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MENIERE'S DISEASE AND MIGRAINE-ASSOCIATED DIZZINESS:

DIFFERENTIAL DIAGNOSIS

by

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ABSTRACT

MENIERE'S DISEASE AND MIGRAINE-ASSOCIATED DIZZINESS:

DIFFERENTIAL DIAGNOSIS

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The objective of the study was to determine if a test battery consisting of electrocochleography and rotary chair testing would differentially diagnose between Meniere's disease and migraine-associated dizziness. A retrospective chart review of 10 patients diagnosed with Meniere's disease and 10 patients diagnosed with migraine-associated dizziness was completed. Comparisons between these two groups were made to determine if statistically significant differences existed in terms of their: 1.) mean rotary chair gain values; and 2.) ECochG SP/AP amplitude ratios.

Results indicated that no statistically significant differences existed between the ECochG SP/AP amplitude ratios of these two groups. Statistically significant differences between these two groups did however exist in the rotary chair gain values at all of the test speeds with the exception of 0.32 Hz. The results suggest that rotary chair gain values have the ability to differentially diagnose between Meniere's disease and migraine-associated dizziness.

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CHAPTER 1:

INTRODUCTION

Controversy in the literature exists regarding the pathophysiology of both Meniere's disease and migraine-associated dizziness. This controversy creates a challenge in terms of accurate diagnosis as well as treatment of each disease. At present, the etiology of each disorder remains unclear. Several theories exist attempting to explain the etiology responsible for these two pathologies. One theory speculates that each disease stems from unique pathophysiologies and the simple overlap in symptoms is responsible for misdiagnosis (Furman, Marcus, & Balaban, 2003). A second theory states that there is a common pathogenesis, which creates similar symptoms in these two disorders. The last, or third theory, speculates that there is an interaction between the two pathologies resulting in one disease causing the other. Differential diagnosis between Meniere's disease and migraine-associated dizziness becomes difficult when the presentation of symptoms is similar and when the pathophysiology of both disorders is not clearly understood.

Patients with Meniere's disease and migraine-associated dizziness may present with similar complaints of vertigo as well as other auditory and vestibular-related symptoms. Diagnosis of Meniere's disease is usually based on the presence of a triad of symptoms, which include vertigo, tinnitus and fluctuating low frequency sensorineural hearing loss (Gianoli, 2001; Rubin, 1993; Thai-Van, Bounaix, & Fraysse, 2001). In some clinical cases, unilateral aural fullness also exists (Gianoli,

2001; Rubin, 1993). While a universal classification for migraine-associated dizziness has yet to be determined, patients present with similar symptoms to Meniere's disease including fluctuating sensorineural hearing loss, vertigo, and tinnitus (Furman et al., 2003; Johnson, 1998; Lee, Lopez, Ishiyama, & Baloh, 2000). Patients with migraine-associated dizziness may also complain of a combination of any of the following symptoms or auras: headache, nausea, vomiting, photophobia, phonophobia, gait ataxia, parestesia, dsyarthria, weakness, and double vision (Johnson, 1998; "Part one", 2004).

While the presentation of symptoms is often similar, some differences between Meniere's disease and migraine exist. The differences in these two pathologies are primarily related to age of onset, gender, prevalence and susceptibility to motion sickness. The onset of Meniere's disease typically occurs between the 4th and 6th decade of life (Fetter, 2000; Gianoli, 2001). In contrast, the onset of migraine typically occurs during the highly productive years, generally beginning between 12 and 30 years of age, with the highest prevalence occurring between 35 to 45 years (Furman et al., 2003; Tusa, 2000). Meniere's disease is evenly distributed between males and females, while migraine occurs more frequently in females (Fetter, 2000; Tusa, 2000). The prevalence of Meniere's disease is extremely low as it occurs in only 0.015% of people, while migraine has a much higher prevalence; occurring in approximately 18% of women and 6% of men within the United States (Lipton, Steward, Diamond, Diamond, & Reed, 2001; Wladislavosky-Waswerman, Facer, Mokri, & Kurland as cited in Ghosh, Gupta & Mann, 2002). One final difference between these two pathologies is the susceptibility to motion sickness. A greater

incidence of motion sickness has been found in patients with migraine in comparison to either a normal-control group or a group of patients with typical tension headaches (Kayan & Hood, 1984).

The purpose of the present study was to determine if a test protocol consisting of electrocochleography (ECochG) and rotary chair testing could differentially diagnose these two similar pathologies (i.e., Meniere's disease and migraine-associated dizziness). As previously discussed, vertigo and hearing loss, among other otologically-related symptoms, are often key presenting symptoms for patients with both Meniere's disease and migraine-associated dizziness. Therefore, a review of the anatomy and physiology of the peripheral and central auditory and vestibular systems is necessary to further understand these pathologies.

Following a review of the peripheral and central auditory and vestibular systems, both Meniere's disease and migraine-associated dizziness will be described in terms of their symptoms, hypothesized pathophysiology, diagnosis strategies, and current treatment strategies. In addition, the two vestibular tests being evaluated in the current study, ECochG and rotary chair testing, will be described. This description will include the clinical utility of each test, the specific test protocols used for each test, and a rationale for why these two tests may be helpful in the diferential diagnosis of these two pathologies.

CHAPTER 2:

LITERATURE REVIEW

Overview of Peripheral Auditory and Vestibular Systems

The auditory and vestibular systems are each divided into peripheral and central nervous system components. The peripheral components of the auditory and vestibular sensory organs are intricately connected and are located in the inner ear within the petrous portion of the temporal bone (Bear, Connors, & Paradiso, 2001; Honrubia & Hoffman, 1997; Shepard & Telian, 1996; Wright & Schwade, 2000). Each system is comprised of an outer "osseous" labyrinth shell (Shepard & Telian, 1996). Encapsulated within this osseous labyrinth shell is a membraneous labyrinth (Shepard & Telian, 1996). The peripheral auditory osseous labyrinth consists of the spiral-shaped cochlea, whose primary function is hearing (Anzai & Lufkin, 1996). As can be seen in Figure 1, the cochlea is a snail-shaped osseous shell that spirals for two and three quarter turns around a central bony pillar named the modiolus (Anzai & Lufkin, 1996; Bear et al., 2001). The modiolus is hollow on its inside (Gelfand, 1997). This hollow inside gives way to a structure known as the internal auditory canal, where the auditory branch of the VIII cranial nerve and cochlear blood supply exit the cochlea and enter the brainstem (Gelfand, 1997).

In contrast, the peripheral vestibular osseous labyrinth consists of two sections: the vestibule and the semicircular canals, also seen in Figure 1, whose primary function is that of balance (Anzai & Lufkin, 1996). The vestibule is located

between the peripheral auditory and vestibular organs (Yost, 2000). Located on one side of the vestibule is the oval window, where the footplate of the stapes is embedded and on the other side are the semicircular canals (Yost, 2000). Within the vestibule, the otolith organs are located. The otolith organs include the utricle and saccule, which provide information to the central nervous system (CNS) concerning linear acceleration (front-to-back motion), also known as pitch, yaw, and roll, of the head and body as well as the influence of gravitational forces (Merchant, 1999). The three semicircular canals (Superior, Lateral (or Horizontal), and Posterior) lay at a 90-degree orientation to one another in 3 separate planes of space (Merchant, 1999; Shepard & Telian, 1996). The semicircular canals provide information to the CNS concerning angular acceleration (side-to-side motion) of the head and body (Merchant, 1999). The vestibular branch of the VIII cranial nerve exits the otolith organs and semicircular canals where it joins with vestibular ganglia within the internal auditory canal and then enters the brainstem (Gelfand, 1997). These peripheral auditory and vestibular organs are found on both the right and left side of the head and are mirror images of each other (Bear et al., 2001; Shepard & Telian, 1996).

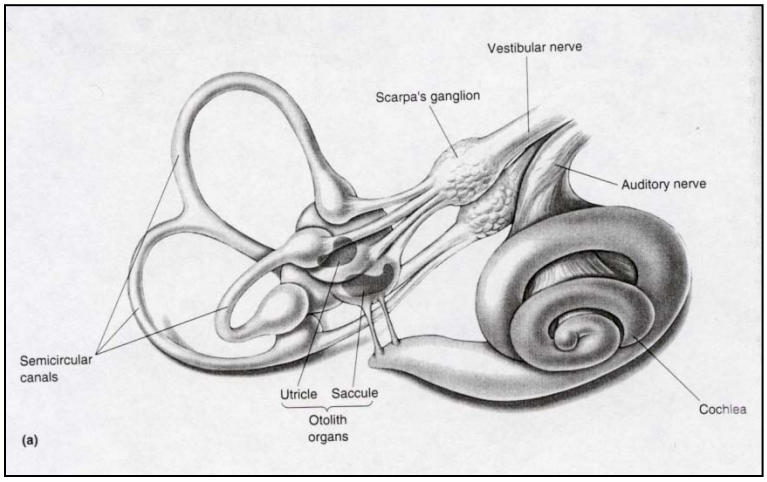

Figure 1. Schematic of peripheral auditory and vestibular system osseous labyrinth from Bear et al., 2001.

Two types of fluid are found within the peripheral components of the auditory and vestibular systems. The osseous labyrinth shell of the peripheral auditory and vestibular organs is filled with perilymph fluid, while the inner membraneous labyrinth is filled with endolymph fluid (Shepard & Telian, 1996). Endolymph fluid flows continuously throughout the peripheral auditory and vestibular systems via the ductus reunions, which connects the auditory and vestibular membraneous labyrinths (Gelfand, 1997). The secretion and absorption sites of these two fluids is currently unknown, however it is speculated that endolymph fluid is secreted in the cochlea via the stria vascularis and absorbed in the endolymphatic sac (Kimura et al., 1963 as cited by Schuknecht, 1974, Schuknecht, 1974). Studies have also indicated that the endolymphatic sac has both absorptive and secretive functions (Gibson & Arenburg, 1997). It is speculated that perilymph is secreted by cerebrospinal fluid and is absorbed by the spiral ligament (Schuknecht, 1974).

The chemical composition of perilymph and endolymph is quite different. Perilymph fluid has a concentration of low potassium and high sodium ions (Gelfand, 1997). The concentration of endolymph fluid on the other hand, is just the opposite, with a high concentration of potassium and a low concentration of sodium ions (Gelfand, 1997). The endolymph fluid system is responsible for bathing the tectorial, otolithic, and cupular membranes and is critical for the sensory transduction process, which will be discussed in detail later in this review (Schuknecht, 1974). The concentration of the perilymph fluid system, in contrast, is responsible for neural excitation and synaptic activity (Schuknecht, 1974).

Even though the peripheral auditory and vestibular systems share many similarities in their structure, each is unique in the following ways: 1.) their function; 2.) the information they supply to the CNS; 3.) the afferent and efferent neural pathways that transmit this information; and 4.) the location within the central nervous system that processes this information. For this reason, the anatomy and physiology of the peripheral and central auditory and vestibular systems will be individually discussed in greater detail.

Peripheral Auditory System: Anatomy

The cochlea is the auditory sensory organ of the inner ear. As shown in a cross-section of the cochlea in figure 2, the cochlea is separated into three fluid-filled chambers: the Scala Vestibuli, the Scala Media, and the Scala Tympani (Bear et al., 2001). These three chambers spiral from the base of the cochlea to the apex. The Scala Vestibuli courses superiorly from the oval window of the vestibule toward the apex where it meets with the Scala Tympani at the helicotrema (Bear et al., 2001;

Gelfand, 1997; Yost, 2000). The helicotrema is a small opening at the apex of the cochlea, which allows communication between the Scala Vestibuli and Scala Tympani (Gelfand, 1997). The Scala Tympani then courses inferiorly from the helicotrema toward the base of the cochlea and terminates at the round window (Bear et al., 2001). Between the Scala Vestibuli and the Scala Tympani is the Scala Media. The Scala Media is separated from the Scala Vestibuli via Reissner's membrane and is separated from the Scala Tympani via the basilar membrane (Bear et al., 2001; Gelfand, 1997). The Scala Vestibuli and the Scala Tympani have an osseous, or bony, outer shell and are filled with perilymph fluid (Gelfand, 1997). In contrast, the Scala Media is a membraneous labyrinth and is filled with endolymph fluid (Bear et al., 2001). Within the Scala Media is the sensory organ of hearing, known as the organ of Corti.

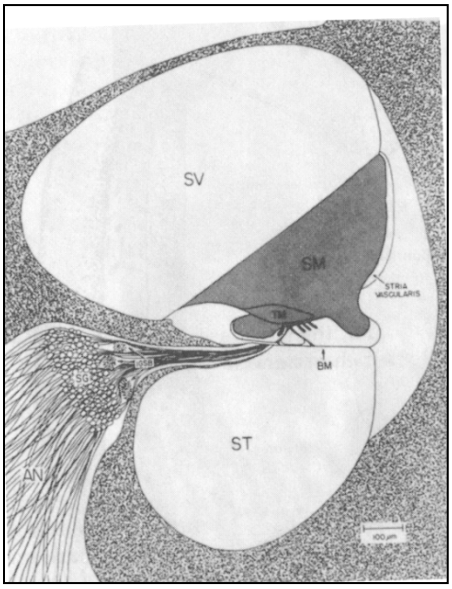

Figure 2. Cross-section of the three cochlear chambers from Gelfand, 1997. SV = Scala Vestibuli, SM = Scala Media, and ST = Scala Tympani

The organ of Corti is the primary sensory receptor of hearing and is located within the Scala Media. Within the organ of Corti there are two types of hair cells: the inner and outer hair cells. Differences between the inner and outer hair cells exist in terms of their location along the basilar membrane, number, shape, and chemical composition. As shown in figure 3, the tunnel of Corti separates the inner and outer hair cells. One row of inner hair cells is located on the medial side of the organ of Corti, while three rows of outer hair cells are located on the lateral side of the organ of Corti (Gelfand, 1997). In a healthy adult cochlea, there are approximately 3500 inner hair cells and over 15,000 outer hair cells (Bear et al., 2001; Ryan, 2002). Each type of hair cell has its own characteristic shape and chemical composition. The inner hair cells are flask-shaped and are comprised of structures such as Golgi apparatus, mitochondria and other organelles, which are suggestive of a high level of metabolic activity (Gelfand, 1997, 1998). In contrast, the outer hair cells are tube-like in shape and contain contractile proteins such as actin, myosin and tubulin, which allow the outer hair cells to contract and elongate (Gelfand, 1997, 1998).

Both the inner and outer hair cells have bundles of stereocilia, or hairs, which are located at the top of the cells (Gelfand, 1997; Ryan, 2002). These stereocilia are anchored in place via a cuticular plate, which is a thickened area of actin filaments located at the top of the hair cells (Gelfand, 1997). Stereocilia from both the inner and outer hair cells are connected via three types of cross-linked actin filaments: side-to-side, row-to-row and tip-to-side filaments (Bear et al., 2001). Side-to-side actin filaments connect hair cells from one side to another within rows of hair cells, while row-to-row actin filaments connect hair cells between rows. Thirdly, tip-to-side actin

filaments connect the tip of one hair cell to the side of the neighboring hair cell (Gelfand, 1998). Collectively, these actin filaments allow the stereocilia to move together as a unit when the hair cells are activated or inhibited (Bear et al., 2001).

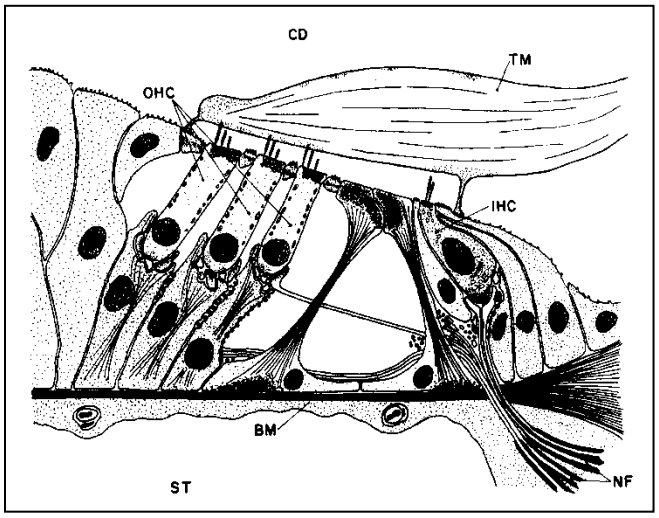

Figure 3. Cross-section of the Organ of Corti from Ryan, 2002. OHC = Outer Hair Cells, CD = Cochlear Duct (Scala Media), TM = Tectorial Membrane, IHC = Inner Hair Cells, ST = Scala Tympani, BM = Basilar Membrane, NF = Nerve Fibers

The basilar membrane is an elastic fibrous membrane which makes up the floor of the organ of Corti as shown in figure 3 (Gelfand, 1997). The basilar membrane has two characteristic physical properties which influence its pattern of movement (Gelfand, 1997). First, the basilar membrane is 5 times wider at its apex than at its base (Bear et al., 2001). Second, the basilar membrane is approximately 100 times stiffer at its base in comparison to its apex (Bear et al., 2001). In other

words, the base of the basilar membrane is narrow and stiff, while the apex is wide and flaccid (Yost, 2000). These two properties become important when discussing the vibration patterns of the basilar membrane and its role in coding frequency-specific information for incoming auditory signals, which will be discussed further in the physiology section.

