5 contains the AR values for the different study groups. A statistically significant difference ($p = 0.012$) between the AR's for the N and MD groups was found on the Kruskal-Wallis Test. The mean AR for oVEMPs for the N group was found to be $12.02 \pm 9.17\%$, with all the ratios below the normative 35% cutoff as suggested by the literature (Welgampola & Colebatch, 2001). The mean AR for the MD only group was $35.67 \pm 27.70\%$, with 53% of subjects qualifying as having a significant asymmetry (Welgampola & Colebatch, 2001). Only 64% of the MD + VN group presented with a significant 100% AR due to the finding that 36% of the subjects had absent responses bilaterally, therefore resulting in an AR which could not be calculated. There appears to be a large variability in responses with a wide interquartile range for both the N and MD groups, but particularly for the MD group. There is one significant outlier in the N group at 34.76%.

In order to further evaluate the statistical difference observed on the Kruskal-Wallis Test, post hoc testing was carried out using individual Mann-Whitney U testing. A statistical difference was found to exist between the N and MD groups ($p = 0.016$).

4. Discussion

The current study aimed to describe cVEMP and oVEMP responses in adults with MD who underwent VN via the retro sigmoid approach, in comparison with an age matched group of adults diagnosed with MD as well as an age and gender matched group of subjects without MD and no other history of vestibular symptoms. Fourteen individuals previously diagnosed with MD and who had undergone a VN, were willing to participate in this study.

In this study, all of the subjects with MD + VN had absent cVEMPs and oVEMPs on the side of the VN.

The finding of absent cVEMP responses in this study replicated the previous research where VEMP responses were absent in all subjects post VN (Welgampola, Rosengren, Halmagyi & Colebatch, 2003; Leveque, Seiderman, Tran, Langagne, Ulmer & Chays, 2010). The inclusion of oVEMP testing into this research protocol was an attempt to validate whether the VN was complete i.e. whether both the superior and inferior vestibular nerves were successfully resected. While the researcher remains aware that these two tests not only assess superior and inferior vestibular nerve function but also the otolith organs and their associated pathways, she acknowledges that any findings would not be definitive in and of themselves. In addition, the absence of results may be due to pre-operative damage to the otolith organs due to pre-existing sequelae from the MD pathology. Unfortunately pre-operative data was not available for use to include in this study. Although oVEMPs have not previously been studied post VN, the absence of results in all subjects appears to echo the previous findings with cVEMPs previously referenced, once again suggesting that the oVEMP response is absent post VN. The absent oVEMP responses together with the absent cVEMPs, suggest that both branches of the vestibular nerve may have been completely resected.

Statistical analysis of the cVEMP findings with the Kruskal-Wallis test found a significant difference in AR's between the N and MD groups, supporting the

previous findings in the literature the cVEMPs are expected to be reduced in subjects with MD (Welgampola & Colebatch, 2005). The absent cVEMP findings in the MD + VN group support previous findings that this response is found to be absent post VN (Welgampola, Rosengren, Halmagyi & Colebatch, 2003; Leveque, Seiderman, Tran, Langagne, Ulmer & Chays, 2010). These findings support the hypothesis that VN via the retro sigmoid approach completely severs the inferior vestibular nerve fibres and that results in the absence of this response (Leveque, Seiderman, Tran, Langagne, Ulmer & Chays, 2010).

Analysis of the oVEMP results using the Kruskal-Wallis and Mann-Whitney U tests, found a significant difference between the AR's of the N and MD groups, with oVEMP responses absent in 100% of subjects post VN. This again echoes previous findings in the literature with regards to cVEMPs, suggesting that the AR may increase with the presence of MD as the amplitude decreases with advanced MD (Welgampola and Colebatch, 2005) with absent results following VN (Welgampola, Rosengren, Halmagyi & Colebatch, 2003; Leveque, Seiderman, Tran, Langagne, Ulmer & Chays, 2010). Although no pre-surgery data was available in this study and the possibility of otolith damage due to MD remains, the absence of oVEMP responses in 100% of subjects with MD + VN, may allow the hypothesis that this surgical approach also completely severs the superior vestibular nerve fibres.

However, it still remains interesting that of the 14 subjects studied, although none of them had any cVEMPs and oVEMPs responses on the operative side, 6 of the subjects reported that they still experienced recurrent periods of dizziness i.e 43% remained symptomatic. This is a finding that is supported by the literature over the past 17 years, initially by Thedinger and Thedinger (1998), and subsequently by Moon and Hain (2005) and again by Angeli, Telischi and Eshraghi (2014), who all found that there is a class of subjects who report residual episodes of vertigo or loss of balance control following VN. Thedinger and Thedinger (1998) and Angeli, Telischi and Eshraghi (2014) found that 20% of subjects continued to report significant dizziness

post surgery, while Moon and Hain (2005) reviewed 3 cases where vertigo had reoccurred in all 3 subjects post VN with initial cessation of symptoms.

