ENHANCING THE ACCURACY IN DIAGNOSING PERIPHERAL VESTIBULAR DISORDERS

by

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DECLARATION

I declare that the contents presented in this thesis are my own work which was done at School of Medical Sciences, Universiti Sains Malaysia unless stated otherwise. The thesis has not been previously submitted for any other degree.

Zuraida Binti Zainun

DEDICATIONS

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LIST OF ABBREVIATIONS

MVVSS	Malay version of Vertigo Symptom Scale
DHT	Dix-Hallpike test
CP	Canal paresis
PVD	Peripheral vestibular disorder
VEMP	Vestibular evoked myogenic potential
SCC	Semicircular canal
VOR	Vestibular-ocular reflex
VSR	Vestibulo-spinal reflexes
ENT	Ear, Nose and Throat
BPPV	Benign paroxysmal positional vertigo
HUSM	Hospital Universiti Sains Malaysia
VNG	Videonystagmography
ENG	Electronystagmography
V-HIT	Video Head Impulse Test
ABBT	Alternate binaural bithermal caloric test
MTST	Monothermal screening test
DP	Directional preponderance
SOT	Sensory Organizational Test
CDP	Computerised Dynamic Posturography
SCM	Sternocleidomastoid
VSS	Vertigo Symptom Scale
DHI	Dizziness Handicap Inventory
ROC	Receiver Operating Characteristic
CCE	Cawthorne–Cooksey exercise
CCCE	Customized Cawthorne-Cooksey exercise
ORL-HNS	Otorhinolaryngology-Head Neck Surgery
PCPVD	Poorly compensated peripheral vestibular disorder
PS	Power Sample
SPSS	Statistical Package for Social Sciences
S.D	Standard deviation
KMO	Kaiser-Meyer-Olkin
SCD	Superior canal dehiscence

LIST OF SYMBOLS

%	percent
ºC	degree Celcius
dBnHL	Decibel for normal Hearing Level
Hz	Hertz
kHz	kilohertz
uV	Microvolt
ms	Millisecond

MENINGKATKAN KETEPATAN DIAGNOSA PENYAKIT VESTIBULAR PERIFERI.

ABSTRAK

Penyakit vestibular periferi merupakan salah satu diagnosa yang begitu lazim di klinik kesihatan dan klinik pakar. Secara klinikal memberi diagnosa yang tepat dan rawatan yang terbaik amatlah sukar. Tanpa diagnosa yang tepat ahli klinikal tidak dapat memberikan rawatan yang optima untuk seseorang pesakit itu. Oleh itu kajian ini telah dijalankan untuk meningkatkan lagi ketepatan diagnosa penyakit vestibular periferi dengan mengkaji dua ujian baru iaitu *vestibular evoked myogenic potential* (VEMP) dan skala simptom vertigo versi Melayu untuk dibandingkan dengan ujian yang sedia ada ujian kalorik dan *Dix-Hallpike test* (DHT). Kajian ini meliputi dua fasa iaitu kajian awalan (terjemahan dan pengesahan borang soal selidik skala simptom vertigo dan penambahbaikan protokol ujian VEMP) dan kajian utama. Skala simptom vertigo versi Melayu (MVVSS) ini mempamerkan soal selidik yang berkualiti dari segi kandungan, pengesahan bentuk dan juga kebolehpercayaan yang tinggi. Protokol yang optimum untuk ujian *vestibular evoked myogenic potential* (VEMP) dapat dihasilkan. Kajian utama melibatkan 40 subjek yang sihat dan 65 pesakit vestibular periferi. Semua subjek dikehendaki untuk mengisi borang soal selidik skala simptom vertigo. Dalam posisi duduk ujian VEMP dijalankan dengan kedudukan elektrod yang aktif di otot *sternocleidomastoid* dan elektrod negatif pada bahagian atas dahi. Nada pecah pada tahap 90 dBnHL (500, 750 dan 1000 Hz) dipersembahkan melalui fon kepala pada kadar lima per saat untuk merekod ujian VEMP. Ujian kalorik dan DHT dijalankan berdasarkan prosidur klinikal piawai. Ujian statistik menunjukkan subjek yang normal dan pesakit vestibular periferi berbeza dalam ujian MVVSS, VEMP and DHT. Sensitiviti dan spesifisiti untuk setiap ujian dikira menggunakan kaedah *Receiver Operating Characteristic* (ROC). Berbanding semua parameter VEMP, amplitud N1 bagi frequensi 750 Hz telah meghasilkan nilai sensitiviti yang paling bagus

(65% bahagian kanan dan 63% bahagian kiri) dan spesifisiti (83% bahagian kanan dan 78% bahagian kiri). Di samping itu juga VEMP merupakan ujian yang paling sensitif. Yang lagi memeranjatkan gabungan antara ujian CP and DHT menunjukkan nilai sensitivity yang rendah (26% sebelah kanan dan 25% sebelah kiri).Gabungan ujian yang baru (MVVSS dan VEMP) menunjukkan nilai sensitiviti yang lebih baik (74% sebelah kanan dan 75% sebelah kiri). Gabungan ke empat-empat ujian tersebut menunjukkan nilai sensitiviti 80% pada kedua-dua belah. Kajian ini menunjukkan kepentingan mengunakan skala simptom vertigo versi Melayu dan VEMP berserta dengan ujian kalorik dan DHT dalam memberi diagnosa kepada pesakit vestibular periferi. Gabungan keempat-empat ujian telah meningkatkan nilai sensitiviti secara drastik dalam mendiagnosa pesakit vestibular periferi berbanding dengan menggunakan ujian kalorik dan DHT sahaja. Oleh itu, ketepatan dalam mendiagnosa penyakit vestibular periferi dapat ditingkatkan dan bilangan pesakit yang didiagnosakan secara salah dapat dikurangkan dengan banyaknya. Kajian ini juga dapat menggalakkan keperluan untuk menjalankan kajian berterusan dalam bidang vestibular ini terutamanya dalam kalangan masyarakat Malaysia.