Overlying the organ of Corti is a gelatinous covering named the tectorial membrane, as shown in figure 3 (Bear et al., 2001; Gelfand, 1997). The tectorial membrane is firmly attached to the inner wall of the cochlea, or spiral limbus, and is only loosely coupled to the organ of Corti (Ryan, 2002). Stereocilia from the tops of the outer hair cells project upward and are embedded within the undersurface of this tectorial membrane (Ryan, 2002). In contrast, stereocilia from the tops of the inner hair cells are either free floating within the organ of Corti or are loosely coupled to the tectorial membrane (Gelfand, 1997; Ryan, 2002). Differences in the coupling patterns between the outer and inner hair cells play an important role in the sensory transduction process, which will be discussed in further detail within the physiology section.

The organ of Corti also contains a number of supporting structures and cells. Supporting the inner hair cells are the phalangeal cells, which are located at the base of the individual inner hair cells (Gelfand, 1998). Supporting the outer hair cells are outer phalangeal cells, which are named Deiters and Hansen's cells (Pickles, 1988; Yost, 2000). Each outer hair cell contains one Deiters cell at its base whose primary function is to provide vertical support for the hair cell (Yost, 2000). On the peripheral edge of the outer hair cells are supporting cells named Hensen's cells (Pickles, 1988).

Along the tops of both the inner and outer hair cells is another support structure known as the reticular lamina. The reticular lamina is responsible for keeping the hair cells aligned and providing upper surface support (Gelfand, 1997, 1998; Yost, 2000). These supporting structures and cells constitute the majority of bulk of the organ of Corti, which keep it firmly attached to the basilar membrane (Ryan, 2002).

Peripheral Auditory System: Physiology

As sound enters the ear, it travels through the external auditory canal where it sets the tympanic membrane into vibration. Movement of the tympanic membrane is transferred through the middle ear space via the ossicular chain: the malleus, incus, and stapes. Incoming sound creates an inward and outward piston-like movement of the stapes footplate, which is embedded within the oval window. This movement results in displacement of cochlear fluids within the membraneous labyrinth (Pickles, 1988). The cochlea's primary function is to transform the mechanical vibrations delivered from the outer and middle ear into electrical, or neural, responses for the brain to decode (Yost, 2000). There are two processes within the cochlea that are responsible for this mechano-electrical transduction process: 1.) the mechanical, or passive, response from the basilar membrane; and 2.) the active, or cochlear amplifier, response from the outer hair cells. The following is a brief description of each of these processes.

Passive / Mechanical Response of the Basilar Membrane

The passive or mechanical response of the basilar membrane begins with the piston-like movement of the stapes at the oval window. This piston-like movement creates a change of pressure within the perilymph fluid of the Scala Vestibuli (Yost,

2000). Because the cochlea is encased within an osseous or bony shell, this pressure change must be compensated (Ryan, 2002). Compensation of fluid pressure occurs in two ways. First, part of this pressure is relieved via the inward and outward bulging of the round window at the base of the Scala Tympani (Ryan, 2002; Pickles, 1988). Second, the remaining pressure travels toward the helictorema and is absorbed by the Scala Media (Ryan, 2002). Absorption of this pressure creates a pressure wave in the endolymph fluid of the Scala Media and results in the displacement of the basilar membrane from its resting position (Ryan, 2002). Displacement of the basilar membrane at the base of the cochlea initiates a pressure wave that travels from the base of the cochlea toward the apex (Bear et al., 2001). This phenomenon is known as the traveling wave (Bear et al., 2001, Gelfand, 1997).

Von Bekesy is responsible for introducing traveling wave theory through a series of experiments leading up to the 1960's (Bear et al., 2001; Gelfand, 1997; Ryan, 2002). Bekesy performed these experiments on both human and animal cadavers and showed that the traveling wave has several important properties, which are dependent, in part, upon the structural characteristics of the basilar membrane (Pickles, 1998). First, Bekesy discovered that the traveling wave always travels from the base of the cochlea toward the apex (Pickles, 1988). Second, the amplitude of the traveling wave increases as it travels away from the base of the cochlea until it reaches its maximum amplitude and then quickly extinguishes (Pickles, 1988). Third, the speed of the traveling wave slowly decreases as it travels from the base towards the apex, which causes the phase of the traveling wave to change along its course (Pickles, 1988). Lastly, Bekesy found that the overall displacement patterns of the

basilar membrane are affected by the frequency of the incoming signal (Pickles, 1988). As shown in figure 4 below, Bekesy discovered that when high frequency signals were delivered to the cochlea, maximal displacement of the basilar membrane occurred near the base (Pickles, 1988). In contrast, when low frequency signals were delivered, the traveling wave grew in amplitude along the basilar membrane and reached its maximal displacement closer to the apex (Pickles, 1988). Based on Bekesy's descriptions of the traveling wave, the basilar membrane has been described as a low-pass filter (Pickles, 1988).

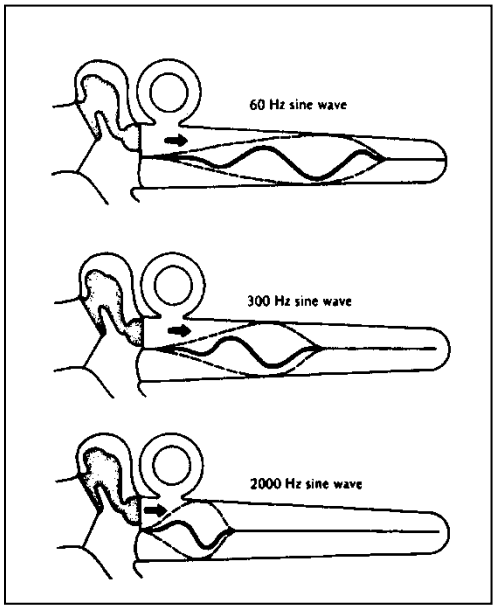

Figure 4. The effect of signal frequency on the displacement pattern of the basilar membrane from Yost, 2000.

The physical properties of the basilar membrane are in part responsible for its frequency selectivity. As previously mentioned, the basilar membrane is approximately 5 times wider at the apex in comparison to the base and is approximately 100 times stiffer at the base in comparison to the apex. These properties result in maximal displacement of the basilar membrane at the stiff, narrow base for high frequency signals and maximal displacement of the basilar membrane at the wider, more compliant apex for low frequency signals (Bear et al., 2001; Ryan, 2002). The basilar membrane is therefore tuned to particular frequencies according to place (Bear et al., 2001). This property is known as tonotopic organization (Bear et al., 2001).

Non-linear Response of the Basilar Membrane

While Bekesy's initial experiments have helped to explain some aspects of the basilar membrane's frequency selectivity properties, subsequent studies have investigated several additional properties of the basilar membrane's vibration pattern, including the effects of stimulus intensity. Several studies have revealed that the basilar membrane has a non-linear pattern of vibration (e.g. Rhode, 1971, 1978; Sellick 1982 as cited in Pickles, 1988; Yost, 2000). In the early 1970's, Rhode (1971, 1978 as cited in Pickles, 1988) was the first individual to discover that the basilar membrane's response was not entirely linear. He demonstrated that the basilar membrane's non-linear patterns of vibration resulted in 2 specific effects: 1) an increase in sensitivity to low-intensity stimuli within the human cochlea and 2) a quite sensitive and sharply tuned frequency response of the basilar membrane at the peak area of displacement (Pickles, 1988).

In 1982, Sellick (as cited by Pickles, 1988) described several specific characteristics related to this nonlinear basilar membrane response. First, he reported that the basilar membrane's response is nonlinear to low intensity signals and becomes linear for higher intensity signals (>80 dB SPL) (Pickles, 1988; Yost, 2000). At these lower intensities, the amplitude of basilar membrane vibration in the peak area of displacement is approximately 100 times greater than the amplitude of displacement that occurs for frequencies above and below this peak area (Bear et al., 2001). Second, Sellick described that this sharp frequency tuning occurs at only one location along the basilar membrane, which coincides with the frequency of the input stimulus (Pickles, 1988; Yost, 2000). Based upon these discoveries, the basilar membrane has been more accurately described as a "bandpass filter" rather than the "low pass filter" initially proposed by Von Bekesy (Pickles, 1988). Third, Sellick (1982, as cited by Pickles, 1988) demonstrated that this nonlinear basilar membrane vibration pattern is physiologically vulnerable. The sharp frequency tuning and enhanced displacement of the basilar membrane in the peak area of the response disappears when the cochlea is damaged (Pickles, 1988). In these cases, the basilar membrane vibration pattern becomes more linear along its length, much like the response patterns of vibration initially reported by Bekesy (Pickles, 1988).

Active Process / Cochlear Amplifier

Several physiological studies have attempted to explain the origin of this sharply tuned frequency response of the basilar membrane and its increased sensitivity to low intensity sounds (Pickles, 1988). It has been speculated that a second "active" process must be present along with the passive or mechanical process

described by Von Bekesy, which is responsible for these properties (Pickles, 1988). This second process has been referred to as the active process, or cochlear amplifier (Bear et al., 2001; Gelfand, 1997). While the mechanisms underlying the active cochlear response are not fully understood, it has been shown that the outer hair cells are the primary contributors to this active process. Three strong pieces of evidence support this hypothesis. First, when the outer hair cells are damaged or missing, the non-linear, sharply tuned frequency response of the basilar membrane disappears and the frequency response tuning curves become much more broadly tuned (Ryan, 2002; Yost, 2000). Second, the non-linear vibration pattern, which occurs at the peak area of the response, becomes more linear when the outer hair cells are damaged (Pickles, 1988). Thirdly, when damage to the outer hair cells takes place, the neural threshold of the hair cells increases by approximately 30 to 40 dB (Davis et al., 1985 & Dallos et al., 1972 as cited by Gelfand, 1998).

This active cochlear response has been specifically attributed to the electromotility properties of the outer hair cells. The outer hair cells contain a motor protein known as prestin, which allows them to change their length and shape when stimulated (Dallos & Fakler, 2002). During depolarization, or excitation phase, the outer hair cells shorten in length by contracting, and during hyperpolarization, or inhibition phase, the outer hair cells lengthen (Dallos & Fakler, 2002; Ryan, 2002). These motility properties are unique to the outer hair cells and directly affect the coupling of the basilar membrane to the tectorial membrane (Yost, 2000).

It is speculated that the changes in length of the outer hair cells during stimulation, results in a pulling and pushing of the basilar membrane from the

tectorial membrane (Bear et al., 2001). The changes in physical coupling between the basilar and tectorial membranes directly affect the vibratory pattern of the traveling wave. Specifically, the amplitude of the traveling wave is increased in the peak area of displacement by approximately 100 fold (Bear et al., 2001). This increased or amplified peak of the traveling wave in a localized region results in an increased sensitivity for low intensity signals and increased frequency selectivity (Yost, 2000). As a result of their contribution, the outer hair cells are said to provide an amplifier to the cochlea (Yost, 2000).

While the outer hair cells are responsible for the sharp frequency tuning and increased sensitivity for low intensity sounds, it is the inner hair cells that are primarily responsible for transferring this information to the central auditory nervous system (CANS). The inner hair cells provide approximately 95% of the afferent information to the CANS (Bear et al., 2001). This is accomplished by inner radial fibers, or type I auditory nerve fibers (Gelfand, 1998). The outer hair cells, in contrast, provide the remaining 5% of afferent information to the CANS. This occurs via outer spiral fibers, or type II auditory nerve fibers (Bear et al., 2001; Gelfand, 1998).

In order for this afferent information to be transferred from the cochlea to the CANS, the outer and inner hair cells must be activated. A discussion of the activation of hair cells requires an understanding of the primary electrical potentials generated within the cochlea. The following is a brief review of the primary electrical potentials measured within the cochlea.

Cochlear Potentials

There are four primary electrical potentials which are generated within the cochlea or the VIII nerve. These are the resting potentials, the summating potential, the cochlear microphonic, and the action potential (Yost, 2000). These electrical potentials are generated by interactions of the various cochlear structures (Yost, 2000). They can be measured using microelectrodes, which can be placed in various cochlear structures or directly on the VIII nerve (Ryan, 2002; Yost, 2000). Each of these potentials will be briefly introduced in this section.

Resting potentials within the cochlea are direct current (DC), or non-alternating, electrical potentials whose measurement is not dependent upon acoustic stimulation (Yost, 2000). The two resting potentials measured within the cochlea are the endocochlear potential and the intracellular potential (Ryan, 2002; Yost, 2000). The endocochlear potential is a measurement of the electrical voltage that exists within the endolymph fluid of the Scala Media (Yost, 2000). The endocochlear potential is a constant positive potential of approximately 80 mV, thus making it the highest electrical potential found within the human body (Ryan, 2002; Yost, 2000). Even though the endolymph fluid is continuous throughout the cochlear and vestibular portions of the inner ear, this potential is only found within the Scala Media (Yost, 2000). In contrast, the intracellular potential is a measurement of electrical voltage that exists within the hair cells (Gelfand, 1998; Ryan, 2002). The intracellular potential is approximately -70 mV, which results in a significant voltage difference of approximately 120- 150 mV between the inside of the hair cells and the endocochlear potential (Gelfand 1998; Ryan, 2002). The electrical voltage difference

or gradient of approximately 120 – 150 mV that exists between the endocochlear and intracellular potentials has been speculated to provide the energy needed for the sensory transduction process (Gelfand, 1998; Ryan, 2002). This high gradient difference facilitates the movement of potassium ions into the hair cells, which initiates the beginning of the depolarization or excitation process (Ryan, 2002). The resting potential and its role in the depolarization process will be discussed in further detail later in this review.

A second electrical potential measured within the cochlea is the summating potential. The summating potential is a DC potential, which is measured as a shift of the baseline voltage in response to acoustic stimulation (Gelfand, 1998; Yost, 2000). The summating potential is primarily generated at the level of the outer hair cells (Ryan, 2002). It has been suggested that measurement of the summating potential may play a significant role in the evaluation and diagnosis of Meniere's disease, which will be discussed in further detail later in this review.

The cochlear microphonic is a third electrical potential measured within the cochlea. Unlike the resting potential and summating potential, the cochlear microphonic is an alternating current (AC) potential (Gelfand, 1998). The cochlear microphonic occurs in response to acoustic stimulation and mimics the intensity and frequency of the incoming stimulus (Yost, 2000). Studies by Tasaki and colleagues have shown that the source of the cochlear microphonic occurs at the level of the cilia-bearing end of the outer hair cells (as cited in Gelfand, 1998).

The fourth electrical potential is the action potential, also called the whole nerve or compound action potential (Gelfand, 1998). The action potential is not a true

cochlear potential because it is generated by auditory neurons, not structures within the cochlea (Yost, 2000). When individual auditory neurons are activated they generate an electrical charge called an action potential (Gelfand, 1997). This action potential is an all-or-none response of the neuron and is the end product of the depolarization process (Gelfand, 1997). In contrast, the compound action potential is the sum of a group of auditory neurons firing simultaneously (Yost, 2000). In conjunction with the summating potential, the compound action potential is also a primary component used in the evaluation and diagnosis of Meniere's disease.

Neural Activation of Hair Cells

Of the four primary cochlear electrical potentials, the resting potentials play a key role in the activation of hair cells, whose end result is the generation of an action potential. The neural activation process differs for the outer and the inner hair cells. For the outer hair cells, neural activation occurs as the result of interactions between the basilar membrane and the tectorial membrane. Upward movement of the basilar membrane moves the organ of Corti towards the overlying tectorial membrane (Bear et al., 2001). Likewise, downward movement of the basilar membrane moves the organ of Corti away from the overlying tectorial membrane (Bear et al., 2001). This upward and downward movement of the basilar membrane creates a shearing action between the basilar membrane and the tectorial membrane. This shearing action results because the basilar membrane and the tectorial membrane have different hinge points (Yost, 2000). The tectorial membrane is hinged to the spiral limbus, while the basilar membrane is hinged to the osseous spiral lamina (Yost, 2000). As the basilar membrane is displaced, the tectorial membrane is dragged along the top of the organ

of Corti (Ryan, 2002). This dragging motion creates a shearing action between the stereocilia of the outer hair cells and the tectorial membrane because the stereocilia of the outer hair cells are embedded in the undersurface of the tectorial membrane (Gelfand, 1998; Ryan, 2002).

Shearing of the inner hair cells on the other hand, occurs as the result of displacement of surrounding fluid in response to basilar membrane movement (Gelfand, 1998). The inner hair cells are sensitive to the velocity of basilar membrane movement (Gelfand, 1998). As the velocity of basilar membrane movement increases, the velocity of surrounding fluid increases (Gelfand, 1998). Because stereocilia of the inner hair cells are free standing, movement of the surrounding fluid creates a drag, which results in a shearing of the stereocilia of the inner hair cells similar to that described for the outer hair cells (Gelfand, 1998; Yost, 2000).

This shearing action of the outer and inner hair cells results in a bending, or deflection, of the stereocilia. When the stereocilia are deflected away from the modiolus, hair cells begin a depolarization, or excitation process (Bear et al., 2001; Gelfand, 1997; Wright & Schwade, 2000). In contrast, when the stereocilia are deflected towards the modiolus, hair cells begin a hyperpolarization, or inhibition process (Gelfand, 1997).