Of the 6 subjects in the current study who remained symptomatic, 2 had absent cVEMP and oVEMP responses on both ears, while a third subject had absent oVEMPs bilaterally, which cannot be fully or definitively explained. The absence of post-operative cVEMPs and oVEMPs on the operative side, as well as the opposite ear, does not fully explain recurrent or residual dizziness in these patients. Possible explanations for these findings as suggested by the literature (Leveque, Seiderman, Tran, Langagne, Ulmer & Chays, 2010) include the development of MD in the unoperated ear, concomitant vestibular disorders such as vestibular migraine, age related changes in the VEMP response itself and incomplete vestibular compensation. Further research to clarify this is needed.

Previous cVEMP and oVEMP research has demonstrated an age effect of the vestibular system with 40% of cVEMP responses decreasing or absent over the age of 60 (Piker, Jacobson, Burkard, McCaslin & Hood, 2013) and 25% of oVEMP responses in otologically and neurologically healthy individuals absent above the age of 60 years (Piker et al, 2011). The researcher in the current study was unable to omit the above age group from the study as 50% of the eligible subjects who had MD + VN were found to be within this age range (mean age = 58.2 years). It should be noted that the mean age of subjects in the largest study to date by Leveque, Seiderman, Tran, Langagne, Ulmer and Chays (2010) included subjects with a mean age of 52 years (age range 31-71 years) and therefore they had similar age related issues. As a result in this current study, age and gender matching was applied to the two comparison groups. Perhaps due to the age range (Singh, Kashyap, Supreetha & Sahana, 2014) of the test subjects (40 – 72 years), the VEMP responses were reduced in some of the participants with no history of vestibular symptoms. In accordance with previous findings (Piker et al, 2011), the age range of the participants in the current study may have resulted in an increase in the variability of the responses.

Due to the time period during which the surgeries were performed, VEMP studies were not a standard part of the pre-operative test battery. The VEMP status of the subjects pre-surgery is therefore unknown.

The test protocol utilized in this study incorporated the use of a 500 Hz tone burst as the test stimulus. Recent research assessing the frequency tuning of the VEMP response in MD suggests that there is a frequency shift in the response from 500 Hz to 1000 Hz in those patients diagnosed with MD (Winters, Campschroer, Grolman & Klis, 2011). The 500 Hz tone burst stimulus frequency was utilized in this study as that was the standard stimulus frequency used in the test protocol of the audiology practice from where the MD group was sourced. Not all subjects were tested with the 1000 Hz stimulus as the diagnosis of MD was often not yet made and only given to the audiologists subsequent to testing. In order to compare test results with the N and MD + VN groups this same test protocol was then used for the other groups.

4.1. Implications of the study and recommendations for further research

Although 100% of the subjects in this study had absent cVEMP and oVEMP responses on the operated ear post VN and the results are suggestive of a successful surgical technique, one cannot definitively say that this is indicative of complete resection. There are other tests available within our assessment battery that look at different frequency responses of the vestibular system such as bithermal calorics (low frequency), rotary chair (variable frequencies) and vHIT (high frequency).

Future research should include pre and post surgery calorics, cVEMP, oVEMP, vHIT studies (in all planes of direction) as well as rotary chair testing in order ascertain vestibular function and central compensation of all five vestibular sensory organs. VEMP testing could further include testing with high frequency stimuli such as 750 and 1000Hz tone bursts as suggested by

Winters (2011), should the response to the 500Hz tone burst test protocol be absent. In this manner it may be possible to determine the origin of vestibular dysfunction in subjects who continue to experience episodes of postural instability and/or ongoing vertigo.

5. Conclusion

This study has found both cVEMPs and oVEMPs to be absent on the post surgery ear in subjects with MD who have undergone VN. The consistency of the results in this group is suggestive of high reliability and validity. As discussed previously this is a finding that is theoretically supported by the literature (Welgampola, Rosengren, Halmagyi & Colebach, 2003; Leveque, Seiderman, Tran, Langagne, Ulmer & Chays, 2010), however the absence of VEMP results may have been influenced by the advanced ages of the research subjects as a factor of the research methodology.

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7. APPENDICES

Appendix A: Letter of Ethical Clearance



UNIVERSITEIT VAN PRETORIA
UNIVERSITY OF PRETORIA
YUNIBESITHI YA PRETORIA

Faculty of Humanities
Office of the Deputy Dean

23 October 2013

Dear Prof Vinck

Project: The impact of selective vestibular section via the retro sigmoid approach on VEMPS in subjects with Meniér's Disease
Researcher: T Henen
Supervisor: Prof B Vinck
Department: Communication Pathology
Reference: 11268884

Thank you for your response to the Committee's letter of 1 July 2013.