ENHANCING THE ACCURACY IN DIAGNOSING PERIPHERAL VESTIBULAR DISORDERS

ABSTRACT

Peripheral vestibular disorder (PVD) is serious and common. Clinically, giving an accurate diagnosis of PVD can be challenging. Without the appropriate diagnosis, clinicians are not able to provide proper management for patients. Therefore, this study was conducted to enhance the accuracy in diagnosing PVD by investigating two new tests, i.e. Vestibular evoked myogenic potential (VEMP) and Malay version of vertigo symptom scale (MVVSS) to be compared with the existing vestibular tests, namely caloric test and Dix-Hallpike test (DHT). This study consisted of two parts: pilot (translation and validation of MVVSS and optimization of VEMP protocol) and main study. MVVSS was found to have adequate content, high test reliability and adequate construct validity. An optimal protocol to record VEMP was also achieved. In the main study, 40 normal participants and 65 PVD subjects participated. They were required to fill in the MVVSS questionnaire accordingly. While sitting, VEMPs were recorded with active electrode on sternocleidomastoid muscle and negative electrode on upper forehead. Tone bursts (500, 750 and 1000 Hz) were delivered via headphones at 90 dBnHL and 5/s rate to record VEMPs. Caloric test and DHT were performed according to the standard clinical procedures. Normal and PVD subjects were found to be statistically different by MVVSS, VEMP and DHT. Sensitivity and specificity of each test was then determined using Receiver Operating Characteristic (ROC) method. Among VEMP parameters, N1 amplitude of 750 Hz stimulus produced the most ideal sensitivity (65% on right and 63% on left) and specificity (83% on right and 78% on left). In fact, VEMP was found to be the most sensitive test. Surprisingly, the combination of canal paresis (CP) of caloric test and DHT yielded low sensitivity values (26% on right and 25% on left). The combination of new tests (MVVSS and VEMP) produced acceptably high sensitivity values (i.e. 74% on right and 75% on left). The combination of all four tests yielded the sensitivity of 80% on both sides. This study demonstrates the usefulness of

having MVVSS and VEMP in conjunction with caloric test and DHT in PVD diagnosis. The combination of all four tests significantly increases the sensitivity to diagnose PVD patients than the use of caloric test and DHT only. Consequently, the accuracy in PVD diagnosis can be enhanced and the number of false negative cases can be reduced greatly. This study also "triggers" the needs of ongoing studies in vestibular field, especially for Malaysian population.

CHAPTER 1

INTRODUCTION

1.1 Background of the study

In daily life, humans perform various activities such as walking, running, driving etc. routinely. In this situation, having an intact balance system is important so that those activities can be conducted conveniently. By definition, balance refers to one's ability to stabilize his/her centre of gravity, parallel to the base of support with minimal movement (Horak, 1987; Shumway-Cook *et al*., 1995). A perfect balance system requires a multidisciplinary and complex integrated system, such as a well functioning brain, proprioception, visual organs and vestibular organs (Murdin *et al*., 2008).

Any disturbances affecting one or more of the balance organs lead to imbalance difficulties (e.g. dizziness, vertigo etc.) (Ba Huy & Toupet, 2001; Luxon, 2003). As a consequence, the quality of life of the affected individuals can be seriously degraded, especially if the episodes end with injuries (MMWR, 2008) or even fatal accidents (Agrawal *et al*., 2009). In fact, balance disorder cases are common (as described later in Section 1.4.1 and 1.4.2) and the number of sufferers increases over time. However, clinically, the diagnosis of balance disorder is challenging. In this situation, the use of test battery is recommended to improve the diagnosis of balance disorders. Having an accurate diagnosis is undoubtedly important so that proper management can be carried out.

Therefore, in general, this study was conducted to enhance the sensitivity of balance (vestibular) assessment in diagnosing subjects with peripheral vestibular disorders (PVD). To achieve this, two new tests, namely Malay Version of Vertigo Symptom Scale (MVVSS) and Vestibular Evoked Myogenic Potential (VEMP) were investigated and compared with the existing clinical vestibular assessments, which were caloric test and Dix-Hallpike test (as described in method sections, Chapter 2). The findings were then discussed (as covered in Chapter 4) and the final conclusions were made accordingly (as shown in Chapter 5). Benefits and clinical implications of the study are also stated in Chapter 5.

1.2   Overview of the vestibular system

1.2.1   Anatomy of the vestibular system

The vestibular system is important to maintain balance perceptions (Luxon, 2003; Martin *et al.*, 2003). This system controls head, neck, ocular and trunk movements in humans (Gleeson, 1997). It is divided into peripheral and central vestibular portions. As shown in Figure 1.1, the peripheral vestibular portion is part of the inner ear and consists of three semicircular canals (anterior, posterior and lateral) and two otolith organs (utricle and saccule) (Luxon, 2003). The central vestibular pathway, on the other hand, starts from vestibular nuclei up to the brain.
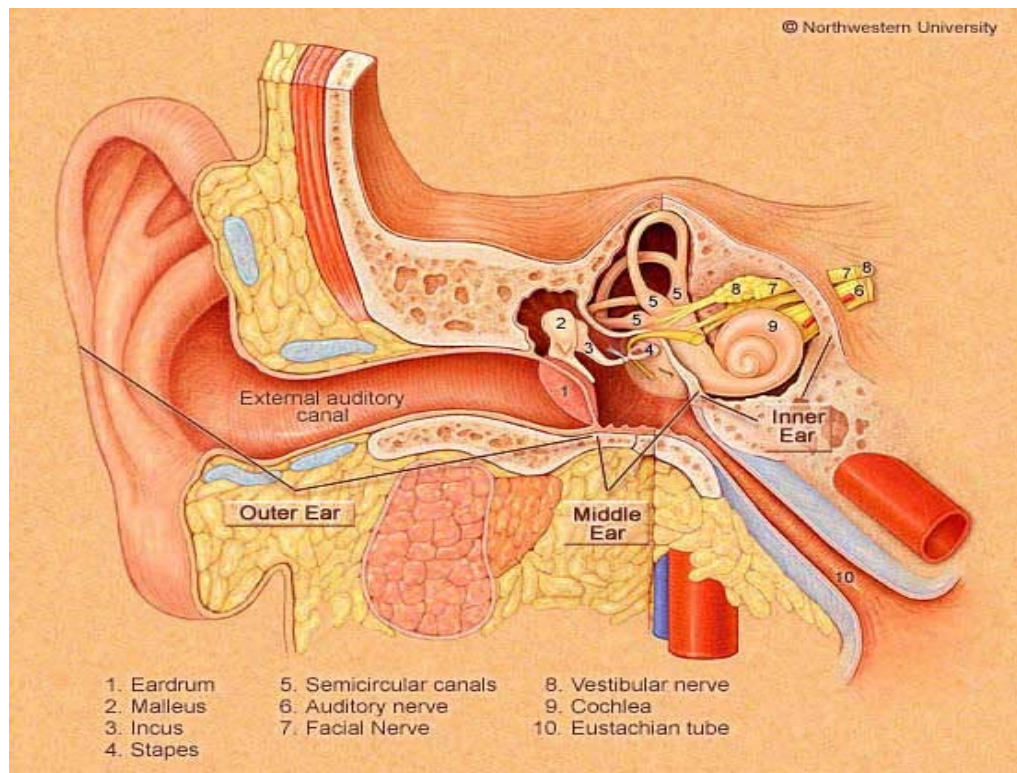
Figure 1.1: Anatomy of a human vestibular system (adapted with permission from www.dizziness-and-balance.com/anatomy/ear-anat.htm)
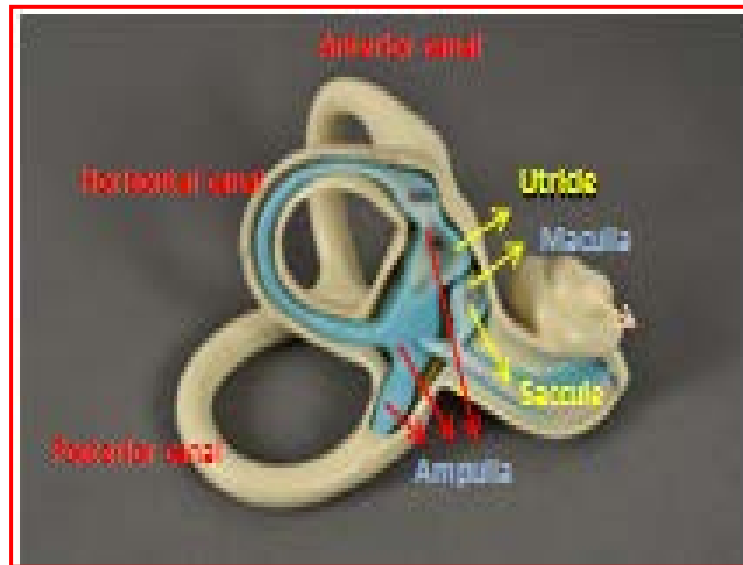
Figure 1.2: Osseous (grey/white) and membranous (blue) labyrinth of the right inner ear