The depolarization process of hair cells within the cochlea is a series of events resulting in the production of a neural discharge known as an action potential. The depolarization process begins when the stereocilia of the hair cells are deflected away from the modiolus. As previously mentioned, the stereocilia on top of the hair cells are connected via tip linkages comprised of actin filaments that connect the stereocilia

as a unit. As shown in the right hand side of figure 5, deflections of the stereocilia away from the modiolus pull on these tip-to-side linkages, which in turn open potassium channels located on the top of the stereocilia (Gelfand, 1997). These potassium channels are selectively permeable and when open, allow an influx of positively charged potassium ions from the surrounding endolymph into the negatively charged cell (Bear et al., 2001; Ryan, 2002; Wright & Schwade, 2000). The incoming potassium ions cause a quick intracellular voltage change from the resting intracellular potential of –70mV to approximately +50mV within the hair cell (Bear et al., 2001). This rapid intracellular voltage change triggers the opening of voltage-gated calcium channels within the hair cell allowing calcium ions to also enter (Bear et al., 2001). The influx of calcium ions into the hair cell causes the release of a neurotransmitter, which as shown in figure 6, travels across the synapse, or synaptic cleft, and initiates a voltage change in the post-synaptic membrane (Bear et al., 2001; Dallos, 1974). Once this voltage change exceeds the post-synaptic cell's threshold, electric current travels the length of the dendrite resulting in depolarization, or initiation of an action potential (Dallos, 1974). The action potential, as mentioned previously, is an all-or-none electrical charge generated by activation of a neuron, which results in neural discharge along the axonal neuron and eventually reaches the level of the CANS (Bear et al., 2001; Gelfand, 1997).

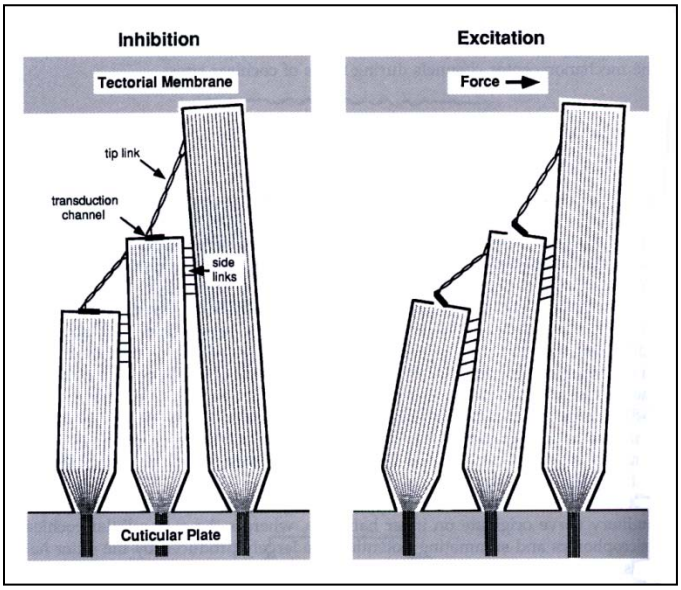

Figure 5. Schematic of changes in the stereocilia tip-to-side linkages on hair cells as a function of inhibition (left) and excitation (right) from Ryan, 2002.

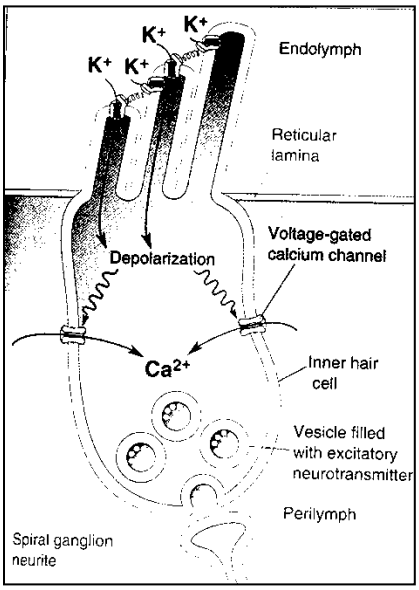

Figure 6. Hair cell activation from Bear et al., 2001. The influx of potassium ions into the cell during excitation triggers calcium ions to enter the cell. This triggers the excitatory neurotransmitter which is responsible for initiating a voltage change in the post-synaptic membrane.

The hyperpolarization process, however, occurs when the stereocilia are deflected toward the modiolus. When this occurs the stereocilia remain upright and the tip-to-side linkages are compressed as shown in the left side of figure 5 (Gelfand, 1997). Because the actin filaments are compressed, potassium channels are unable to open. This prevents potassium from entering the hair cell. Therefore, the resting potential within the hair cell remains the same and no action potential is created (Bear et al., 2001). When an action potential is not elicited, the CANS recognizes this as an inhibitory response (Gelfand, 1997).

Central Auditory System: Anatomy

The ascending auditory pathway is a complex pathway responsible for sending auditory information from the hair cells of the peripheral auditory system to the central auditory cortex. While this pathway is not fully understood, it is known that the auditory-vestibular nerve, or VIII cranial nerve, relays neural information from the hair cells to the level of the brainstem (Gelfand, 1998). From here, the ascending auditory pathway becomes much more complex. As shown in figure 7, neural information travels through a combination of many structures, or tracts, before reaching the primary auditory cortex. These structures include the cochlear nucleus, the superior olivary complex, the lateral lemniscus, the inferior colliculus, and the medial geniculate body (Bellis, 1996). This figure is a simplification of the ascending auditory pathway, however it should be noted that the CANS is a complex system for integrating and analyzing incoming auditory information. The ascending auditory pathway is often referred to as a redundant pathway because there are both ipsilateral and contralateral pathways that carry the same information through similar nuclei to the auditory cortex (Gelfand, 1997). Given the topic of literature review, only a brief overview of the central auditory anatomy and physiology will be presented.

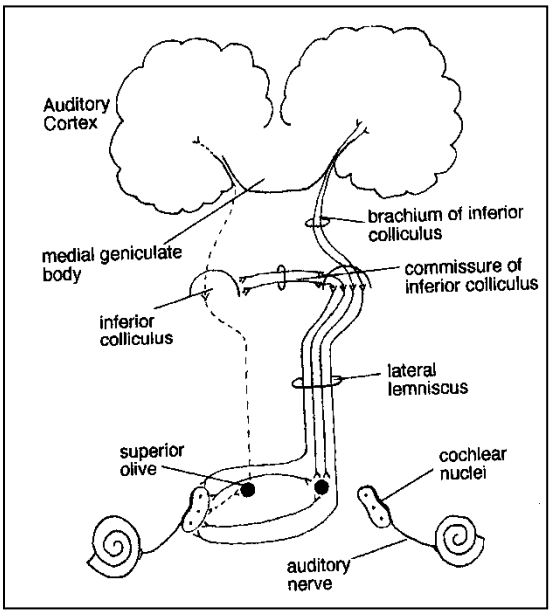

Figure 7. Ascending central auditory pathways from Bellis, 1996.

From the hair cells, the VIII cranial nerve exits the cochlea via the habenula perforata and travels through the internal auditory meatus (Gelfand, 1998). Within the internal auditory meatus, the VIII nerve resembles a twisted trunk, with fibers in the core of the trunk carrying low frequency information from the apex of the cochlea and fibers on the outside of the trunk carrying high frequency information from the base of the cochlea (Gelfand, 1998). The VIII nerve exits the internal auditory meatus and enters the brainstem at the level of the lower pons (Gelfand, 1998).

Upon entering the brainstem, the VIII nerve synapses with neurons located in the cochlear nucleus (Bear et al., 2001; Gelfand, 1998; Yost, 2000). The cochlear nucleus is located at the cerebellopontine angle and consists of three divisions: the anterior ventral cochlear nucleus (AVCN), the posterior ventral cochlear nucleus (PVCN), and the dorsal cochlear nucleus (DCN) (Bellis, 1996). Neurons within each

of the 3 divisions of the cochlear nucleus receive ipsilateral stimulation from the auditory nerve (Yost, 2000).

Output from the cochlear nuclei travels to either the superior olivary complex or bypasses the superior olivary complex and goes to the lateral lemniscus and the inferior colliculus. The superior olivary complex is located within the pons, medial to the cochlear nucleus (Bellis, 1996). The superior olivary complex receives both ipsilateral and contralateral information from the cochlear nucleus with approximately 80% of the fibers coming from contralateral stimuli (Bellis, 1996). The superior olivary complex consists of many groups of nuclei, with the 2 primary structures for the auditory pathway being the medial superior olivary nucleus and the lateral superior olivary nucleus (Chermak & Musiek, 1997).

The superior olivary complex is also responsible for efferent innervation of the Organ of Corti (Gelfand, 1997). The olivocochlear bundler, or Rasmussens's bundle, gives rise to both crossed and uncrossed efferent pathways (Gelfand, 1997). The uncrossed olivocochlear bundle arises in the lateral superior olivary complex and innervates ipsilateral inner hair cells by making connections on the afferent nerve endings (Gelfand, 1997; Yost, 2000). In contrast, the crossed olivocochlear bundle however arises in the medial superior olivary complex and innervates the contralateral outer hair cells (Gelfand, 1997; Yost, 2000).

From the superior olivary complex, axons extend to the lateral lemniscus of the pons (Yost, 2000). The lateral lemniscus contains both ascending and descending fibers, however, it is viewed as a primary ascending auditory pathway (Bellis, 2003; Chermak & Musiek, 1997). The lateral lemniscus is located from the pons in the

brainstem to the inferior colliculus in the midbrain (Bellis, 1996; Chermak & Musiek, 1997). It consists of both dorsal and ventral nuclei (Bellis, 1996; Chermak & Musiek, 1997). The lateral lemniscus receives both ipsilateral and contralateral information from the cochlear nuclei and superior olivary complex (Bellis, 2003).

The inferior colliculus is the next major nuclei in the ascending auditory pathway. The inferior colliculus is comprised of 3 areas: the central nucleus, the dorsal cortex, and the paracentral nuclei (Yost, 2000). The central nucleus constitutes the core of the inferior colliculus, and is surrounded by the paracentral nuclei (Chermak & Musiek, 1997). The right and left inferior colliculi are connected via commissural fibers named the brachium (Bellis, 2003). The inferior colliculus collectively receives contralateral and ipsilateral neural input from the cochlear nuclei, superior olivary complex and lateral lemniscus (Chermak & Musiek, 1997).

From the inferior colliculus, axons extend to the medial geniculate body in the thalamus by way of the brachium of the inferior colliculus (Bear et al., 2001; Bellis, 1996). The medial geniculate body is located on the inferior portion of the thalamus (Bellis, 2003; Chermak & Musiek, 1997). The thalamus is known as a “gateway station” because it serves as a connection between the brainstem and the auditory cortex (Bellis, 2003). Projections from the medial geniculate body, also known as auditory radiation fibers, are responsible for supplying neural information to the primary auditory cortex where auditory sensation and perception occur within the cerebrum (Bellis, 1996).

The auditory areas of the cortex are located in the cerebrum on the upper surface of the temporal lobe, also known as the supratemporal plane, within a deep

groove named the fissure of Sylvius (Bellis, 2003; Yost, 2000). Projections from the medial geniculate body arrive at the auditory cortex areas by way of structures such as the internal capsule, insula, and external capsule (Bellis, 2003). The auditory areas of the cortex are divided into two main areas: the primary auditory cortex and the auditory association cortex (Bellis, 2003). The primary auditory cortex is also known as Heschl's Gyrus, while the auditory association cortex is also known as Wernicke's area (Bellis, 2003). These two auditory areas of the cortex are connected via an axonal bundle (Bellis, 2003). The right and left auditory cortices are connected via that corpus callosum (Rappaport & Provencal, 2002).

Central Auditory System: Physiology

Action potentials generated at the level of the inner hair cells transfer neural information via the VIII cranial nerve to the central auditory cortex for sensation and perception of auditory information (Bellis, 1996). The individual action potentials generated by the VIII cranial nerve fibers collectively constitute a Compound Action Potential (CAP). This CAP codes the incoming information present in the auditory stimulus in 3 ways: frequency specificity, intensity (rate of firing), and timing information (phase-locking) (Bellis, 2003). Because each auditory nerve fiber is exclusively connected to an inner hair cell, auditory nerve fibers preserve the tonotopic organization of the basilar membrane and relay this frequency specific information to the cochlear nuclei (Bellis, 2003; Phillips, 2001). This tonotopic organization is preserved not only in the cochlear nucleus, but also upward throughout the ascending auditory pathways to the auditory cortex (Bellis, 1996). Stimulus intensity is neurally coded by the rate of individual auditory nerve firing. As

the intensity of an incoming stimulus increases, the basilar membrane is displaced across a broader distance and is displaced with greater amplitude (Bear et al., 2001). Both of these changes in the pattern of basilar membrane displacement result in an increase in the rate and number of auditory nerves firing (Bear et al., 2001). The CANS interprets this increase in rate and number of auditory nerves firing as a perceived increase in stimulus intensity, or loudness (Bear et al., 2001). Lastly, auditory nerve fibers provide information regarding temporal information present in the signal via phase-locking (Bellis, 2003). Phase-locking occurs when auditory neurons fire synchronously in-phase with the incoming stimulus frequency, or in other words, the auditory neurons fire at whole number multiples of the period of the stimulus (Bear et al., 2001). The phase-locking properties of the auditory neurons however are only effective for auditory stimuli below 4k Hz (Bear et al., 2001).

From the VIII cranial nerve, auditory information is first processed by the CANS at the level of the cochlear nucleus (Bellis, 2003). The cochlear nucleus has two primary responsibilities: enhancement of the incoming neural signal and innervation of other nuclei within the brainstem (Bellis, 2003; Yost, 2000). Enhancement of the incoming neural signal within the cochlear nucleus occurs due to the presence of specialized cells such as bushy cells, pauser units, chopper units, and build-up units (Bellis, 2003; Phillips, 2001). Each of these cell units respond uniquely to the incoming stimuli and provide information regarding signal duration, onset of the stimulus, and contrast enhancement (Bellis, 2003). For example, bushy cells which are located in the AVCN, preserve the timing of incoming stimuli via phase-locking, much like the auditory nerve fibers (Phillips, 2001). Chopper units, which

are located in the PVCN, respond at regular intervals throughout the incoming stimuli, thus supplying information regarding stimulus duration (Bellis, 2003). Located within the DCN are pauser units and build-up units, both of which help decode stimulus duration (Bellis, 2003). Pauser units relay information regarding stimulus duration by responding with initial spikes during stimulus onset, then pause from responding and lastly respond gradually throughout the remainder of the stimulus (Bellis, 2003). Build-up units respond in a similar fashion to pauser units, however, they lack the initial spiked response that occurs during stimulus onset (Bellis, 2003).

Neurons in the cochlear nucleus also enhance incoming signals via amplitude modulation, wherein the peaks within the signal are made higher and the troughs in the signal are made lower (Bellis, 2003). This results in the enhancement of important components within the incoming signal (Bellis, 2003). The cochlear nucleus is also the source of innervation for many other nuclei within the brainstem as it makes both ipsilateral and contralateral connections with the superior olivary complex, lateral lemniscus and inferior colliculus (Chermak & Musiek, 1997).

Because the superior olivary complex receives both ipsilateral and contralateral connections, it plays a fundamental role in binaural listening (Bellis, 2003). The primary function of the superior olivary complex is that of sound localization, lateralization, and listening in background noise (Bellis, 2003; Yost, 2000). These functions are accomplished by means of interaural timing delays, interaural phase differences, and interaural intensity differences as well as by specific neuronal response patterns (Bear et al., 2001; Bellis, 2003; Yost, 2000). Sound

localization is achieved as the result of interaural time (phase) differences and interaural intensity differences (Bellis, 2003). Because the distance between the two ears is approximately 20 cm, when a sound is presented in a horizontal plane of space to either the right or the left, the sound will reach the ipsilateral ear before the contralateral ear (Bear et al., 2001). Neurons within the superior olivary complex receive input from both cochleas, therefore when the signal reaches one ear before the other, these neurons are able to detect interaural time delays and can detect the source of the signal (Bear et al., 2001). The signal also reaches each ear with different phases. The interaural phase or time delay differences can only be detected for sounds whose frequencies are below 2000 Hz because at these lower frequencies the sound waves are much longer than the distance between the ears (Bear et al., 2001). A different strategy must be utilized for signals greater than 2000 Hz (Bear et al., 2001).

For sounds above 2000 Hz, the superior olivary complex achieves sound localization by detecting interaural intensity differences (Bear et al., 2001). Intensity differences occur between the ears because the head casts a sound shadow, which is an area of reduced sound pressure on the ear furthest away from the sound source (Bear et al., 2001). Depending on the angle in which the sound is presented, the head casts shadows in different directions (Bear et al., 2001). For example, sounds that are presented directly to one ear, or at a 90º angle of the head, cast a much larger shadow than sounds presented from 45º (Bear et al., 2001). As a result of these areas of reduced sound pressure, or head shadows, neurons within the superior olivary complex that are sensitive to intensity differences are able to effectively localize the sound source (Bear et al., 2001). Interaural intensity differences are not effective cues

for sound localization of low frequency sounds (< 2000 Hz) because the wavelengths of these sounds are long enough to diffract around the head and do not create a head shadow effect (Bear et al., 2001).