I am pleased to be able to tell you that the above application was **approved Research Ethics Committee** at an ad hoc meeting on 23 October 2013.

The Committee requests you to convey this approval to the researcher.

Sincerely

Prof Sakhela Bulhungu
Chair: Postgraduate Committee &
Research Ethics Committee
Faculty of Humanities
UNIVERSITY OF PRETORIA
e-mail:sakhela.bulhungu@up.ac.za

Appendix B: Informed Consent Form

INFORMED CONSENT FORM

The impact of selective vestibular section via the retro sigmoid approach on VEMPs in Menière's patients

Please complete the following:

Surname: _____

Name: _____

Age: _____ **ID number:** _____

I hereby agree to participate in this project and acknowledge that the data will be used for research purposes. I am aware that I may withdraw from this project, at any time, should I want to.

Signature

Date



Appendix C: Cover letter

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!
!
!



18 May 2014

Faculty of Humanities
Department of Communication Pathology

Dear participant,

I am a post-graduate student at the University of Pretoria, conducting a research study entitled: ***The impact of selective vestibular section via the retro sigmoid approach on VEMPs in subjects with Menière's Disease***

I would like to invite you to participate in my study. The purpose of the current study is to answer the question: How are cVEMPs and oVEMPs affected by selective vestibular neurectomy using the retro sigmoid approach in the treatment of patients with Meniere's disease?

Below please find an outline of the research procedures and protocols.

Procedures:

The auditory part of the study will take approximately 30 minutes and will include:

- Assessment of post-operative hearing function using:
 - Otoloscopic examination – visual physical examination of the external ear and the tympanic membrane to determine the health and status of the outer ear, tympanic membrane and middle ear.
 - Pure Tone Audiometry including air conduction and bone conduction thresholds – this will determine the current hearing status of the research subject and whether there has been any deterioration in hearing in comparison to pre-operative hearing status.

The vestibular part of the study will take approximately 30 minutes and will include:

- Both cVEMPS and oVEMPS in order to objectively assess the presence of residual otolith (saccul and utricle), superior and inferior vestibular nerve function – these tests will indicate any left over balance function on the side of the surgery.

Risks and Discomforts

All the tests to be performed are non-invasive and should result in minimum discomfort. Should you become fatigued suitable rest and bathroom breaks will be provided. Participants will be permitted to perform all tasks at their own pace.

Benefits

There will be no personal benefit or financial gain for either the researchers or the research subjects in this study.

Participants' Rights

Participation is voluntary; and participants may withdraw from participation in this study at any time and without negative consequences.

Should you consent to be part of the study, testing will be conducted at my private practice at 10 Bedford Gardens Medical Suites, Bedford Gardens, Johannesburg, during May and June 2014. I will schedule appointments at your convenience. I would really appreciate your participation in this study as it will contribute to the management and care of patient's diagnosed with Menière's Disease in the future.

I thank you in anticipation.

Tammy Henen
Student

Prof Bart Vinck
Supervisor/Head: Dept of Communication Pathology

Mrs Barbara Heinze
Co-supervisor

University of Pretoria
PRETORIA 0002
Republic of South Africa

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Appendix D: Data Collection Sheet

DATA COLLECTION SHEET

SUBJECT NUMBER: _____

GROUP: _____

IMPEDANCE

| | RIGHT | LEFT |
|---------------|-------|------|
| TYMPANOMETRY | | |
| REFLEX 1000Hz | | |

AUDIOGRAM

| | 125 Hz | 250 Hz | 500 Hz | 1000 Hz | 2000 Hz | 3000 Hz | 4000 Hz | 6000 Hz | 8000 Hz |
|-----------------------|--------|--------|--------|---------|---------|---------|---------|---------|---------|
| AIR CONDUCTION LEFT | | | | | | | | | |
| BONE CONDUCTION LEFT | | | | | | | | | |
| AIR – BONE GAP LEFT | | | | | | | | | |
| AIR CONDUCTION RIGHT | | | | | | | | | |
| BONE CONDUCTION RIGHT | | | | | | | | | |
| AIR – BONE GAP RIGHT | | | | | | | | | |

cVEMP:

| | Trial 1 | Trial 2 |
|-------------------------|---------|---------|
| Right P1 latency | | |
| Right N1 latency | | |
| Right P1 – N1 Amplitude | | |
| Left P1 latency | | |
| Left N1 latency | | |
| Left P1 – N1 Amplitude | | |
| Asymmetry ratio | | |

oVEMP:

| | Trial 1 | Trial 2 |
|-------------------------|---------|---------|
| Right N1 latency | | |
| Right P1 latency | | |
| Right N1 – P1 Amplitude | | |
| Left N1 latency | | |
| Left P1 latency | | |
| Left N1 – P1 Amplitude | | |
| Asymmetry ratio | | |