As illustrated in Figure 1.2 above, the vestibular organs (also known as labyrinthine organs) are formed by bony and membranous labyrinths. According to Baloh (1998), the bony or osseous section contains fluid known as perilymph and the membranous section has endolymph. Each of them has a specific sensory organ. That is, cupula is a sensory organ for semicircular canals (SCCs) and macula is for otolith organs (Baloh, 1998).

1.2.2 Physiology of the vestibular system

The SCCs are responsible for controlling rotational movements and dynamic stability (Seikel *et al.*, 2005). When the head moves, the endolymph flows to a certain direction and this stimulates the cupula. This action results in either a stimulatory or an inhibitory response. The response is dependent on the direction of motion and location of that particular SCC. Movement of hair cells of cupula towards the ampulla (that houses the cupula) is called "ampullofugal" and movement of the hair cells away from the ampulla is known as "ampullopetal" (Lorne *et al*., 2003).

The direction of the head rotation or movement and the endolymph fluid are oppositional. As an example, when we turn our head to the right, the endolymph fluid inside the left posterior SCC moves towards the ampulla (ampullopetal). This indirectly causes movement of the cupula towards the utricle (utriculopetal) and an inhibitory response occurs. Simultaneously, the right posterior SCC exhibits an oppositional response where movement of the endolymph fluid is away from the ampulla ('ampullofugal'). This results in utriculofugal movement that causes an excitation effect (ibid).

A similar condition occurs in the right and left anterior SCC. In lateral SCC, the opposite condition occurs, whereby the utriculofugal movement will cause an inhibitory response and the utriculopetal movement will cause an excitatory response (Baloh, 1998; Lorne et al., 2003). This oppositional condition is illustrated in Figure 1.3 below. The electrical responses then travel along the central vestibular portion for further actions.
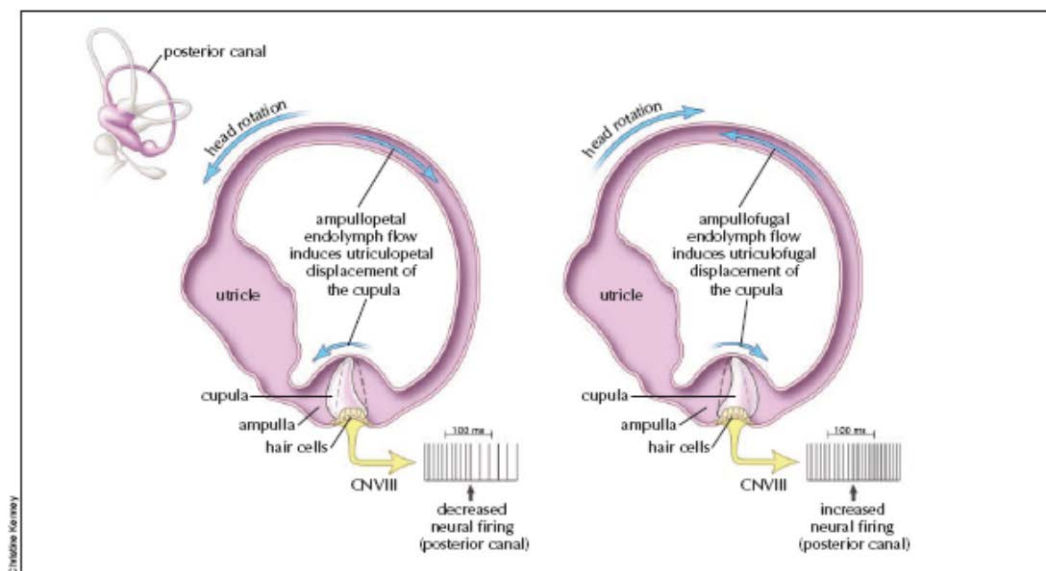
Figure 1.3: Physiological changes: Inhibitory and exhibitory firing of the posterior SCC in the left side (adapted with permission from Lorne *et al*., 2003)

The otolith organs, on the other hand, play a major role in balancing the human body during linear movements (Ba Huy & Toupet, 2001). Specifically, utricle and saccule are

responsible to control the body balance during horizontal and vertical movements, respectively. Their sensory organ, macula contains otoconia and vestibular hair cells. For example, when an individual moves up or down (as in an elevator), the otoconia of saccule moves and causes movement of the vestibular hair cells that will result in an inhibitory or excitatory action. The nerve impulses are then transmitted to the central portion of the vestibular system for further processing.

The central vestibular portion consists of vestibular nuclei, vestibular-ocular pathways, vestibulospinal pathways, vestibulocolic pathways, vestibule-autonomic pathways, vestibulocerebral pathways, vestibulocerebellum and perihypoglossal nuclei (Furman, 2000). The vestibular nuclei play an important role in processing the vestibular signals. They receive afferent fibres from the vestibular, eye and somatosensory organ and project efferent fibres to the motor centres (Parent, 1996). The sensory inputs are integrated and then transmitted to the motor centres for the eye, postural and spatial orientation in the body (Furman, 2000).