Sound localization also occurs as the result of excitatory and inhibitory neural response patterns within the superior olivary complex. In some areas within the superior olivary complex, ipsilateral information results in an excitatory response pattern while contralateral information results in an inhibitory response pattern (Bellis, 2003; Yost, 2000). In combination, some of these response patterns cancel each other out, thus supplying information regarding sound localization (Yost, 2000). In cases of unilateral stimulation, intensity differences result between ears, which enhance the inhibitory / excitatory response patterns that are responsible for sound localization (Bellis, 2003). The efferent innervation patterns, which originate within the superior olivary complex, are speculated to play a role when listening in background noise. According to studies by Dewson (1996) and Nieder & Nieder (1970), the olivocochlear bundle may activate the outer hair cells to contract and elongate resulting in a dampening or enhancement of the basilar membrane response and thus enhance our ability to hear in background noise (as cited by Chermak & Musiek, 1997).

The next step in the ascending auditory pathway is the lateral lemniscus. Like the superior olivary complex, the lateral lemniscus receives both ipsilateral and contralateral information (Bellis, 2003). The major function of the lateral lemniscus is its role as a primary auditory pathway within the brainstem (Bellis, 2003; Chermak & Musiek, 1997)

The inferior colliculus is the next stage for processing of auditory stimuli in the afferent pathway. Similar to the cochlear nucleus and the superior olivary complex, the inferior colliculus maintains tonotopic organization thus preserving frequency selectivity (Phillips, 2001). The inferior colliculus is also responsible for sound localization, binaural processing, and serves as a pathway for information traveling to the thalamus and cortex (Bellis, 2003). The inferior colliculus assists in sound localization because it is made up of monaural cells that only respond to ipsilateral information and binaural cells that only respond to contralateral information (Yost, 2000). The inferior colliculus processes sound by integrating information from lower brainstem structures (Yost, 2000). The inferior colliculus also contributes to further enhancement of the incoming signal via amplitude modulation, much like that described for the cochlear nucleus (Bellis, 2003). Lastly, the inferior colliculus serves as pathway for relaying information to the thalamus and cortex. The afferent neural information from the inferior colliculus is sent via two ascending pathways: the primary pathway and the diffuse pathway (Bellis, 2003). These two pathways are differentiated in that the primary pathway is tonotopically organized and has very sharp frequency tuning, while the diffuse pathway exhibits little tonotopicity and is broadly tuned (Bellis, 2003). Each of these two pathways is responsible for projecting information for different functions such as coordination of eye, head, and body movements in response to sound stimuli to different areas within the thalamus and cortex (Bellis, 2003).

The thalamus is often referred to as the primary gateway to the auditory cortex (Bellis, 2003). Within the thalamus is the medial geniculate body, or auditory nucleus

of the thalamus. The medial geniculate body is responsible for multimodality integration, in that information arriving from lower brainstem structures is integrated with information arriving from non-auditory areas such as the limbic system (Bellis, 2003). Secondly, the medial geniculate body, like the cochlear nucleus and inferior colliculus, is responsible for further enhancement of amplitude modulation wherein the peaks and troughs are made higher and lower respectively, resulting in the enhancement of components in the signal (Bellis, 2003). Thirdly, it appears that speech stimuli with slowly varying acoustic features, such as /ba/ versus /wa/, which are related to the duration of formant transitions, are coded at the level of the medial geniculate body (King, McGee, Rubel, Nicol, and Kraus, 1995 as cited in Bellis, 2003).

The primary auditory cortex and the auditory association cortex receive information from the level of the thalamus as well as interconnections between the cortices (Bellis, 2003). Like all other levels of the ascending auditory pathway, tonotopic organization is continued within the auditory areas of the cortex (Bellis, 2003). Collectively, the primary auditory cortex and auditory association cortex are responsible for complex processing of both contralateral and ipsilateral auditory stimuli, however, each auditory area is responsible for contributing unique information. Neurons within the primary auditory cortex are responsible for numerous components of signal processing, such as coding for stimulus intensity, frequency, timing, and binaural listening (Bellis, 2003).

The primary auditory cortex codes stimulus intensity via three mechanisms: preferential responses, firing rate increases, and place or amplitopic coding (Bellis,

2003). Preferential responses occur in the primary auditory cortex in that cells respond preferentially to specific increases in intensity (Bellis, 2003). Secondly, in response to increases in stimulus intensity, cells within the auditory cortex also increase their firing rates (Bellis, 2003). Lastly, the auditory cortex utilizes "amplitopic" coding for identifying stimulus intensity (Bellis, 2003). For amplitopic coding, cells fire with similar firing rates, however different groups of cells are responsible for firing in response to specific stimulus intensities (Bellis, 2003).

Frequency coding is achieved due to the tonotopic organization that exists within the primary auditory cortex (Bellis, 2003). The primary auditory cortex is organized into iso-frequency bands, all of which contain neurons that have similar characteristic frequencies (Phillips, 2001). Neurons responsible for coding low frequencies are located within the posterior auditory cortex, while neurons responsible for coding high frequencies are located anteriorly (Bellis, 2003). Within these isofrequency bands are also ear-dominance bands (Bellis, 2003). These ear-dominance bands respond to ear-specific information (Bellis, 2003).

Thirdly, the primary auditory cortex is responsible for timing, or temporal coding. Cells within the primary auditory cortex have the ability to fire synchronously with stimulus onset, which yields information regarding voice onset time, place of articulation and spectro-temporal transitions (Bellis, 2003). The final role of the primary auditory cortex is its contribution to binaural listening. Similar to the function of the superior olivary complex, the auditory cortex also makes use of interaural differences in timing and intensity to achieve localization (Phillips, 2001).

Overall, the primary auditory cortex is responsible for the convergence of processed auditory information from lower levels of the central auditory system (Bellis, 2003). The primary auditory cortex further processes this auditory information for the discrimination and extraction of fine acoustic information present in the signal (Bellis, 2003). This auditory information is also used by the primary auditory cortex for further sound localization (Bellis, 2003).

Connected to the primary auditory cortex is the auditory association cortex, or Wernicke's area (Bellis, 2003). The primary function of Wernicke's area is the processing and analyzing of language. More specifically, Wernicke's area is responsible for the recognition, comprehension and formulation of language including the tasks of reading and writing (Bellis, 2003). Damage to Wernicke's area often results in loss of perception of word meaning and speech recognition (Carlson, 1980).

As previously discussed, patients with both Meniere's disease and migraine-associated dizziness often present with vestibular-related symptoms. For this reason, a brief review of the anatomy and physiology of the peripheral and central vestibular system will be presented.

Peripheral Vestibular System: Anatomy

The peripheral vestibular system is comprised of an outer osseous labyrinth shell, which is filled with perilymph fluid and includes the 3 semicircular canals and the vestibule (Wright & Schwade, 2000). Suspended within this osseous shell is the membraneous labyrinth, which is filled with endolymph fluid and houses the 5 sensory organs: the 3 semicircular canals and the 2 otolith organs, the utricle and the saccule (Hain, Ramaswamy, & Hillman, 2000). Located within these 5 sensory

organs are specialized sensory receptors. The sensory receptor for the semicircular canals is known as the crista ampularis, while the sensory receptor for the otolith organs is known as the macula (Goebel, 2001). The right and left vestibular labyrinths are mirror images of each other and the sensory receptors within each work together as pairs (Goebel, 2001). For example, when stimulation occurs, the brain compares the input from the right peripheral vestibular system to the input from the left peripheral vestibular system (Goebel, 2001). Further detail of this comparison will be discussed in the physiology section below.

The three semicircular canals are each named according to their position in space: the lateral or horizontal semicircular canal, the anterior semicircular canal, and the posterior semicircular canal (Goebel, 2001; Wright & Schwade, 2000). In humans, the lateral, or horizontal, semicircular canal lies at an approximately 30-degree angle relative to the eyes (Honrubia & Hoffman, 1997). Together, the three semicircular canals are orientated in orthogonal planes, meaning they lie at right angles to one another (Bear et al., 2001; Goebel, 2001; Wright & Schwade, 2000). As shown in figure 8, each semicircular canal originates at the utricle and compromises approximately 2/3 of a circle before terminating at a dilated or ampulated end (Anniko & Takumida, 2001; Honrubia & Hoffman, 1997; Shepard & Telian, 1996). The anterior and posterior semicircular canals share a common crus before terminating at separate ampullae which results in 5 semicircular canal openings into the utricle (Wright & Schwade, 2000). The sensory receptor organs for the semicircular ducts are located within the ampulated end of each semicircular canal (Wright & Schwade, 2000).

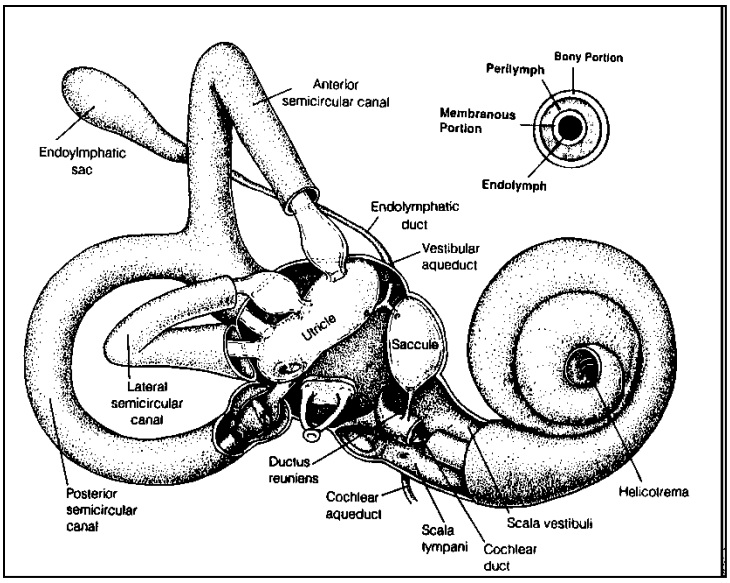

Figure 8. The peripheral vestibular sensory organs including the three semicircular canals and the utricle and saccule from Hain et al., 2000.

The otolithic organs, the utricle and saccule, are located within the vestibule of the vestibular system (Merchant, 1999). As shown in figure 8, the utricle and saccule are aligned such that the utricle lies posterior to the saccule (Wright & Schwade, 2000). While these two organs come into contact, they have no communication with one another (Honrubia & Goodhill, 1979). Because the semicircular canals originate at the utricle, the utricle communicates via 5 openings with the semicircular canals (Honrubia & Goodhill, 1979). The saccule, in contrast, communicates with the cochlear duct via the ductus reunions and with the endolymphatic duct via the saccular duct (Honrubia & Goodhill, 1979). The sensory receptor organ within the utricle is located on the superior portion of the utricular wall and is horizontally oriented (Wright & Schwade, 2000). In contrast, the sensory

receptor organ within the saccule is located along its bony wall and is vertically oriented (Wright & Schwade, 2000).

The crista ampularis and the macula are the primary sensory receptors of balance and are located within the ampulated end of the semicircular canals and within the otolith organs, respectively (Herdman & Tusa, 1999; Merchant, 1999). There are approximately a total of 23,000 hair cells in the three cristae and 4,000 hair cells in the two maculae (Honrubia & Hoffman, 1997). Within these sensory receptor organs are two types of hair cells: Type I and Type II hair cells. These hair cells are similar to the hair cells found within the cochlear. However, differences do exist between these two types of vestibular hair cells. Specifically, they differ in terms of their physical characteristics as well as their afferent and efferent innervation patterns. Type I hair cells are flask shaped and are surrounded by a single, large chalice-like terminal known as a calyx, which envelopes the base of the hair cell (Honrubia & Hoffman, 1997; Merchant, 1999). This calyx can envelope up to as many as five type I hair cells (Highstein, 1996). Type II hair cells, in contrast, are cylindrical in shape and have a cluster of nerve endings at the base of the hair cell (Hamid, 1993; Merchant, 1999; Wright & Schwade, 2000). Type I hair cells send direct afferent vestibular nerve information to the CNS via the chalice-like terminal located at the base of the hair cell, while Type II hair cells send afferent information to the CNS via the cluster of nerve endings located at the base of the hair cell (Wright & Schwade, 2000). The calyx of the type I hair cells makes an afferent connection with one VIII nerve fiber, while up to 30 to 40 type II hair cells make afferent connections with one much finer VIII nerve fiber (Highstein, 1996). The efferent innervation pattern for

these two types of hair cells is quite different. Type I hair cells receive indirect efferent innervation via the afferent nerve located below the cell body; whereas the Type II hair cells receive direct efferent innervation to the base of the hair cell (Anniko & Takumida, 2001; Merchant, 1999; Wright & Schwade, 2000).

Both the Type I and Type II vestibular hair cells have bundles of cilia located at the top of the cells, which are held in place by a cuticular place (Honrubia & Hoffman, 1997; Merchant, 1999). Vestibular hair cells have two types of cilia: stereocilia and kinocilia (Wright & Schwade, 2000). The stereocilia are arranged in a stairstep fashion in that they are aligned from shortest to tallest, with the tallest apical projection being the kinocilium (Wright & Schwade, 2000). The stereocilia of each of the hair cells extends within the endolymph fluid of the membraneous labyrinth, while the remaining portions are surrounded by perilymph fluid (Barber & Stockwell, 1980).

The crista ampularis of the semicircular canals is comprised of blood vessels, nerve fibers, and supporting tissues with a collection, or mound, of hair cells sitting on top, as shown in figure 9 (Goebel, 2001). Overlying the crista ampullaris is a gelatinous plug known as the cupula (Goebel, 2001; Herdman & Tusa, 1999). The cupula is made up of a highly specialized gelatinous substance, which gives it elasticity (Anniko & Takumida, 2001). The cupula's greatest compliance occurs at its center where it is thinner (Anniko & Takumida, 2001; Highstein, 1996). The cupula serves as a tight covering, or divider, which covers the crista ampularis and separates the endolymph fluid between the semicircular duct and the crista ampularis (Goebel, 2001; Hamid, 1993). The cupula also closes off the opening from the semicircular

canal into the utricle (Wright & Schwade, 2000). Embedded within the cupula are the tall stereocilia from hair cells of the crista ampularis, (Anniko & Takumida, 2001).

The distribution of type I and type II hair cells within the crista is such that type I hair cells are predominantly located within the central area of the crista, while type II hair cells are located more peripherally (Highstein, 1996). The alignment of hair cells within all 3 ampullae is in the same direction, however the orientation of hair cells within each ampulla differs (Honrubia & Hoffman, 1997). Hair cells within each ampulla are aligned such that they are parallel to their axis (Highstein, 1996). Hair cells in the horizontal canals are oriented or polarized so that their kinocilia, the tallest of the stereocilia, face the utricle, while hair cells within the anterior and posterior canals are oriented so their kinocilia face away from the utricle (Highstein, 1996; Honrubia & Hoffman, 1997; Wright & Schwade, 2000). Because the hair cells within these semicircular canals are oriented in different patterns, depolarization of these hair cells is dependent upon the direction of endolymph fluid movement.

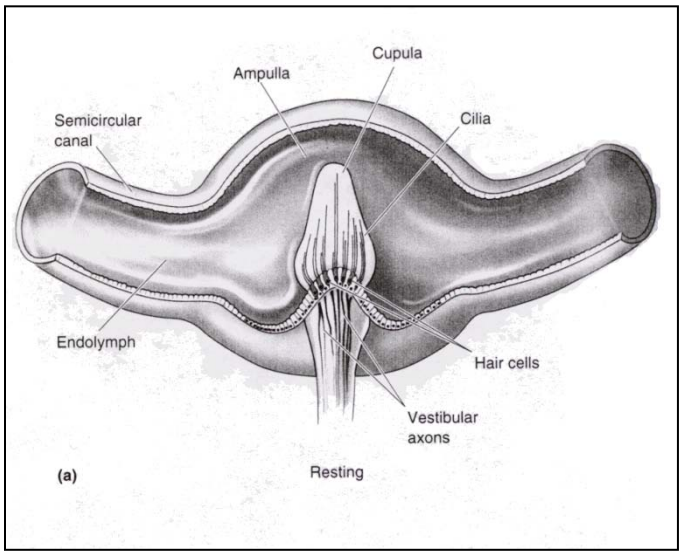

Figure 9. Crista ampularis of the semicircular canal, which contains the hair cells, stereocilia and cupula from Bear, Connors & Paradiso, 2001.

The macula of the utricle and saccule is comprised of a mound of hair cells with an overlying gelatinous covering known as the otolithic membrane, as shown in figure 10 (Bear et al., 2001). In both the utricle and the saccule, hair cells from the macula extend upward and are embedded within the otolithic membrane (Goebel, 2001). Unique to the otolithic organs is the presence of otoconia, or calcium carbonate crystals, which are embedded within and cover the otolithic membrane (Bear et al., 2001; Shepard & Telian, 1996). The density of these otoconia is more than twice that of water, which results in an increase in the density of the otolithic membrane in comparison to the surrounding endolymph fluid (Honrubia & Goodhill, 1979; Honrubia & Hoffman, 1997). Because of this density difference, the otolith organs play an important role in detecting linear acceleration information and static

tilt (gravitational pull) related to head and body movement. The role of both the utricle and saccule in detecting these head movements will be discussed further in the physiology section of this review.