1.3 Overview of Dizziness

1.3.1 Definition and prevalence

"Dizziness" is a general term (Baloh, 1998) and covers symptoms such as "sensation of faintness and whirling or an inability to maintain normal balance in a standing or seated position" (Mosby, 2006: 580). According to Drachman and Hart (1972), dizziness can be divided into four subtypes:

      i)   Vertigo - a feeling or sensation of one or surrounding spinning

      ii)   Presyncopal and light-headedness

      iii)   Disequilibrium

      iv)   Other forms of dizziness.

Dizziness is one of the general symptoms that are commonly reported by patients to the clinicians at all levels. Most of these patients are either seen at the 'Ear, Nose and Throat' (ENT) or the Neurology clinics or departments for further management (Kroenke *et al.,* 1992). According to Cormick et al (1995), the possibility and risk for a person to exhibit symptoms of dizziness is quite high. About 93 per 1000 people are affected each year. In the USA, the predictive rate for dizziness receiving consultation is 76 per 1000 people each year for people aged 75 years and above (Lawson *et al.,* 1999).

In the United Kingdom (UK), symptoms of dizziness had been reported by 40% of the population (Coles and Sinclair, 1988), and involved 1 in 4 of the Welsh community in the age range of 50-65 years. In London, the complaint of imbalance is 20% among 25-64 year olds (Patrick and Peach, 1989). An epidemiological study of a German population revealed that almost 24% of total dizziness cases were diagnosed to have vestibular vertigo (Sheykholeslami and Kaga, 2002).

Dizziness can be chronic and difficult to treat (Yardley *et al.*, 1998). The problems or difficulties associated with dizziness become more prominent among working people. Yardley *et al.* (1998) found that one in five working people experienced dizziness symptoms. From this figure, almost 40% of dizzy people face a problem in carrying out their jobs (ibid). In addition, it was also found that the dizziness is an age-related illness, whereby, patients experiencing dizziness symptoms are more likely to be adults (Yardley *et al.,* 1998).

Dizziness is common among the population (age range of 18-65 years old) (Yardley *et al.*, 1998) and with more female sufferers than men (Kroenke *et al.,* 1992; Yardley *et al*., 1998; Hofman *et al*., 1999; Tinetti *et al*., 2000). Most of the prevalence studies also found that the elderly people are more likely to experience and be affected by dizziness symptoms. For

example, a study by Fife and Baloh (1993) found that 65% of people who are above 60 years old experience symptom of dizziness and unsteadiness.

Among the subtypes of dizziness, vertigo is one of the most commonly reported symptoms of the vestibular disordered patients (Baloh, 1998). Vertigo is defined as "an illusion of movement that is commonly present with a sense of rotation or sometimes a feeling of linear displacement or tilt" (Baloh, 1998: 1841). Research into this particular symptom in terms of frequency, duration and aggravation factors will be useful for accurate diagnosis and the appropriate treatment strategies (Baloh, 1998).

1.3.2 Aetiological factor

The prevalence for the causes of dizziness varies depending on the age, site of study (primary, secondary or tertiary centres), and the definition and classification used for dizziness itself. Complaints of dizziness potentially have a variety of possible etiological factors based on otological, neurological and medical disorders (Pagarkar and Davies, 2004). The most common cause of dizziness is peripheral vestibular disorder (PVD) (Hoffman *et al*., 1999; Kroenke *et al*., 2000; Kwong and Pimlott, 2005).

In primary care settings, acute labyrinthitis (or vestibular neuritis) is the most common diagnosis made for the PVD (Madlon-Kay, 1985) and most of the symptoms associated with PVD are manageable (Kroenke, 1992). In tertiary referral centres, diagnosing dizziness symptoms as recurrent peripheral vestibular disorder i.e. recurrent benign paroxysmal positional vertigo (BPPV), recurrent vestibulopathy (Kroenke, 2000), or Meniere's disease (Kwong and Pimlott, 2005) are dominant (Drachman and Hart, 1972; Madlon-Kay, 1985; Nedzelski *et al*., 1986; Katsarkas, 1994).

1.4 Vestibular disorders

Any disturbance or malfunction of the vestibular system leads to vestibular disorders. There are three types of vestibular disorders which depend on the site of lesion. These are peripheral, central, and mixed vestibular disorders. Several factors have been considered as aetiological factors for vestibular disorders such as ageing, genetic inheritance, head trauma and hormonal related factors (i.e. premenstrual or oral contraceptive users) (Murofushi *et al*., 1996; Streubel *et al.,* 2001). Apart from these factors, there are still a great number of vestibular disorders with unknown aetiology (Yardley *et al,* 1998).

It has been well demonstrated that patients with vestibular disorders have difficulties in maintaining balance during rotary and/or linear movements (Luxon, 2003). Any disturbance involving the vestibular system may lead to unsteadiness, vertigo, oscillopsia, nausea, vomiting and other self-limiting symptoms. For instance, a patient with a saccular dysfunction may experience difficulties dealing with linear movements and orientation to gravity (Strupp *et al.,* 1998). In other words, patients with vertigo commonly experience sweating, nausea and vomiting compared to other subtypes of dizziness (Baloh, 1998), and are more likely to be diagnosed as suffering from vertigo than from another form of dizziness.

People who experience vestibular problems may or may not recover over time. The estimated duration for central compensation in unilateral vestibular disorder cases is about 4-6 weeks (Strupp *et a*l., 1998). Such difficulties may seriously affect the quality of life of the individual (Agrawal *et al*., 2009). There is also an economical impact, with treatments of fall incidents among the elderly costing more than seven million US dollars annually (National Institute on Deafness and Other Communication Disorders, 1989). Untreated cases of balance disorders may lead to the involvement of psychological symptoms (Furman and Jacob, 1997). Consequently, the cases may become more complicated and difficult to manage.

1.4.1 Peripheral vestibular disorder and its prevalence

PVD is the most common of vestibular disorder cases (McClure *et al*., 1977; Herdman *et al*., 1993; Parnes and Price-Jones, 1993; Dumas *et al*., 1994). By definition, PVD is a disturbance of the peripheral pathway of the vestibular system (such as vestibular organs or vestibular nerve) (Lawson *et al*., 1999). It may include acute vestibular neuritis, vestibular labyrhintitis, benign paroxysmal positional vertigo (BPPV) or Meniere's diseases. Typically, patients with PVD will experience symptoms of vertigo, hearing problems, tinnitus, abnormal eye movement (nystagmus) and unsteadiness (Baloh, 1998).

Past studies (McClure *et al.,* 1977; Herdman *et al*., 1993; Parnes and Price-Jones, 1993; Dumas *et al.,* 1994) estimated that between 17-30% of vertiginous patients who sought treatment in vestibular clinics were categorized as having unclassified PVD. More recently, Murdin and Davies (2008) reported that among people who were diagnosed to have PVD, 40% of them had unknown cause, 21% of them had BPPV and 13% of them were found to have Meniere's disease.

Classification and subsequent prevalence rates suggest that BPPV is the most common form of PVD. Froehling *et al.* (1991) estimated that the ratio of BPPV was 64 in 100,000 people in the USA. Among the Japanese population, the estimated ratio of BPPV was 10.7 in 100,000 people (Mizukoshi *et al*., 1988). The least diagnosed form of PVD is Meniere's disease. The prevalence of this disease was between 5-11% in referral or specialized centres (DeWaele et al, 1999a; 1999b). This finding is in line with a recent Malaysian study that found a similar prevalence rate of Meniere's disease (Zainun *et al*., 2009).

In Malaysia, information regarding the prevalence of PVD is lacking. What is known of PVD indicates that it is more common than central vestibular disorder. A retrospective study in Hospital Universiti Sains Malaysia (HUSM) by Zainun *et al.* (2009) found that 73.6% of

vestibular disorders to be PVD, 17.6% were central vestibular disorder, 1.1% mixed vestibular disorders, and the remaining 7.7% were unknown. According to Yin *et al.* (2008), among 2169 patients, 33.8% of them were diagnosed as peripheral vertigo, 17.2% central vertigo, 26.8% unclassified vertigo and 22.2% vertigo of unknown origin. It was also found that vertigo was more prevalent among older patients (Yin *et al.*, 2008). Another study of vertiginous patients in Malaysia showed that 22% of them experienced BPPV, followed by 16.5% suffering from Meniere's disease (Zainun *et al.,* 2009).

1.4.2 Central vestibular disorder and its prevalence

According to Furman and Whitney (2000), the most common central vestibular diseases (CVD) are migraine-associated dizziness, trauma, ischemic disease (vertebrobasilar insufficiency and brain-stem stroke), and degenerative diseases that affect the cerebellum. Symptoms of CVD differ from PVD. People suffering from CVD often exhibit different features of nystagmu*s*, have different neurological signs, have severe postural instability, and show gradual impairment of symptom (Hotson and Baloh, 1998). CVD patients also exhibit less nausea and vomiting (Chan et al, 1997).

With reference to features of nystagmus for CVD, Tierney *et al.* (1997) found the features to be non-rotary, inclined towards the vertical type, may be of any direction, and are non-fatigability. In addition, it has been demonstrated that patients with CVD show a slower improvement when undergoing vestibular rehabilitations if compared to subjects with PVD (Konrad *et al.*, 1992).

1. 5   Classification of Peripheral Vestibular Disorder

The latest consensus (Morera *et al*., 2008) concerning the classification of PVD divided the diseases according to single-episode or recurrent attacks of vertigo. "Single episode" cases are divided into the following sub categories:

a. associated with hearing loss (i.e. vestibular labyrhintitis, Ramsay-Hunt syndrome).

b. without hearing loss (i.e. vestibular neuritis).

Cases of recurrent attacks of vertigo are subcategorized as:

a. with hearing loss (i.e. Meniere's disease, vertigo-migraine, autoimmune, syphilis, perilymphatic fistula).

b. without hearing loss such as BPPV, perilymphatic fistula, spontaneous, migraine-associated vertigo, Paroxysmal vertigo of childhood, transient ischaemic attack, and vertebrobasilar insufficiency.

1.5.1 Benign Paroxysmal Positional Vertigo (BPPV)

BPPV is identified as a lesion of the inner ear with positional related vertigo with recurrent attacks (Bhattacharyya *et al*., 2008). It is very common among PVD patients (Katsarkas and Kirkham, 1978; McClure, 1985; Noere, 1994). Typical symptoms include sudden vertigo attacks in short duration (i.e. a few minutes), positional related, rotary nystagmus, fatigability and reversal of the nystagmus direction in sitting position, and rapid recovery associated with nausea and vomiting (Dix and Hallpike, 1952; Schuknecht and Ruby, 1973; Brandt, 1990).

BPPV has many types, and is dependent upon which part of the SCC that is affected (i.e. anterior, posterior or lateral SCC). Posterior canal BPPV is the most common type and its typical features include vertigo and rotary nystagmus (Brandt and Daroff, 1980; Gacek, 1985). These symptoms can be identified effectively by using a provocative test of posterior

canal such as Dix-Hallpike test (DHT). This test is simple and can be conducted in the general clinics. Lateral canal BPPV, on the other hand, is predictably presented with horizontal nystagmus as revealed by a provocation test of horizontal semicircular canal such as the roll test (McClure, 1985).

1.5.2 Other types of PVD

Apart from BPPV there are several other common diagnoses such as Meniere's disease, acute vestibular neuritis and vestibular labyrhintitis. Typical symptoms for Meniere's disease include fullness of the ear, tinnitus, loss of hearing, vertigo for long duration (i.e. minutes to hours), unsteadiness, floating sensation, nausea, vomiting and nystagmus (Babon, 1985).

Vestibular neuritis is characterized by acute onset of vertigo with severe symptoms prolonged up to days or weeks, nystagmus, unsteadiness, nausea, no hearing loss (sometimes present in certain patients), tinnitus and aggravated by head movements (Kitamura, 1981; Brandt, 1999). Many of the studies showed that the common site of lesion is at the superior vestibular nerve (Murofushi *et al.,* 1996). However, Darlot *et al.* (1997) found that there are cases where vestibular neuritis involved the inferior vestibular nerve. The period of recovery from this illness varies and most of the reported data show evidence that positive recovery can be achieved in cases involving the superior vestibular nerve (Okinaka *et al*., 1993; Strupp *et al.,* 1998; Bergenius and Perols, 1999).

Vestibular labyrinthitis is usually caused by a viral infection and has a similar presentation as to vestibular neuritis (Pagarkar and Davies, 2004). The difference is that many patients with vestibular labyrinthitis often complain of hearing loss. Patients suffering from vestibular neuritis, on the other hand, rarely complain of hearing disorder (ibid).

Another form of PVD is classified as 'unknown'. This classification identifies PVD conditions with the following characteristics: having several symptoms of another PVD classification, however these symptoms are insufficient for diagnosis; having symptoms of more than one classification – a form of hybrid of classifications; or experiencing symptoms similar to one or more classification compounded with presenting uncommon symptoms or aetiology. Cases involving either one of these features are insufficient for clinical categorization due to the rarity of occurrence. The deviation of treatment and rehabilitation for people in this category is subjective to the presenting symptoms and site of lesion (ibid).

1.6. Vestibular Assessments

Investigation for the aetiological factor and site of lesion in vestibular disordered patients is compulsory as the information becomes the foundation for decision making in further treatment and rehabilitation. Clinically, patients with vestibular disorders will undergo routine assessments that include clinical examination, objective tests and subjective tests.