In the macula, the distribution and orientation of hair cells varies systematically (Bear et al., 2001). Both the distribution and orientation of hair cells within the macula is affected by the curved, bowl-shaped center, or central area, of the macula known as the striolar region (Anniko & Takumida, 2001; Honrubia & Hoffman, 1997). A greater proportion of Type I hair cells are found within this striolar region in comparison to the more peripheral sensory receptor areas (Anniko & Takumida, 2001; Honrubia & Goodhill, 1979). In addition, the orientation and polarization of hair cells in the saccule and utricle is different within this striolar region. In the saccule, the kinocilia of the hair cells is directed, or polarized, away from the striolar region, whereas in the utricle, the kinocilia of the hair cells is directed and polarized toward the striolar region (Highstein, 1996).

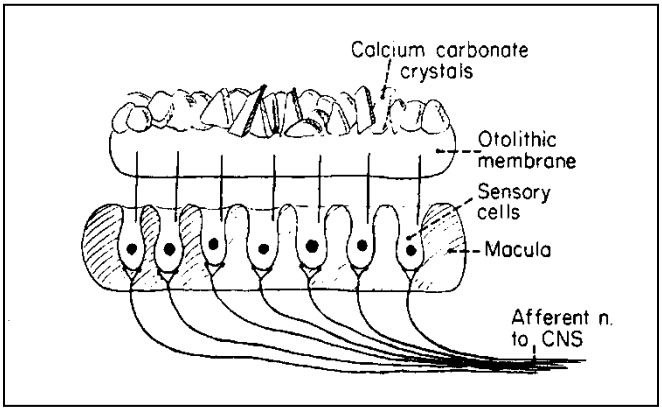

Figure 10. Macula of the otolith organs which contains the hair, or sensory cells, the otolithic membrane and the otoconia, or calcium carbonate crystals from Goebel, 2001.

Peripheral Vestibular System: Physiology

The primary function of the peripheral vestibular system is to transform mechanical movements of the head and body into electrical, or neural, responses for the brain to decode. The vestibular system supplies information regarding head and body movement, balance and equilibrium for the CNS, which then triggers appropriate reflexive eye and body movements (Bear et al., 2001). The semicircular canals and otolith organs are responsible for this mechano-electrical transduction process and each provides unique information regarding the position of the body and head in space. The otolith organs provide information regarding static tilt and linear acceleration, while the semicircular canals provide information regarding velocity and angular acceleration.

The otoconia, or calcium carbonate crystals, found within the otolith organs are responsible in part for our body's sensitivity to static tilt and linear acceleration. As reviewed previously, the density of otoconia is greater than that of its surrounding endolymph fluid. Because of this density difference, the otoconia, which completely cover the surface of the macula, produce a weight upon the underlying hair cells in response to gravitational forces and linear acceleration (Honrubia & Hoffman, 1997). During either linear acceleration or changes in head angle, the weight of the otoconia cause the otolithic membrane to undergo shifts on the surface of the macula, resulting in the deflection of the underlying hair cells (Bear et al., 2001; Honrubia & Hoffman, 1997; Wright & Schwade, 2000). Because force is equal to mass times acceleration, the large mass of the macula in combination with any given acceleration produces enough force to shear, or bend, the vestibular hair cells (Hain et al., 2000).

The otolith organ's sensitivity to linear acceleration is also affected by the position of the macula within each utricle and saccule. The macula is orientated horizontally in the utricle, roughly parallel to the lateral semicircular canals, while the macula within the saccule is oriented vertically (Barber & Stockwell, 1980). This anatomic configuration makes the saccule more sensitive to linear accelerations in the occipitocaudal axis and to anterior-posterior movement (Hain et al., 2000; Highstein, 1996). In contrast, the utricle is more sensitive to lateral accelerations in the interaural axis, anterior-posterior motion, and head tilt (Hain et al., 2000; Highstein, 1996). The macula found within each of these otolith organs is maximally sensitive to movement within its own plane of space (Barber & Stockwell, 1980). For example, both the utricle and the saccule play a role in detecting gravitational pull due to the presence of otoconia on both maculae. However, because the gravitational field is a type of linear acceleration, more force is exerted upon the horizontal utricle, while less force is exerted upon the vertical saccule (Hain et al., 2000).

In order to correctly identify head movement, the CNS compares information from all 5 sense organs. Information from both the utricle and the saccule are often compared to determine head position. The otolith organs are paired bilaterally in a push-pull configuration (Highstein, 1996). Two types of pairing configurations exist within the otolithic organs: contralateral and ipsilateral. With contralateral pairing, the right and left utricular maculae act as a pair as they lie in approximately the horizontal plane together, and similarly the right and left saccular maculae act as a pair in that they lie in the vertical plane together (Shepard & Telian, 1996). Because the vestibular systems on each side of the head are mirror images of one another, any

particular movement results in an equal and opposite response from its contralateral partner (Bear et al., 2001; Rubin & Brookler, 1991). Therefore, for any given head movement, one macula is sending an excitatory signal to the CNS, while its contralateral partner is sending an inhibitory signal (Highstein, 1996).

With ipsilateral pairing, this push-pull configuration occurs within each macula due to the difference in polarization patterns of hair cells within individual maculae (Hain et al., 2000). The polarization and orientation of hair cells within the striolar region of the macula differs in comparison to more peripherally located hair cells. Hair cells in the saccular macula are directed and polarized away from the striolar region, while hair cells in the utriclar macula are directed and polarized toward the striolar region (Highstein, 1996). This variability in the hair cell's polarization makes the macula sensitive to multiple directions and results in the stimulation of different configurations of macular hair cells with different head movements (Honrubia & Hoffman, 1997). Therefore, during any particular head movement, some hair cells are excited, some hair cells are inhibited, and others are unaffected within the same macula (Barber & Stockwell, 1980).

While the otolith organs detect information regarding linear acceleration and static tilt, the semicircular canals are responsible for detecting information regarding angular acceleration (Hain et al., 2000). Angular acceleration includes side-to-side head movement and head rotation (Bear et al., 2001). Detection of angular acceleration occurs as the result of displaced endolymph fluid within the semicircular canals. During periods of little or no head movement, there is an equal amount of pressure on either side of the cupula located within each semicircular canal (Barber &

Stockwell, 1980). As the head turns either side-to-side or front-to-back, endolymph within the semicircular canals is displaced in the opposite direction of head movement. For example, as the head is turned rightward, the semicircular canals move rightward and the endolymph fluid initially remains stationary (Highstein, 1996). Next, inertia generates a lag in fluid movement, which results in a leftward endolymph movement and subsequent pressure being exerted upon the cupula (Bear et al., 2001; Goebel, 2001). This difference in pressure on either side of the cupula causes the elastic cupula to bend (Barber & Stockwell, 1980; Bear et al., 2001; Highstein, 1996). Because cilia from the hair cells are embedded within the cupula, pressure changes of the cupula deflect the cilia, which cause either excitation or inhibition of the hair cells (Bear et al., 2001; Hain et al., 2000). It is the direction of endolymph movement that dictates whether excitation or inhibition of the hair cells takes place (Bear et al., 2001).

In the late 1800s, Ewald performed a series of experiments and is responsible for discovering the implications of the direction of endolymph flow (Honrubia & Hoffman, 1997). These experiments consisted of applying both positive and negative pressure within the semicircular canals of pigeons resulting in both ampullopetal and ampullofugal endolymph flow (Honrubia & Hoffman, 1997). Ampullepetal endolymph flow occurs when endolymph fluid is displaced toward the ampulla, while ampullofugal endolymph flow, in contrast, occurs when endolymph fluid is displaced away from the ampulla (Hain et al., 2000; Hamid, 1993). From these experiments stemmed 3 primary findings known as Ewald's laws of canal function. First, it was found that both eye and head movements occur within the same plane as both the

canal being stimulated and the direction of endolymph flow (Honrubia & Hoffman, 1997). Second, Ewald discovered that in the horizontal canal, ampullopetal endolymph flow resulted in greater neural excitation than did ampullofugal endolymph flow (Honrubia & Hoffman, 1997). Thirdly, it was discovered that just the opposite occurred within the anterior and posterior canals in that ampullofugal flow resulted in greater neural excitation and ampullopetal flow resulted in neural inhibition (Honrubia & Hoffmand, 1997).

Excitation of vestibular hair cells in the horizontal semicircular canal takes place when endolymph fluid is displaced toward the ampulla, known as ampullopetal endolymph flow (Hain et al., 2000; Hamid, 1993). In contrast, inhibition of the hair cells in the horizontal semicircular canals occurs when the endolymph fluid is displaced away from the ampulla, or in an ampullofugal direction (Hain et al., 2000; Hamid, 1993). For the anterior and posterior semicircular canals, direction of endolymph flow for excitation is the exact opposite. Ampullopetal endolymph flow results in inhibition of the hair cells, while ampullofugal endolymph flow results in their excitation (Goebel, 2001; Honrubia & Hoffman, 1997). This mismatch in excitation patterns is a result of the differences in hair cell orientation within each semicircular canal. Due to this mismatch in excitation patterns, when one canal is inhibiting another canal is undergoing depolarization, resulting in at least 2 canals coding any given head movement (Goebel, 2001).

Typically, it is the ear leading the head turn that sends an excitatory response to the CNS, while the trailing ear sends an inhibitory response. For example, with a right head turn, the right semicircular canal undergoes excitation, while the left

semicircular canal undergoes inhibition (Goebel, 2001). The CNS determines the direction of angular acceleration by comparing differences in inhibition versus excitation between each of the 3 semicircular canals, as well as by comparing differences between the right and left peripheral vestibular systems. Comparisons between the right and left peripheral vestibular systems are possible because each semicircular canal is paired with another semicircular canal on the contralateral side within the same plane of space (Bear et al., 2001; Herdman & Tusa, 1999).

The two lateral or horizontal semicircular canals are paired together, while the right anterior semicircular canal is paired with the left posterior semicircular canal and the left anterior semicircular canal is paired with the right posterior semicircular canal as shown in figure 11 (Herdman & Tusa, 1999). This configuration is known as a push-pull arrangement similar to that described for the otolith organs (Hain et al., 2000). During any particular head movement, the cupula in each pair is displaced in opposite directions resulting in the excitation of one semicircular canal and the inhibition of its contralateral partner (Hain et al., 2000; Herdman & Tusa, 1999). This configuration allows the three sets of semicircular canals to sense head movement within their respective planes, and therefore collectively head rotations in all directions can be detected (Bear et al., 2001). Specifically, the horizontal semicircular canals are responsible for detecting left and right head movement, the right anterior and left posterior semicircular canals are responsible for detecting right forward and left backward head movement, and the left anterior and right posterior are then responsible for detecting left forward and right backward head movement (Herdman & Tusa, 1999). Because the canals are depolarized in response to only

movement within their plane of space, the CNS can easily determine the direction of head movement (Barber & Stockwell, 1980).

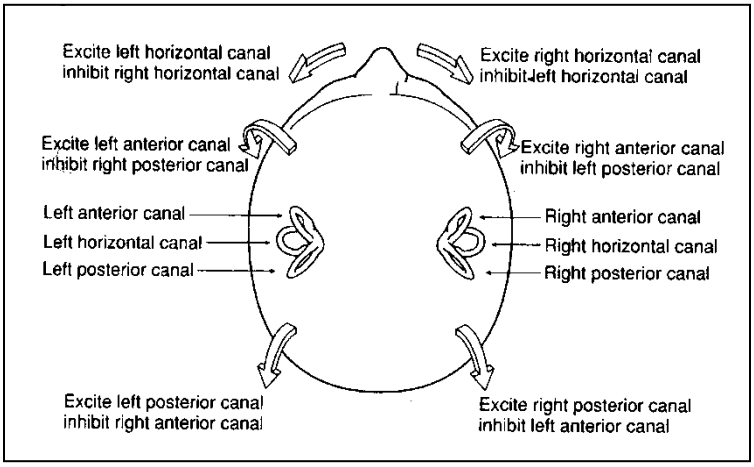

Figure 11. Semicircular canal pairs from Herdman & Tusa, 1999. During head movements the semicircular canals are paired as follows: the right and left horizontal semicircular canals; the right anterior and left posterior semicircular canals; and the right posterior and left anterior semicircular canals.

There are 3 main advantages to this push-pull configuration. First, this push-pull arrangement results in sensory redundancy, which provides protection if disease should affect one of the peripheral vestibular systems (Hain et al., 2000). Second, this pairing allows the CNS to ignore common-mode noise such as changes in neural firing bilaterally due to changes in body temperature or body chemistry (Hain et al., 2000). Third, this pairing of the semicircular canals aids in compensation when

sensory overload occurs, and thus increases the dynamic range of the system (Hain et al., 2000).

Neural Activation of Vestibular Hair Cells

Excitation and inhibition of vestibular hair cells occurs much like the excitation and inhibition of auditory hair cells. The primary difference between activation of these two types of hair cells is the mode of activation. With auditory hair cells, hair cells are activated in response to endolymph fluid pressure changes and depolarization occurs when hair cells are displaced toward the modiolus. With vestibular hair cells however, hair cells are activated in response to forces parallel to the tops of the hair cells, i.e. shifts in otoconia within the utricle and saccule as well as changes in endolymph fluid pressure exerted on the cupula within the semicircular canals (Honrubia & Hoffman, 1997). Within both otolithic organs as well as all 3 semicircular canals, depolarization occurs when the hair cells are deflected toward the kinocilium, with the direction of hair cell polarization varying depending upon its location (Highstein, 1996). Vestibular hair cells then undergo a similar depolarization process as compared to auditory hair cells, which leads to the firing of an action potential as outlined previously (Highstein, 1996).

Hyperpolarization, or inhibition, of vestibular hair cells occurs when the stereocilia are deflected away from the kinocilium (Highstein, 1996). During hyperpolarization, neurotranmitter release decreases resulting in a decrease of neural firing (Goebel, 2001; Highstein, 1996). The CNS decodes this hyperpolarization phase as no head movement.

While the initiation of head movement results in the increasing and decreasing of vestibular neural excitation and inhibition, it should be noted that a small amount of spontaneous neural activity occurs when no head movement is taking place. Hoagland made this discovery in the 1930s, by observing that organs within fish generated some amount of spontaneous activity (Honrubia & Hoffman, 1997). This finding has since been confirmed in other sensory systems including the vestibular system in that some neural activity occurs during periods when sensory cells are at rest (Honrubia & Hoffman, 1997; Wright & Schwade, 2000). At their resting state, a human vestibular hair cell's average spontaneous firing rate is at approximately 75 impulses per second (Barber & Stockwell, 1980). This spontaneous rate increases during depolarization to approximately 400 – 450 impulses per second and then decreases during hyperpolarization (Cohen & Gizzi, 2003).

Differences between the discharge patterns of Type I and Type II hair cells also exist. With Type I hair cells, the discharge patterns are irregular, while Type II hair cells discharge with more regularity (Cohen & Gizzi, 2003). The significance of these discharge differences lies in their function. The irregular discharging Type I hair cells, which are primarily located within the striolar region of the macula and the central portion of the crista, discharge in bursts and pulses, which initiate compensatory head movements upon stimulation (Cohen & Gizzi, 2003). The regular discharging Type II hair cells, which are located peripherally in both the macula and crista, are responsible for contributing to eye movement elicited during the vestibulo-ocular reflex (VOR) (Cohen & Gizzi, 2003).

Central Vestibular System: Anatomy

The peripheral vestibular system is innervated by the vestibular portion of the eighth cranial nerve, which is made up of bipolar ganglion cells located within Scarpa's ganglion (Honrubia & Goodhill, 1979). The vestibular portion of the eighth cranial nerve is comprised of approximately 20,000 vestibular nerve axons and is located within the internal auditory canal (Bear et al., 2001). It is separated into the superior division of the vestibulocochlear nerve and the inferior division of the vestibulocochlear nerve (Hamid, 1993). The superior division is responsible for innervation of the lateral and superior semicircular canals, the utricular macula, and the anterior superior portion of the saccular macula (Goebel, 2001; Hamid, 1993). The inferior division, in contrast, is responsible for innervation of the posterior semicircular canal and the main portion of the saccular macula (Goebel, 2001; Hamid, 1993). Like the auditory portion of the VIIIth nerve, these vestibular fibers exit the internal auditory meatus and enter the brainstem at the level of the lower pons (Hain et al., 2000).

Upon entering the brainstem, the vestibular portion of the VIIIth nerve synapses with neurons located in the contralateral and ipsilateral vestibular nucleus as well as the cerebellum (Barber & Stockwell, 1980; Wright & Schwade, 2000). The vestibular nucleus is located in the dorsolateral portion of the brainstem (Wright & Schwade, 2000). It consists of four major nuclei: the superior, inferior (descending), lateral, and medial nuclei, among several other minor nuclei (Goebel, 2001; Wright & Schwade, 2000). These four major nuclei in combination with several minor nuclei are also referred to as the vestibular nuclear complex (Schubert & Minor, 2004). As

fibers from the VIIIth cranial nerve enter the vestibular nuclei, they bifurcate into ascending and descending tracts, which are distributed to these major nuclei in a highly organized fashion (Wright & Schwade, 2000). The superior division of the vestibular branch of the VIIIth nerve makes connections with the superior and medial vestibular nuclei, while the inferior branch makes connections with the medial, lateral, and inferior vestibular nuclei (Schubert & Minor, 2004). In addition, connections between the ipsilateral and contralateral vestibular nuclei are made via commissural fibers, which allow the relay of information between the two sides (Hain et al., 2000).

The vestibular nuclei also receive afferent information from a variety of other structures in addition to the vestibular portion of the VIIIth nerve. For example, the cerebellum makes afferent connections with the vestibular nuclei. Information originates at the level of the fastigial nucleus, exits via the inferior cerebellar peduncle, and projects to the vestibular nuclei (Bhatnagar & Andy, 1995). The cerebellum is second in line to the vestibular branch of the VIIIth nerve for supplying the vestibular nuclei with information (Wright & Schwade, 2000). Afferent projections to the vestibular nuclei are also received from the spinal cord, reticular formation, contralateral vestibular nuclei, and mesencephalic nuclei (Barber & Stockwell, 1980; Brodal, 2004).

From the vestibular nuclei, axons extend to the cerebellum, the spinal cord, oculomotor nerves, and various other locations within the brainstem (Bhatnagar & Andy, 1995). Information from the brain stem enters the cerebellum via one of three peduncles: the inferior, middle, and superior cerebellar (Bhatnagar & Andy, 1995).

Information from the vestibular nuclei and direct connections from the vestibular portion of the VIIIth nerve enter the cerebellum via the inferior cerebellar peduncle (Bhatnagar & Andy, 1995). The medial and inferior vestibular nuclei are the nuclei primarily responsible for relaying information to the cerebellum (Brodal, 2004). Fibers which project from the vestibular nuclei to the cerebellum are referred to as vestibulocerebellar fibers (Brodal, 2004).

The cerebellum is comprised of 3 primary sections: the flocculonodular, the anterior, and the posterior sections (Bhatnagar & Andy, 1995; Brodal, 2004). The flocculonodular lobe is the only section relevant to central vestibular function and is therefore the only section that will be reviewed. The flocculonodular lobe is located on the inferior surface of the cerebellum and consists of the nodulus at the midline, which is connected to the paired flocculi as shown in figure 12 (Bhatnagar & Andy, 1995; Brodal, 2004). Because the flocculonodular lobe primarily receives afferents from the peripheral vestibular system and the vestibular nuclei, it is also referred to as the vestibulocerebellum (Brodal, 2004).

Other structures within the cerebellum, such as the fastigial nucleus and the vermis, also receive incoming vestibular information (Bhatnagar & Andy, 1995). The vermis is a narrow strip located on both sides of the midline within the cerebellum as shown in figure 12, (Brodal, 2004). The fastigial nucleus is one of four main nuclei within the cerebellum (Brodal, 2004).

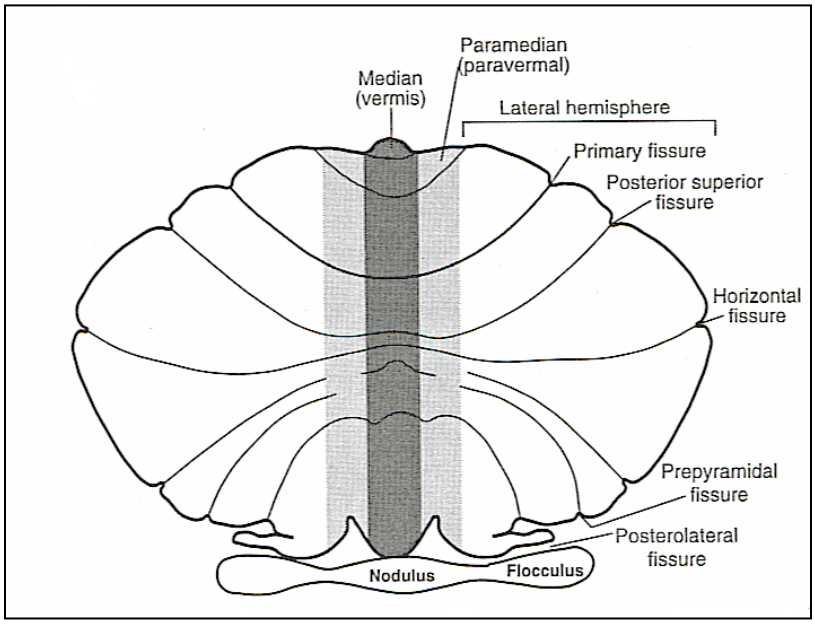

Figure 12. Schematic of the cerebellum including the vermis and the flocculonodular lobe consisting of the nodulus and paired flocculi, from Bhatnagar & Andy, 1995.

The reticular formation is located within the central portion of the brainstem (Martin, 1996). Located within the reticular formation is the paramedian pontine reticular formation (PPRF). The PPRF is located lateral to the sixth (trochlear) nucleus and makes connections with the oculomotor nuclei (Barber & Stockwell, 1980; Brodal, 2004). Within the PPRF is the center for horizontal eye movements (Barber & Stockwell, 1980; Brodal, 2004).

There are three major pathways in which information is relayed from the vestibular nuclei to the spinal cord. These are the lateral vestibulospinal tract, the medial vestibulospinal tract, and the reticulospinal tract (Honrubia & Hoffman, 1997). The lateral vestibulospinal tract originates in the lateral vestibular nuclei on

the ipsilateral side; the medial vestibulospinal tract originates in the medial, superior, and inferior vestibular nuclei on the contralateral side; and the retriculospinal tract originates in the reticular formation (Hain et al., 2000; Wright & Schwade, 2000). Each of these tracts makes specific connections with structures in the spinal cord.

Information from the vestibular nuclei is also relayed both ipsilaterally and contralaterally to the oculomotor (cranial nerve III), trochlear (cranial nerve IV), and abducens (cranial nerve VI) motor nuclei (Bhatnagar & Andy, 1995; Goebel, 2001; Honrubia & Hoffman, 1997; Scaravilli, 2003). This information is relayed via the ascending tract of Deiters and the medial longitudinal fasciculus (MLF) (Hain et al., 2000). The ascending tract of Deiters relays information from the vestibular nuclei to the abducens nucleus, while the MLF relays information from the vestibular nuclei to the remaining motor nuclei (Hain et al., 2000). The MLF is a large fiber bundle, which lies on the floor of the fourth ventricle and extends from the spinal cord to the midbrain and thalamus (Honrubia & Hoffman, 1997). The superior and medial vestibular nuclei are the primary nuclei responsible for making afferent connections with the MLF (Brodal, 2004). Indirect connections between the vestibular nuclei and the oculomotor nuclei also exist via the reticular formation (Brodal, 2004).

The oculomotor, trochlear, and abducens motor nuclei make connections with and activate the extraocular eye muscles (Goebel, 2001). There are six extraocular muscles, which form 3 complimentary pairs, and are responsible for all eye movements as shown in figure 13 (Barber & Stockwell, 1980; Schubert & Minor, 2004). The six extraocular muscles include the four rectus muscles: the medial, lateral, superior and inferior rectus muscles and the two oblique muscles: the superior

and inferior oblique muscles (Barber & Stockwell, 1980). The three complimentary pairs of extraocular muscles are: (1) the medial rectus and the lateral rectus muscles; (2) the superior rectus and inferior rectus muscles; and (3) the superior and inferior oblique muscles (Barber & Stockwell, 1980; Schubert & Minor, 2004).

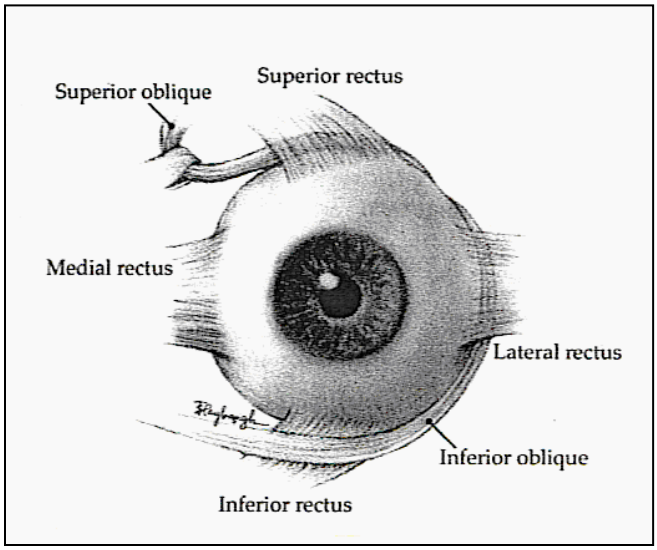

Figure 13. Six extraocular muscles from Schubert & Minor, 2004.

Central Vestibular System: Physiology

The overall purpose of the central vestibular system is that of balance function. Balance function, however, is not exclusively dependent on the vestibular system. With normal functioning vestibular systems, intricate communication between the vestibular, visual and somatosensory systems is responsible for normal balance function (Goebel, 2001). These three systems work together to integrate incoming signals for the interpretation of head and body movement, and then elicit the appropriate motor activities including head, eye, and body movements (Bear et

al., 2001). The central vestibular system's contribution to the maintenance of balance function, as well as its interactions between the visual and somatosensory systems will be reviewed.

While the peripheral vestibular system provides information regarding head movement, the central vestibular system relays this information to the visual and somatosensory systems to initiate two reflexes: the vestibulo-ocular reflex (VOR) and the vestibulo-spinal reflex (VSR) (Hain et al., 2000). These reflexes play a key role in maintaining equilibrium as they are responsible for initiating appropriate compensatory eye movements and somatosensory balance control.

The role of the central vestibular system is initiated at the level of the vestibular branch of the VIIIth nerve. The vestibular branch of the VIIIth nerve is responsible for relaying neural information regarding head and body movement from the maculae and cristae of the peripheral vestibular system to various structures within the central vestibular system. At rest, individual vestibular nerve fibers have resting discharge rates between 70 to 90 spikes per second, which increase up to approximately 400 spikes per second during stimulation (Honrubia & Hoffman, 1997). During ongoing stimulation, this high neural discharge rate is not maintained, but rather slowly reduces to a level of adaptation (Honrubia & Hoffman, 1997). In contrast, when stimulation terminates, this firing rate drops to a level below the spontaneous rate before returning to its original resting, or spontaneous rate (Honrubia & Hoffman, 1997). This information is relayed through the internal auditory canal to various relay stations within the central vestibular system (Hain et al., 2000).

Both the vestibular nucleus and the cerebellum receive afferent information from the vestibular branch of the VIIIth nerve. The vestibular nucleus is responsible for coordinating this incoming afferent information with output motor neurons and interacts closely with both the visual and somatosensory systems (Hain et al., 2000). Individual nuclei within the vestibular nucleus are each responsible for different functions. The superior and medial nuclei are responsible for relaying information which contributes to the vestibulo-ocular reflex (VOR) (Hain et al., 2000). In contrast, the caudal portions of the medial vestibular nuclei, dorsal portions of the lateral vestibular nuclei, and the inferior vestibular nuclei play a key role in coordinating head and eye movements necessary for the vestibulo-spinal reflex (VSR) (Cohen & Gizzi, 2003).

Individual nuclei within the vestibular nucleus are also responsible for receiving information from specific components of the peripheral vestibular system. The otolith organs primarily relay information to the lateral vestibular nuclei, which is the primary nucleus for the VSR (Cohen & Gizzi, 2003; Hain et al., 2000). The anterior semicircular canal primarily relays to the superior vestibular nucleus, while the remaining semicircular canals project to the medial, ventral lateral, and inferior vestibular nuclei (Cohen & Gizzi, 2003).

From the vestibular nuclei, further processing takes place within the cerebellum. Overall, the cerebellum is responsible for regulation of the VOR and the VSR (Wright & Schwade, 2000). More specifically, the cerebellum calibrates the VOR and helps maintain both balance and posture (Schubert & Minor, 2004; Wright & Schwade, 2000). Specifically, fibers from the vestibulocerebellum are responsible

for adjusting the gain, or sensitivity, of the VOR (Brodal, 2004). The cerebellum also plays a role in the initiation of both eye and head movements due to its close interaction with the vestibular nucleus (Wright & Schwade, 2000). In communicating with the vestibular nucleus, the cerebellum exerts both excitatory and inhibitory information, with the majority of information being inhibitory (Wright & Schwade, 2000).

While the cerebellum as a whole plays an important role related to our equilibrium, each component within the cerebellum has a unique function related to balance function. The components of the cerebellum are the nodulus, flocculus, vermis, and fastigial nucleus. The nodulus of the cerebellum is responsible for adjusting the duration of VOR responses (Hain et al., 2000). The flocculus, in contrast, is responsible for adjusting and maintaining the sensitivity, or gain, of the VOR (Hain et al., 2000). The vermis is responsible for making connections with sections of the brainstem, which communicate with the spinal cord (Bear, Connors & Paradiso, 1996). Lesions within the vermis commonly result in gait ataxia with truncal instability (Hain et al., 2000). Lastly, the fastigial nucleus influences posture control as well as controls saccadic accuracy (Brodal, 2004; Goebel, 2001). The fastigial nucleus is also responsible for supplying efferent information to the vestibular nuclei and the reticular formation (Brodal, 2004).

Another structure found within the brainstem, known as the reticular formation, is responsible for connecting the vestibular nuclei with visceral reflex centers. These reflex centers include the nuclei of origin of the vagus nerve, the phrenic nucleus, the salivatory nuclei, and the sympathetic chain ganglia (Wright &

Schwade, 2000). These connections are responsible for vestibular evoked symptoms such as nausea, vomiting, sweating and pallor that are often produced in the presence of vestibular dysfunction (Wright & Schwade, 2000). The reticular formation also integrates information regarding eye position, retinal slippage and the position of the head (Brodal, 2004). The paramedian pontine reticular formation (PPRF), which is located within the reticular formation, is the center for horizontal eye movements and makes afferent connections with the abducent and oculomotor nuclei for coordination of their activity (Brodal, 2004).

There are three primary tracts that are responsible for relaying information from the vestibular nuclei to the spinal cord. The lateral vestibulospinal tract is primarily responsible for postural control through communication with various levels of the spinal cord (Wright & Schwade, 2000). This tract assists in controlling the antigravity muscles of the neck, trunk, and limbs (Wright & Schwade, 2000). The medial vestibulospinal tract is responsible for stabilization of the head during movement as well as in response to gravity through communication with cervical levels of the spinal cord (Wright & Schwade, 2000). Lastly, the reticulospinal tract is responsible for balance reflex motor actions (Hain et al., 2000).

The medial longitudinal fasciculus (MLF) is responsible for connecting the vestibular nuclei to the ocular motor nuclei as well as interconnecting the ocular motor nuclei for coordinated extraocular activity (Brodal, 2004, Hain et al., 2000). Axons from the ocular motor nuclei extend to the extra-ocular muscles and are responsible for initiating their movement (Brodal, 2004; Hain et al., 2000). Each motor nuclei makes specific connections with the extra-ocular muscles. For example,

the abducens nucleus controls the ipsilateral lateral rectus muscles, and the trochlear nucleus controls the contralateral superior oblique muscles (Barber & Stockwell, 1980; Cohen & Gizzi, 2003; Schubert & Minor, 2004). Lastly, the oculomotor nucleus is responsible for activating the remaining extra-ocular muscles which include: the ipsilateral medial rectus, inferior rectus, inferior oblique, and the contralateral superior rectus muscles (Barber & Stockwell, 1980; Cohen & Gizzi, 2003).

Elicited eye movements generally occur in pairs with each pair of eye muscles responsible for its own unique movements. The first pair of eye muscles, the medial rectus and the lateral rectus muscles, lie in the horizontal plane and are responsible for rotating the eyes horizontally (Barber & Stockwell; Schubert & Minor, 2004). The second pair, the superior rectus and inferior rectus muscles, lie in the vertical plane and are responsible for rotating the eyes vertically (Barber & Stockwell, 1980; Schubert & Minor, 2004). The final pair, the superior and inferior oblique muscles, also lie in the vertical plane, and rotate the eyes both torsionally and with a vertical component (Barber & Stockwell, 1980; Schubert & Minor, 2004). Specifically, the superior oblique muscle is responsible for downward torsional rotation of the eyes, while the inferior oblique muscle is responsible for upward rotation of the eyes (Schubert & Minor, 2004). These pairs of eye muscles work together complimentarily. One of the muscles acts as the agonist, which pulls the eye in the direction of movement; while the other muscle acts as the antagonist, which pulls the eye in the opposite direction of movement (Barber & Stockwell, 1980). During any

particular movement, the agonist contracts, while the antagonist simultaneously relaxes (Barber & Stockwell, 1980).

The pathway extending from the peripheral vestibular components up to the extra-ocular muscles is highly organized. These connections are organized such that each semicircular canal and otolith organ is paired with specific pairs of eye muscles (Honrubia & Hoffman, 1997). This pairing produces compensatory, conjugate eye movements in the same plane of canal stimulation (Honrubia & Hoffman, 1997). For example, when head rotation stimulates the left posterior semicircular canal and inhibits the right anterior semicircular canal, the ipsilateral superior oblique and the contralateral inferior rectus muscles are stimulated while the ipsilateral inferior oblique and contralateral superior rectus are inhibited (Honrubia & Hoffman, 1997). This pattern of stimulation results in conjugate eye movements within the same plane of the left posterior canal (Honrubia & Hoffman, 1997). These eye movements generally occur as a reflexive response known as the vestibulo-ocular reflex (VOR), which will be described in further detail below. Specific connections between the semicircular canals and their paired eye muscles are much more understood in comparison to connections between the ototlith organs and the extra-ocular eye muscles (Honrubia & Hoffman, 1997).