Clinical examination for diagnosing vestibular-related diseases usually involves seven tests, which are: Dix-Hallpike test, head thrust test, roll test, head shaking test, straight line test, Romberg test and Fukuda test. Further confirmation of diagnosis requires the use of objective and subjective balance assessments. The common objective tests for vestibular assessment include videonystagmography (VNG) or electronystagmography (ENG), vestibular-evoked myogenic potential (VEMP), posturography, rotational chair and video head impulse test (V-HIT). These objective tests are performed to identify the most likely site of lesion in vestibular disordered patients. The subjective assessment involves the use of specific vestibular-related questionnaires such as vertigo symptom scale, dizziness handicap inventory and so on. In this situation, patients describe the symptoms that they are experiencing in a systematic manner by filling up the questionnaire. This assessment provides clinicians with useful information regarding the patients' symptoms from their point of view.

The VNG test is specifically used to evaluate the horizontal semicircular canal. The VEMP test is utilized to determine the site of lesion, either at the inferior vestibular nerves, saccule and also central lesions (Halmagyi *et al.*, 1994). The rotational chair method is used for horizontal SCC. For general evaluation of balance or posture (for peripheral or central lesion), posturography is employed (Furman. 1994). Video Head Impulse Test (V-HIT) is used to determine lesions at either the anterior, posterior or lateral SCC (MacDougall *et al.*, 2009).

1.6.1   Caloric test

The caloric test is part of the VNG/ENG test. It is performed to evaluate the horizontal canal function (Mehra, 1964; Riesco-MacClure, 1964). According to Fitzgerald and Hallpike (1942), there are two types of caloric tests: alternate binaural bithermal caloric test (ABBT) and monothermal screening tests (MTST). ABBT method uses both warm and cool water, while MTST uses warm or cold water alone. The second method is found to be more rapid and offers more comfort to patients.

Caloric test interpretation is calculated using the Jonkees' formula with two main values: 'canal paresis' (CP) and 'directional preponderance' (DP) (Riesco-MacClure, 1964). Final results are based on the comparison between both horizontal canal sides and total response for both vestibular organs. The normal range for CP and DP varies and depends on the methods utilized. The normal range for CP is between 20-33% and DP is between 22-33% (Jongkees, 1948; Souza *et al.*, 2000).

Any abnormal value of CP is suggestive of peripheral vestibular disorder (Riesco-MacClure, 1964; Zajonk and Roland, 2005). Significant abnormal CP values are indicative of either Meniere's disease (Hulshof and Baarsma, 1981), vestibular neuritis (Bergenius and Borg,

1983), acoustic neuroma (Bergenius and Borg, 1983), or migraine stroke (Grad and Baloh, 1989).

For vestibular disorders, DP is considered as a less sensitive test (Kroenke *et al*., 1992; Hoffman *et al*., 1999). DP with value higher than the normative value is usually found in central vestibular disorder, cortex lesion, brainstem lesion and PVD (Fitzgerald and Hallpike, 1942; Coats, 1965; Eviatar and Wassertheil, 1971; McGee, 1986). Past research regarding Meniere's disease found that the patients have abnormal DP (Thomas and Harrison, 1971; Hulshof and Baarsma, 1981). Abnormal DP was also found in healthy people (Baloh *et al.,* 1977).

1.6.2   Other objective vestibular tests

Computerised Dynamic Posturography (CDP) is one of the specialized clinical tools used to determine the balance status of individuals (Nashner *et al*. 1982). It is an objective test that focuses on the assessment of posture and motor system of subjects (Monsell *et al*., 1997). Specifically, CDP evaluates an individual's body and postural control in specific situations.

In CDP, scores from the sensory organizational test (SOT)) are used to determine the contribution of sensory organs (i.e. visual, somatosensory, vestibular & proprioception) in maintaining body control (Monsell *et al*., 1997; Black, 2001; Clackamas, 2007). CDP has been found to be useful in clinical diagnosis (Nashner *et al*., 1982; Dodd *et al*., 2003; Ionescu *et al.,* 2005), rehabilitation (Shepard *et al*., 1993; Monsell *et al*., 1997), rehabilitation assessment (Monsell *et al*., 1997), post traumatic assessment (ibid), ability to work (ibid) and assessment part for research purposes.

Rotational chair test method is considered as a fundamental test for bilateral peripheral vestibular disorder. This is a counterpart of the caloric test used to identify unilateral peripheral vestibular disorder, specifically the status of the horizontal semicircular canal.

Apart from evaluating the functions of vestibular organs, the rotational chair test has also been used for rehabilitation. However, if compared to other vestibular tests, this test is extremely expensive. This is one of the reasons why this test is rarely used in balance clinics or centres.

Video Head Impulse Test (V-HIT) is one of the prevailing objective vestibular tests available (MacDougall *et al*., 2009). This test is considered as a high-frequency test whereby it is able to evaluate the anterior, posterior and horizontal semicircular canals in a very fast and easy manner. Patients will be more comfortable as there is no irritation due to water irrigation or spinning conditions which are present in the caloric test and rotating chair test. Furthermore the V-HIT is able to assess the function of vestibulo-ocular reflex.

1.7   Vestibular evoked myogenic potential (VEMP)

1.7.1   Overview of VEMP

The earliest known studies related to VEMP were conducted four decades ago. These studies investigated neck muscles and their relation to vestibular potential (Bickford *et al*., 1964; Cody, 1964; Yoshie and Okudaira, 1969). Following these studies, efforts concentrated on vestibular evoked myogenic potentials (Colebatch and Halmagyi, 1992; Colebatch and Rothwell, 1993; Halmagyi and Colebatch, 1995; Robertson and Ireland, 1995; Wu *et al*., 1999). More current studies found that, if an electrode is placed on sterno-cleidomastiod (SCM) muscles or other locations (e.g. forehead or sternum) and a loud sound is introduced via the headphone to the ear, the saccule is stimulated (Murofushi *et al*., 1995; Sheykholeslami and Kaga, 2002). The sound is then transmitted to the inferior vestibular nerves, lateral vestibular nucleus, medial vestibulo-spinal tract, and terminates at the motor neurons of the SCM muscles. Figure 1.4 shows the pathway of the sacculocolic reflex of VEMP.

VEMP that is recorded from the SCM muscles is also known as cervical VEMP. In fact, VEMP has several types including ocular VEMP (Rosengren *et al.,* 2008), galvanic VEMP (Murofushi *et al.,* 2003) and skull tap VEMP (Brantberg *et al*., 2008). Among these variants, the cervical VEMP has been acknowledged as the most convenient test due to its simplicity and reliability (Maes *et al*., 2010; Versino *et al*., 2001). That is, it can be performed using the existing auditory evoked potential machine (that is commonly used to record the auditory brainstem response) without the need of extra equipment. In fact, it is a non-invasive procedure and the electrodes are placed on "comfortable" locations of the subjects. The VEMP waveform is also robust and stable over time (Maes *et al*., 2010; Versino *et al*., 2001). In the current study, the word "VEMP" actually refers to the cervical VEMP.
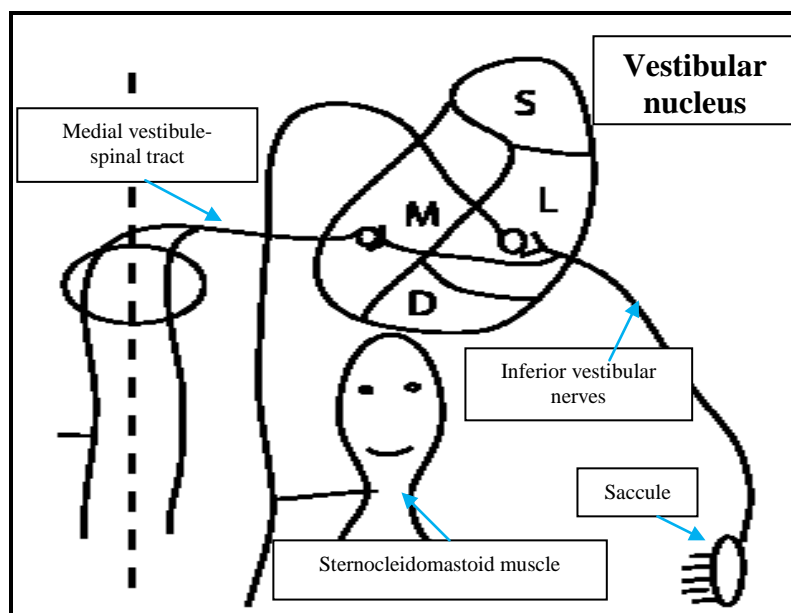
KEYS

S   Superior vestibular nucleus

M   Medial vestibular nucleus

L   Lateral vestibular nucleus

D   Dorsal vestibular nucleus

Figure 1.4: Sacculocolic reflex of VEMP pathway. Sound stimulates the saccule, which activates the inferior vestibular nerve, lateral vestibular nucleus, 11th nerve nucleus, and then the sternocleidomastoid muscle (mostly ipsilaterally). (Adapted with permission from www.dizziness-and-balance.com/ testing/vemp.html)

The typical VEMP of a normal individual is shown in Figure 1.5. In general, there are three prominent peaks of waveforms: inhibitory (P1@p13), excitatory (N1@n23), and a third peak that is assumed to originate from the cochlea (Welgampola and Colebatch, 2005). The first two peaks are considered to originate from the vestibular or balance organs. The information from these peaks is useful for the evaluation of the saccule and inferior vestibular nerves. VEMP recorded from the neck is believed to be almost completely unilateral (Colebatch *et al.,* 1994; Wilson and Boyle, 1995; Murofushi *et al.,* 1996; Uchino *et al.,* 1997; Kushiro *et al.,* 2000) and can be obtained from patients with severe to profound hearing loss. This suggests the non-auditory origin of the evoked response (Murofushi *et al.,* 1999).
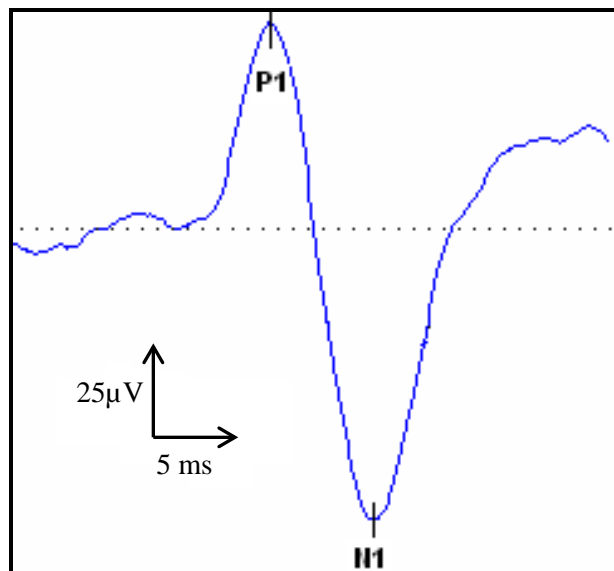
Figure 1.5: A typical Vestibular Evoked Myogenic Potential (VEMP) of a normal individual. Prominent peaks, P1 and N1 are shown.

1.7.2 Diagnostic value and clinical significance of VEMP

Clinically, the VEMP test is one of the objective tests to evaluate the function of saccule, inferior vestibular nerve and central vestibular organs (Halmagyi et al., 1994). This test can actually evaluate other organs of the vestibular system that cannot be assessed by typical clinical tests such as the caloric or rotational chair test. Abnormal VEMPs have been found in cases of Meniere's disease (DeWaele *et a*l., 1999a; DeWaele *et al.,* 1999b), vestibular

neuritis (Murofushi *et al*., 1996), superior canal dehiscence (Streubel *et al*., 2001), Wallenberg syndrome (Itoh *et al*., 2001), and vestibular schwannoma (Murofushi *et al*., 1998). Central pathologies such as brainstem infarcts (Chen and Young, 2003) and multiple sclerosis (Shimizu *et al*., 2000) produce VEMPs with prolonged latencies. These findings illustrate the importance of VEMP in making clinical diagnoses.

1.8 Self-reported questionnaire

Clinically the diagnoses of vertigo and balance disorders are very challenging and complicated. For clinical purposes, it is valuable if the clinician has a detailed knowledge and understanding of the severity level as to whether patients have vestibular disorder solely, or if it is mixed with psychological involvement such as anxiety disorders or depression (Baloh, 1998). Subjective patient assessments are self-administered, inexpensive and are non-hazardous methods for monitoring and evaluating a patient's condition and rehabilitation progress.

In this regard, having a simple self-administered questionnaire serves at least two advantages. First, in a busy clinic, some important questions regarding vertigo and other associated symptoms may have been left out unintentionally by the clinician. In this situation, having a reliable questionnaire can be very helpful in documenting relevant and important information in a systematic manner. Second, since the questionnaire employs some rating scales and scores are derived, the questionnaire is also useful to document the patient's improvement or progress between appointments. This may lead to better management and for patient's services of vestibular disorders.

Accurate diagnosis of PVD should utilize subjective patient assessment. This assessment is also one of the important elements in clinical practice. It is especially pertinent for the chronic and complicated disorders which have a great impact on a patient's life. The

subjective assessment can assist clinicians in understanding the physical, social and psychological aspects of the patients (Yardley, 1994).