Vestibulo-Ocular Reflex (VOR)

The VOR is a reflex responsible for keeping images stationary on the retina in order to maintain clear vision during active head motion (Brodal, 2004; Hain et al., 2000). This reflex functions by sensing movements of the head and then eliciting compensatory eye movements that are conjugate, opposite in direction, and equal in

velocity to the head movement (Bear et al., 2001; Brodal, 2004; Goebel, 1993). The VOR optimally functions from 0.1 to 8 – 10 Hz (Cohen & Gizzi, 2003). Outside of this frequency range, VOR function is poor due to mechanical limitations of the head (Goebel, 1993). The VOR pathway is comprised of the peripheral vestibular labyrinth, the brainstem and the visual system. The VOR is therefore useful in the assessment of vestibular function as it reflects the integrity of these systems (Wright & Schwade, 2000).

The pathway of the VOR is commonly described as a 3-neuron arc as shown in figure 14 (Shepard & Telian, 1996). The 3-neuron arc is comprised of: 1.) afferent fibers originating from the peripheral vestibular system; 2.) neurons from the vestibular nuclei which relay information to the appropriate oculomotor nuclei; and 3.) motor neurons whose axons extend to the extraocular muscles (Brodal, 2004). The main function of the VOR is to sense head rotations, estimate its velocity, and relay this information to the oculomotor nuclei for appropriate reflexive eye movements (Goebel, 1993). These compensatory reflexive eye movements occur in the plane of the stimulated canal and prevent oscillopsia, which is visual blurring in response to head rotation (Goebel, 1993; Shepard & Telian, 1996).

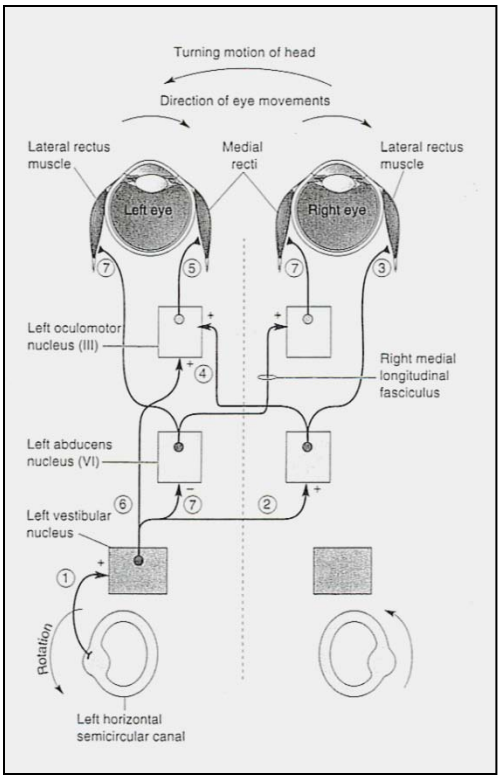

Figure 14. Pathway of the VOR during leftward head movement from Bear, Connors, & Paradiso, 2001.

The VOR is initiated at the level of the peripheral vestibular labyrinth where the sensation of head rotation occurs. In the event of leftward head movement, as shown in figure 14, depolarization of cupular hair cells in the left horizontal semicircular canal and hyperpolarization of cupular hair cells in the right horizontal semicircular canal results. Depolarization of hair cells in the left cupula leads to an increased neural discharge to the ipsilateral vestibular nuclei. Secondary neurons in the vestibular nuclei responsible for initiating compensatory eye movements (i.e. the superior and medial vestibular nuclei) project information regarding this head

movement both ipsilaterally and contralaterally to the appropriate oculomotor nuclei (i.e. cranial nerve nuclei III, IV, or VI) via the MLF (Goebel, 1993). From there, a third neuron connects the appropriate oculomotor nuclei to its paired agonist / antagonist extra-ocular muscle group for the production of compensatory eye movements (Goebel, 1993; Goebel, Isipradit, & Hanson, 2000). For leftward head movement, information is relayed to the abducens and oculomotor nuclei, which are responsible for control of the medial and lateral rectus muscles resulting in compensatory eye movements to the right (Wright & Schwade, 2000). In this instance, the right lateral and left medial rectus muscles are excited and act as the agonist muscle group, while the left lateral and right medial rectus muscles are inhibited and act as the antagonist muscle group (Honrubia & Hoffman, 1997).

For small head rotations, the eyes are able to move in the opposite direction and at the same velocity of head movement with accuracy, thus enabling objects to remain on the same position of the retina (Brodal, 2004). However, for larger head rotations the appropriate direction and velocity of eye movement cannot be maintained in response to head movement (Brodal, 2004). In this instance, the eyes reach their maximum level of excursion and must quickly move in the direction of the head turn to re-fixate on the visual target (Brodal, 2004). This fast component of eye movement in the direction of the head turn is called a saccade (Brodal, 2004). The slow phase eye movement in the opposite direction of head turn is initiated by the vestibular system and is a function of the velocity of the stimulus (Cohen & Gizzi, 2003, Wright & Schwade, 2000). In contrast, the fast, corrective saccade is considered restorative and is controlled by the central vestibular system, specifically

the reticular formation (Cohen & Gizzi, 2003, Wright & Schwade, 2000). A combination of these slow and fast eye phases are known as nystagmus (Cohen & Gizzi, 2003). Nystagmus are often measured in the assessment of the integrity of the VOR and are named according to the direction of the fast component (Shepard & Telian, 1996).

In order for the VOR to function accurately, the velocity of eye movement needs to match the velocity of head movement within 3 degrees per second (Kingma, 2003). This allows the image to move over the retina slowly enough to maintain its integrity (Kingma, 2003). Accurate VOR function enables the visual system to perceive details of the image during head rotation (Kingma, 2003). The sensitivity or accuracy of the VOR is measured as a function of gain (Hain et al., 2000). Gain is calculated as a ratio between eye velocity and head velocity (Schubert & Minor, 2004). A gain of -1 is indicative of eye velocity and head velocity in an equal and opposite direction (Schubert & Minor, 2004). In order to maintain gaze stabilization during all ipsilateral and most contralateral head movements, the function of only one intact labyrinth is necessary (Goebel et al., 2000).

When the accuracy of the VOR decreases to approximately 2 - 5 degrees per second, vision may be obscured (Goebel et al., 2000, Hain et al., 2000). As a result, oscillopsia may be reported (Goebel et al., 2000). Oscillospia is characterized by a bobbing of visual images during head rotation (Goebel, 2001). Impaired VOR function results in decreased gross and fine visual detail during high velocity head movements, such as walking or riding in a car (Goebel, 2001; Goebel et al., 2000).

In the event of impaired VOR function, the vestibulocerebellum serves as a feedback system and aids in readjusting the VOR. The vestibulocerebellum receives information regarding the velocity of head movement when oscillopsia or retinal slippage occurs (Brodal, 2004). The velocity of head movement is then altered (made faster or slower) by adjusting the gain within the cerebellum, thus stabilizing the image (Brodal, 2004).

Ve*stibulo-Spinal Reflex (VSR)*

The central vestibular system is also responsible for initiating the vestibulospinal reflex (VSR). The VSR is responsible for maintaining postural control during standing and stabilization during walking and running (Cohen & Gizzi, 2003). This reflex is comprised of a collection of several reflexes and functions via a feedback circuit between the brainstem and spinal cord (Bhatnagar & Andy, 1995; Hain et al., 2000). Due to the complexity of the VSR and its irrelevance to the present study, this reflex will not be reviewed.

Concluding a review of the peripheral and central auditory and vestibular anatomy and physiology, the pathophysiology of both Meniere's disease and migraine-associated dizziness will now be reviewed. The purpose of trying to differentially diagnose patients as either Meniere's disease or migraine-associated dizziness is due to their differences in pathophysiologic manifestation, which ultimately leads to differences in treatment. For this reason both Meniere's disease and migraine-associated dizziness will be described in terms of symptoms, hypothesized pathophysiology, diagnostic strategies, and current treatment strategies.

Meniere's Disease

Symptoms and Clinical Features

Meniere's disease was first introduced in 1861 by Dr. Prosper Meniere, who described his work in a number of articles in The Medical Journal of Paris (Ghosh et al., 2002; Meniere, 1861 as cited by Paparella & Djalilian, 2002). Classic Meniere's disease is characterized by a triad of symptoms, including vertigo, tinnitus, and fluctuating low frequency sensorineural hearing loss, with the presence of aural fullness in some instances. Two variations of classic Meniere's disease exist: cochlear Meniere's disease and vestibular Meniere's disease. Cochlear Meniere's disease is characterized by the absence of vertigo, while vestibular Meniere's disease is characterized by the absence of cochlear symptoms (i.e. hearing loss and tinnitus) (Arenburg, 1993). Studies indicate however, that in the majority of cases, vestibular Meniere's disease is more closely associated with migraine (Rassekh & Harker, 1992 as cited by Baloh, 1997).

The course of Meniere's disease is variable among patients. Some patients experience mild Meniere's disease with either one attack or several attacks which are generally short in duration and separated by many years which are symptom free. Others, in contrast, experience progressive Meniere's disease with symptoms that increase in severity and eventually result in damage to the intralabyrinthine structures (Gianoli, 2001; Halmagyi, Cremer, & Curthoys, 2003). A Meniere's disease attack typically begins with the onset of unilateral aural fullness, a decrease in hearing sensitivity, tinnitus, and the eventual onset of rotational vertigo (Fetter, 2000). The vertigo that occurs with Meniere's disease generally lasts from approximately 30

minutes to 4 hours and then a sensation of disequilibrium often persists for several days after the acute symptoms abate (Committee on Hearing and Equilibrium, 1995; Gianoli, 2001). Patients often experience nausea accompanied by vomiting during bouts of vertigo and disequilibrium (Arenburg, 1993). At the conclusion of a Meniere's disease attack, normal hearing sensitivity returns, which is accompanied by a reduction in aural fullness and tinnitus (Fetter, 2000; Halmagyi et al., 2003). After numerous Meniere's disease attacks however, these symptoms often become permanent (Fetter, 2000; Halmagyi et al., 2003).

In the early stages of Meniere's disease, patients may exhibit one or two of the four classic symptoms, however as the disease progresses, both the amount of symptoms as well as their severity increases (Gianoli, 2001). When the disease has progressed to a point in which no usable hearing is present in the affected ear and vertigo and tinnitus are no longer experienced, the patient is said it have "burned out" Meniere's disease (Halmagyi et al., 2003). In many cases, once the afflicted ear has reached the "burned out" phase, the contralateral ear becomes involved. Numerous studies have reported that bilateral Meniere's disease subsequently develops in either 30% (Keshner, 2000), 40% (LaRouere, Seidman, & Kartush, 1997), or 50% (Halmagyi et al., 2003) of cases.

The true incidence of Meneire's disease is unknown (Costa, Sousa, & Piza, 2002; Kayan & Hood, 1984). According to recent criteria, Meniere's disease is believed to be a rare condition (Kayan & Hood, 1974). Limited information regarding the true incidence of Meniere's disease is thought to be the result of inconsistencies in both diagnosis and presentation of the disease (Costa et al., 2002)

Pathophysiology

The Committee on Hearing and Equilibrium (1995) define Meniere's disease as "an idiopathic syndrome of endolymphatic hydrops." Endolymphatic hydrops is described as the progressive retention of endolymph fluid in the endolymphatic space (Gianoli, 2001). Because endolymphatic hydrops can only be definitively diagnosed histopathologically, it is functionally defined as the presence of episodic vertigo, hearing loss, aural fullness, and tinnitus (Committee on Hearing and Equilibrium, 1995).

The underlying pathophysiology of Meniere's disease is currently unknown. There appears to be agreement in the literature that Meniere's disease can be attributed to the progressive retention of endolymph fluid within the endolymphatic space (Gibson & Arenburg, 1997; Schuknecht, 1974). However, controversy exists regarding the underlying etiology which results in this progressive retention of endolymph fluid. Two common theories speculate that the retention of excessive endolymph fluid can be attributed to either: 1.) endolymphatic sac dysfunction; or 2.) an obstruction of the endolymphatic duct (Gibson & Arenburg, 1997; Schuknecht, 1974).

Endolymphatic Sac Dysfunction.

Schuknecht (1974) theorized that Meniere's disease can be attributed to endolymphatic sac dysfunction. As reviewed previously, endolymph fluid is both absorbed and secreted in the endolymphatic sac where it travels via the endolymphatic duct and enters the membraneous labyrinth in the vestibule. Schuknecht (1974) theorized that the endolymphatic duct and sac lose their

reabsorptive function, leading to the slower accumulation of endolymph fluid within the membraneous labyrinth. This accumulation of endolymph fluid results in distention of the endolymphatic space and displacement and distortion of internal structures such as Reissner's membrane, the scala vestibuli, and the saccule (Schuknecht, 1974). Histopathological reports indicate that Reissner's membrane may herniate through the apex and balloon into the vestibule at the basal end (Schuknecht, 1974). Continued distention of the endolymphatic space is speculated to eventually give rise to ruptures of the endolymphatic membrane, resulting in the endolymph fluid spilling into the perilymphatic space (Schuknecht, 1981). As endolymph enters the perilymphatic space, these two fluids mix resulting in a decrease of potassium within the endolymph fluid and an increase in potassium within the perilymph fluid (Thai-Van et al., 2001).

The symptoms of vertigo and fluctuating hearing loss are attributed to the toxic effect of potassium on the sensory structures which are normally bathed in perilymph fluid (Schuknecht, 1974). These symptoms have been speculated to result from one of three hypotheses: 1.) a nutritional or metabolic deficiency in the apical region; 2.) an alteration of motion mechanics in the cochlear duct; or 3.) potassium intoxification (Schuknecht, 1974). Potassium intoxification is attributed to the rupturing of Reissner's membrane as discussed above. Upon rupture, potassium-rich endolymph spills into the scala tympani where it enters the Organ of Corti (Schuknecht, 1974). Low frequency hearing loss is attributed to the toxic effect endolymph has on the sensory structures within the Organ of Corti, while the

sensation of vertigo is attributed to potassium intoxification of the vestibular nerve (Schuknecht, 1974).

Cessation of symptoms is speculated to occur in response to the healing of the membrane rupture (Schuknecht, 1974). Upon healing, the accumulation of endolymph fluid begins again and symptoms are perceived following subsequent membrane ruptures. Schuknecht (1991 as cited by Costa et al., , 2002, Schuknecht, 1991 as cited by LaRouere et al., 1997) summarizes the endolymphatic sac dysfunction hypothesis in 5 steps: 1.) a decrease of endolymph reabsorption attributed to endolymphatic sac dysfunction; 2.) over accumulation of endolymph fluid resulting in endolymphatic hydrops; 3.) membrane rupture resulting in intermingling of endolymph in the perilymphatic space which results in both auditory and vestibular symptoms; 4.) healing of the membrane rupture; and 5.) continued distortion and atrophy.

Controversy exists in the literature regarding this theory because several histopathological reports on patients with Meniere's disease are not consistent with this theory. Specifically, Sperling, Paparella, Yoon, & Zelterman (1993, as cited by Paparella & Djalilian, 2002) report that approximately 2/3 of temporal bones with Meniere's disease were reviewed and indicated no evidence of Reissner's membrane rupture. Costa et al. (2002) suggest that if this theory is true, ruptures in both the cochlear duct and the saccule would need to occur simultaneously in order to account for the concurrent cochlear and vestibular symptoms.

Obstruction of the Endolymphatic Duct.

A second theory regarding the etiology of Meniere's disease was proposed by Gibson and Arenburg (1997). These authors theorize that blockage of the endolymphatic duct by metabolic debris leads to the manifestation of Meniere's disease. This theory is based upon the assumption that the endolymphatic sac operates on both a reabsorptive and a secretory function. It is speculated that the cochlea produces metabolic debris that is responsible for obstructing the endolymphatic duct (Gibson & Arenburg, 1997). Upon obstruction, the endolymphatic sac receives an inadequate amount of endolymph fluid, which initiates the production of a hormone called saccin as well as glycoproteins (Costa et al., 2002; Gibson & Arenburg, 1997). Saccin is responsible for activating the production of endolymph fluid, while glycoproteins attract endolymph fluid (Gibson & Arenburg, 1997). It is speculated that the increased production of endolymph fluid derived from the production of saccin, is responsible for clearing the obstruction (Gibson & Arenburg, 1997). The subsequent symptom of vertigo is attributed to a large flow of endolymph fluid into the endolymphatic sac following the cleared obstruction (Gibson & Arenburg, 1997).