Over the last two decades there are several specific disease questionnaires that have been developed for dizziness; specifically the dizziness handicap inventory (DHI) (Jacobson and Richardson, 1990), vertigo symptom scale (VSS) (Yardley *et al*., 1992), medical outcome study SF-36 (Ware *et al.,* 1992), activities-specific balance confidence scale (ABC) (Powell and Myers, 1995), UCLA dizziness questionnaire (Honrubia 1996; Perez 2003), the vertigo symptom index (Black 2000), the vestibular activities of daily living scale (Cohen and Kimball, 2000) and verbal or visual analog scales (Herdman *et al.,* 2003). For the purpose of this study the VSS is used as it has been widely accepted with good validity and reliability values.

1.8.1 Vertigo Symptom Scale

The vertigo symptom scale (VSS) (Appendix 4) by Yardley *et al*. (1992) is one of the disease-specific subjective questionnaires to quantify balance disorder, somatic anxiety, and autonomic severity symptoms (Yardley *et al*., 1992). Since its development, validation tests have been carried out amongst the United Kingdom population (Yardley, 1992; Yardley, 1998). The VSS has been translated into six other languages, apart from English; Dutch, French, German, Spanish, Swedish, and Turkish (Yardley, 1994; Yardley, 1999). The VSS has also been used as part of the treatment evaluation in vestibular disordered patients (Hotson and Baloh, 1998). It has been used extensively for research purposes as well (Yardley *et al.*, 1994a; Yardley *et al.*, 1994c; Yardley *et al.,* 1998; Mendel *et al.,* 1999; Guerraz *et al*., 2001; Godemann *et al.*, 2005; Holmberg *et a*l., 2005).

The first version of the VSS by Yardley *e. al*., (1992) contained 36 items. After consideration of a few factors, two items were retracted: "feeling of being spaced out" and "bowel sensations", and leaving 34 items for use (Yardley *et al*., 1999). The original VSS

comprised of 24 different symptoms (vertigo, somatic and autonomic symptom) and these symptoms were clustered into four different sub-scales (Yardley *et al.,* 1992):-

l- Acute vertigo - Dizziness with minimum duration of one hour and related with ataxia, nausea or vomiting.

II- Vertigo and unsteadiness for a short duration

III-Autonomic arousal symptoms (e.g., heart pounding, excessive sweating, hot or cold spells, feeling faint or short of breath)

IV- Somatic symptoms e.g., diverse pains and somatic sensations

This VSS questionnaire is able to quantify a patient's frequency of symptoms using a Likert-like scale. Responses are rated between 0 (never) to 5 (more than once a week) for all symptoms associated with vertigo for the past one year, or since the attack. This is especially useful for patients with recent attacks of vertigo. Three main questions relating to vertigo: 'feeling things are spinning or moving around', 'light-headed' and 'unsteady about to loss balance' were measured in detail for their specific duration of the symptom (Yardley *et al.,* 1992a; Yardley *et al.,* 1992b). Some of the subscales especially for the vertigo scale showed high reliability for the 'weighted short duration' ($\alpha=0.85$) and 'unweighted acute vertigo scale' ($\alpha= 0.83$). These two subscales were noted to be highly associated, and correspond with patient disability and the clinical diagnostic impact of presented symptoms (Yardley *et al.,* 1992).

Previous studies indicated that two main subscales of the VSS: vertigo and somatic anxiety are sensitive enough to discriminate between symptomatic and healthy patients (Yardley et al., 1994b; Yardley *et al*., 1994; Yardley et al., 1995; Yardley *et al*., 1998; Yardley *et al*., 1998; Guerraz *et al*., 2001).

For the purpose of this study the abridged version of VSS with 34 items is used because it has been proven in term of its usefulness and validity. This abridged version was utilized in

one cross-cultural validation study amongst Mexican patients. The researchers found two items that were evidenced to be less relevant (Yardley *et al.,* 1999). As a consequence, these two items were excluded.

This questionnaire has been shown to be useful in terms of clinical investigation and evaluation. It was able to isolate balance disorders amongst psychiatric patients during routine follow-up or referral, and to evaluate anxiety and panic disorder in neuro-otology clinics (Yardley *et al*., 1999). By considering all these important findings and reasons, it is clear that the subjective questionnaire is clinically important for the accurate diagnosis of vestibular disorders in general, and PVD specifically.

1.8.2   Importance of subjective measures

The usefulness of questionnaire in identifying patients with vestibular disorders has been demonstrated elsewhere (Holmberg *et al*., 2005). For instance, a study by Holmberg *et al.* (2005) found that normal and labyrinthine disordered subjects produced lower scores in dizziness handicap inventory (DHI) questionnaire. In contrast, subjects experiencing phobic postural vertigo had higher scores, indicative of more impairment or disability.

Clinical diagnosis and objective tests of balance disorder alone are inadequate for assessing the severity and impact of a patient's dizziness. Utilizing a symptom-specific subjective measurement is essential in giving patients accurate identification of symptoms and status, as well as being helpful in deciding further treatment methods, clinical judgment and disease monitoring. As mentioned previously, the VSS is a well established tool for the evaluation of vestibular disorders and the associated symptom of autonomic arousal and somatosensation. VSS also focuses on all the primary and secondary symptoms of vestibular disorder, including anxiety and autonomic symptoms (Yardley *et al.,* 1992a; Yardley *et al*., 1999).

By using this self-administrated questionnaire, patients with vestibular disorders are able to express and score their recent and current symptoms or problems. Items of the VSS address symptoms which might have been overlooked in the initial appointment with the clinician. The majority of the items related to the autonomic symptom in the VSS are related to vertigo rather than other subtypes of dizziness (Baloh, 1998). Autonomic symptoms such as nausea and vomiting are typical features of PVD (Baloh, 1998).

Detailed measurement of dizziness and its related symptoms and will guide the clinicians in making an accurate diagnosis and specifying the site of lesion (Baloh, 1998). For clinical purposes it is valuable if the clinician has a clear view and cut off point/level as to whether patients have vestibular disorder solely or if it is mixed with psychological involvement such as anxiety disorder or depression (Asmundson *et al*., 1998).

Furthermore, detailed information regarding the duration of particular symptoms is really important for the clinician to have a clear idea of the course of the disease and to narrow down the symptoms accurately (Eaton and Roland, 2003). For example, in Meniere's disease, questions regarding the patient's quality of life are used to monitor and evaluate the patient's status during the treatment course (Soderman *et al*., 2002).

The VSS has been used as the assessment tool for dizzy patients who have undergone vestibular rehabilitation. In one study (Yardley *et al*, 2004) research participants were randomly selected from 20 general practices in the Southern England. In this interventional study, primary care nurses gave instruction and explanation in two home visits to all participants. Results of this study indicated some improvement of the patient's symptoms, handicap and balance control (Yardley *et al.,* 2004).

Hence, one of the purposes of this study was to develop a valid Malay Version of VSS (MVVSS) for accurate diagnoses amongst a Malay-speaking population. Having a reliable