In the early stages of Meniere's disease, the endolymphatic sac and duct are presumed to operate as mentioned above, however in later stages of the disease it is speculated that the system is no longer able to fully repair itself (Gibson & Arenburg, 1997). In this instance, the endolymphatic duct remains blocked, and vertigo is no longer experienced, such as is the case in "burned out" Meniere's patients (Gibson & Arenburg, 1997). The continued production of glycoproteins is believed to be destructive to the endolymphatic sac, while the continued production of saccin

initiates secretion of endolymph fluid (Gibson & Arenburg, 1997). The continued production of endolymph fluid results in persistent endolymphatic hydrops, which has an adverse effect on hearing (Gibson & Arenburg, 1997).

Diagnosis

Currently, the diagnosis of Meniere's disease is not made on the basis of clinical testing outcomes, but rather in response to case history and course of disease. The American Academy of Otolaryngology Head and Neck Surgery diagnostic criteria for Meniere's disease defines four levels of Meniere's disease diagnosis: Certain, Definite, Probable and Possible Meniere's disease (Committee on Hearing and Equilbrium, 1995; Bamiou & Luxon, 2003). All diagnoses are made primarily upon the exclusion of all other causes (Committee on Hearing and Equilbrium, 1995; Bamiou & Luxon, 2003). Table 1 briefly reviews the four levels of Meniere's disease classifications.

Certain Meniere's disease
Definite Meniere's disease plus histopathological confirmation
Definite Meniere's disease
Two or more definitive episodes of vertigo
At least one audiometrically documented occasion of hearing loss
Tinnitus or aural fullness in the suspect ear
Probable Meniere's disease
One definitive episode of vertigo
At least one audiometrically documented occasion of hearing loss
Tinnitus or aural fullness in the suspect ear
Possible Meniere's disease
Episodic vertigo characteristic of Meniere's disease without documentation of hearing loss OR;
Sensorineural hearing loss, fluctuating or fixed, with disequilibrium but without definitive episodes

Table 1. Diagnostic classifications of Meniere's disease from the American Academy of Otolaryngology Head and Neck Surgery Committee on Hearing and Equilibrium (1995).

Classification of Meniere's disease is dependent upon strict criteria of vertiginous spells and documentation of hearing loss. When at least 2 definitive vertiginous spells occur, each greater than 20 minutes in duration, a diagnosis of definitive Meniere's is given (Committee on Hearing and Equilibrium, 1995). Audiometric documentation of hearing loss must be documented in the suspect ear (Committee on Hearing and Equilibrium, 1995). Hearing loss can reportedly take on a number of configurations, such as higher (poorer) thresholds in the lower frequencies and/or higher (poorer) thresholds in the suspect ear in comparison to the non-suspect ear (Committee on Hearing and Equilibrium, 1995). A significant change in hearing sensitivity has been reported as a 10 dB HL change in thresholds at 500, 1k, 2k, and 3k Hz as well as a $\geq$ 15% change in word recognition score (Committee on Hearing and Equilibrium, 1995). Documentation of fluctuations in hearing sensitivity is not needed as fluctuations are not present in all cases of Meniere's disease (Committee on Hearing and Equilibrium, 1995).

Treatment

Treatment of Meniere's disease includes a combination of one or more of the following: dietary changes, pharmacological therapy, surgical therapy (both conservative and ablative), and psychological support. Dietary changes include restriction of salt, water, alcohol, caffeine, and nicotine intake as well as avoidance of stress and an increase in physical exercise (Fetter, 2000; Shepard & Telian, 1996, Thai-Van et al., 2001). Pharmacological therapies include the use of a variety of medications including: benzodiazepines, antiemetic agents, vasodilators, diuretics, calcium antagonists, and aminoglycosides among others (Thai-Van et al., 2001). Each

pharmacological therapy functions uniquely in that each impacts the system differently which may result in varying outcomes such as central vestibular sedation, selective treatment of vertigo, reduction of stress and anxiety, regulation of inner ear fluid equilibrium, and maintenance therapy (Thai-Van et al., 2001). Aminoglycoside treatment, one specific form of pharmacological therapy, involves the injection of gentamicin into the inner ear through the oval or round window to selectively damage the vestibular portion of the inner ear (Thai-Van et al., 2001). This method is known as a chemical labyrinthectomy (Thai-Van et al., 2001). Because the vestibular portion of the inner is more sensitive to this therapy than the cochlear portion, vestibular ablation can be achieved without damaging hearing; however in many cases some amount of hearing is generally damaged (Thai-Van et al., 2001; Mattox, 2000).

Approximately 75% of Meniere's disease patients will respond positively to dietary changes and pharmacological therapy (Mattox, 2000). For the remaining 20-25% of Meniere's disease patients, surgical therapy is the remaining option. Surgical therapy is a last resort in treating Meniere's disease and is only recommended for those patients with persistent, debilitating vertigo (Fetter, 2001; Shepard & Telian, 1996). There are two categories of surgical therapy: nondestructive and radical. Nondestructive surgical therapy aims to eliminate vestibular function while maintaining cochlear function (Thai-Van et al., 2001). It includes endolymphatic sac surgery and tympanostomy tube (Thai-Van et al., 2001). Endolymphatic sac surgery involves placement of a shunt, which drains the endolymphatic sac into either the subarachnoid space or the mastoid cavity thus alleviating excessive endolymph (Thai-Van et al., 2001). A tympanostomy tube is simply a ventilation tube placed in the

tympanic membrane (Thai-Van et al., 2001). While the tympanostomy tube has been found to be an effective treatment, there is no explanation why other than possibly the placebo effect (Thai-Van et al., 2001).

In contrast, radical surgical therapy aims to eliminate vestibular function without necessarily conserving cochlear function. It includes either a labyrinthectomy or a vestibular neurectomy (Thai-Van et al., 2001). Labyrinthectomy involves removing the entire labyrinth including all cochlear structures; therefore both vestibular and hearing functions are eliminated (Arenburg, 1993; Thai-Van et al., 2001). Labyrinthectomy is generally only advised when there is not a viable amount of hearing worth preserving (Arenburg, 1993). Vestibular neurectomy, in contrast, involves sectioning the vestibular portion of the VIIIth nerve, leaving the auditory portion intact (Thai-Van et al., 2001). In doing this, hearing is preserved while the debilitating vertigo is eliminated (Thai-Van et al., 2001). Vestibular neurectomy is currently the most successful surgical procedure with a 90 – 95% success rate (Fetter, 2000). One final form of treatment is psychological therapy. Psychological therapy is often sought for coping with disabling vertigo (Fetter, 2000).

Migraine-associated Dizziness

Symptoms and Clinical Features:

The International Headache Society defines migraine as a “disabling primary headache disorder” characterized by a unilateral throbbing headache in association with nausea and intolerance to light and sound (“Part One”, 2004). Migraine headaches are often accompanied by focal neurological symptoms called auras (Evans & Olesen, 2003). Auras can be experienced either before, concurrently, or

even after a migrainous attack (Evans & Olesen, 2003). Aura symptoms include visual disturbances, numbness, weakness, aphasia, vertigo, and tinnitus among others (Evans & Olesen; "Part One", 2004). Approximately one-fifth of migraine sufferers experience auras with their migraine (Welch, Cutrer & Goadsby, 2003). Visual disturbances are the most common type of aura (Welch et al., 2003).

Specific factors have been found to trigger or aggravate migraine headaches. Stress, anxiety, hypoglycemia, fluctuating estrogen, smoking, lack of sleep and foods such as chocolate, aspartame, aged cheeses, yeast, canned soups, and monosodium glutamate (MSG) have all been reported as possible triggers for migraine (Bruegel, 2003; Tusa, 2000). Factors reported to aggravate migraine include stress, alcohol consumption and other environmental factors such as bright lights, weather changes, and smoking ("Part One", 2004).

Several investigators have reported a close association has been found between migraine headaches and dizziness (e.g., Cutrer & Baloh, 1992; Dieterich & Brandt, 1999; Kayan & Hood, 1984). Kayan and Hood (1984) report vestibulocochlear symptoms in 118 of 200 (59%) unselected migraine patients and in only 35 of 116 (30%) tension headache patients. Of their 200 migraine patients, 78 patients (39%) reported only vestibular symptoms, 31 patients (15.5%) reported both vestibular and cochlear symptoms, while 9 patients (4.5%) reported strictly cochlear symptoms (Kayan & Hood, 1984). Vestibular symptoms associated with migraine can occur as an aura to the migraine headache. These symptoms occur either during the migraine headache or independent of the migraine headache (Cutrer & Baloh, 1992).

Cochlear symptoms have also been reported in cases of migraine headaches. Symptoms such as unilateral sensorineural hearing loss, unilateral aural fullness, and tinnitus have been reported in patients diagnosed with episodic vertigo related to migraine (Dieterich & Brandt, 1999; Thaker, Anjaneyelu, & Deka, 2001). Viirre and Baloh (1996) reported on 13 patients with sudden hearing loss which was associated with both migraine headache and vertigo. The hearing loss in these cases was unilateral and severe to profound in nature. Reploeg and Goebel (2002) reported hearing loss as a symptom in 5 of 81 patients (6%) with migraine-associated dizziness and aural fullness in 8 of the 81 patients (10%). Kayan and Hood (1984) also report phonophobia, or a fear of certain sounds, in 162 out of 200 (81%) migraine patients in comparison to 14 of 116 (12.1%) tension headache patients. Cochlear symptoms associated with migraine are generally less common in comparison to the presence of vestibular symptoms (Baloh, 1997).

The prevalence of migraine-associated dizziness in the general population has been reported between 5.5% and 6.5% (Furman & Whitney, 2000; Thaker et al., 2001). Similar to the characteristics of general migraine, migraine-associated dizziness has been reported more frequently in females when compared to their male counterparts. Reportedly, women are diagnosed with vertigo approximately 5 times more often than men (Furman et al., 2003). Out of 344 patients with vertigo, Thaker et al. (2001) diagnosed 19 patients with vertigo related to migraine (Thaker et al., 2001). In this instance, the incidence of migraine-associated dizziness was greater in females (10.3%) in comparison to males (2%). Cutrer and Baloh (1992) also found a greater incidence of women diagnosed with migraine-associated dizziness in

comparison to men. These authors studied 90 patients with episodic vertigo related to migraine and found that 76.9% were females while the remaining 23.1% were males. Lastly, Dieterich and Brandt (1999) reported a 1.5:1 greater incidence of migraine-related dizziness in females versus males.

The mean onset of vertigo in migraine-associated dizziness has been reported as 37.7 years for women and 42.4 years for men (Dieterich & Brandt, 1999). Similarly, Cutrer and Baloh (1992) report an overall mean onset of vertigo to be 35 years, while Reploeg and Goebel (2002) report a mean onset of vertigo of 36.6 years.

Pathophysiology

The pathophysiology responsible for both the migraine headache as well as dizziness associated with migraine is not completely understood. The pathophysiology for migraine headache is often attributed to either vascular abnormalities or ion channel dysfunction (Baloh, 1997). Vascular abnormalities include vasodilatation of extracranial vessels, which occur simultaneously with migraine headache (Baloh, 1997). In contrast, ion channel dysfunction is often associated with inherited migraine headaches and involves abnormal voltage-gated calcium channels (Baloh, 1997). These abnormal calcium channels result in the over accumulation of extracellular potassium, which initiates a spreading wave of depression (Baloh, 1997).

The pathophysiology underlying migrainous aura is speculated to stem from a spreading depression of neuronal activity (Welchet al., 2003). Studies indicate that cortical blood flow decreases as much as 25 to 30% during these spreading waves of depression (Lauritzen et al. & Olesen et al, as cited by Welch et al., 2003). However,

further studies indicated that this decrease in cortical blood flow has also been found in migraine patients who do not experience auras (Woods et al., as cited by Welch et al., 2003). The temporal relationship between the manifestation of the preceding aura, or a decrease in cortical blood flow, and the subsequent migraine are unknown at this time (Welch et al., 2003).

The pathophysiology underlying both the vestibular and cochlear symptoms, which often accompany migraine headache, are controversial. Five hypotheses exist attempting to explain the presence of these vestibular and cochlear symptoms: 1.) vascular, 2.) metabolic; 3.) ionic channel dysfunction; 4.) neuropeptide release and, 5.) calibration of vestibular inputs (e.g., Baloh, 1997; Thakar, Anjaneyeylu, & Deka, 2001).

Vascular.

Baloh (1997) hypothesizes that vasospasms of the cochlear and vestibular branches of the internal auditory artery are responsible for the vestibular and cochlear symptoms that often accompany migraine headaches. These vasospasms lead to ischaemia, which is speculated to affect the secretion and absorption of both the endolymph and perilymph fluid (Saxena, 1978 as cited by Kuritzky, Toglia, & Thomas, 1981). Parker (1995) speculated that the cochlear and vestibular symptoms seen with migraines arise from a decrease of blood flow throughout the peripheral cochlear and vestibular systems (Parker, 1995)

Metabolic.

Kuritzky et al. (1981) speculated that the cochlear and vestibular symptoms associated with migraine headaches could be attributed to a metabolic cause

involving serotonin. Specifically, these investigators speculated that both the levels of serotonin and their synaptic functions could be altered while an individual is experiencing a migraine, thus leading to vestibular and cochlear symptoms.

Ion channel disorder.

Baloh (1997) speculated that the presence of abnormal voltage-gated calcium channel dysfunction in the inner ear may also be responsible for the migraine headache as well as the vestibular and cochlear symptoms that may accompany this headache. These defective ion channels are thought to result in reversible hair cell depolarization leading to vestibular and cochlear symptoms (Baloh, 1997). This reversible depolarization leads to asymmetries in neural firing, which results in the sensation of vertigo.

Neuropeptide release.

Cutrer and Baloh (1992) hypothesized that the release of neuropeptides is a possible underlying pathophysiology of vestibular symptoms for patients whose symptoms occur independent of the migraine headache or whose vestibular symptoms are not consistent with typical aura characteristics. These investigators believed that the release of neuropeptides increased the excitability of the vestibular sensory system. As a result of this increased excitability, the ipsilateral neural firing rate increases, which create an asymmetry in neural firing. This asymmetry in neural firing is perceived by the brain as vertigo (Cutrer & Baloh, 1992). In contrast, for patients whose vestibular symptoms occur in a time-locked fashion with the symptom of headache, these investigators presume that the pathophysiology underlying the migraine headache and the vestibular symptoms are the same. Specifically, these

symptoms are due to a spreading wave of depression or vasospasm as opposed to the release of neuropeptides (Cutrer & Baloh, 1992).

Calibration of vestibular inputs.

Thakar et al. (2001) proposed that during a migraine attack, the calibration or gain of the VOR becomes altered. This alteration would result in miscommunication of vestibular input from the maculae and cristae of the peripheral vestibular system to the vestibulocerebellum and vestibular nuclei, thus creating symptoms of disorientation, motion intolerance and vertigo (Thakar et al., 2001).

Diagnosis

Migraine headache is diagnosed based on case history and the course of symptoms, similar to that of Meniere's disease. The International Headache Society (IHS) defines 6 primary types of migraine: migraine without aura, migraine with aura, migraine associated with childhood syndromes, retinal migraine, complications of migraine, and probable migraine ("Part One", 2004). As with Meniere's disease, all diagnoses are based upon the exclusion of all other causes (Johnson, 1998). The diagnostic levels for migraine are outlined in Table 2.

1.1 Migraine without aura
1.2 Migraine with aura
1.2.1 Typical aura with migraine headache
1.2.2 Typical aura with non-migraine headache
1.2.3 Typical aura without headache
1.2.4 Familial hemiplegic migraine (FHM)
1.2.5 Sporadic hemiplegic migraine
1.2.6 Basilar-type migraine
1.3 Childhood periodic syndromes that are commonly precursors of migraine
1.3.1 Cyclical vomiting
1.3.2 Abdominal migraine
1.3.3 Benign paroxysmal vertigo of childhood
1.4 Retinal migraine
1.5 Complications of migraine
1.5.1 Chronic migraine
1.5.2 Status migrainosus
1.5.3 Persistent aura without infarction
1.5.4 Migrainous infarction
1.5.5 Migraine-triggered seizure
1.6 Probable migraine
1.6.1 Probable migraine without aura
1.6.2 Probable migraine with aura
1.6.5 Probable chronic migraine

Table 2. Diagnostic classifications of migraine from the International Headache Society, 2004

Oftentimes patients with migraine-associated dizziness do not fall into one of the specific diagnostic classifications listed above. Cutrer and Baloh (1992) report that in 91 patients diagnosed with migraine-associated dizziness, 41 (45.1%) had migraine with aura, 40 (44.0%) had migraine without aura, and 10 (11.0%) had migrainous aura without headache. Similarly, Dieterich and Brandt (1999) studied 90 patients diagnosed with episodic vertigo associated with migraine and found that only 7 (7.8%) patients met the diagnositic criteria of basilar migraine. These patients, however, were given a diagnosis of dizziness related to migraine based upon

management of symptoms with traditional migraine treatment (Dieterich & Brandt, 1999).

Based upon the available research to date, it appears that the majority of patients who experience vertigo associated with their migraine fall into one of 3 main categories of migraine. These are: 1.) migraine without aura; 2.) migraine with aura and; 3.) basilar artery migraine. Each of these will be reviewing below.

Migraine without aura, also referred to as common migraine is diagnosed as at least 5 attacks fulfilling the following criteria: 1.) headache lasting from 4 to 72 hours; 2.) headache with at least 2 of the following characteristics: unilateral, pulsating, moderate or severe pain, and disruption of physical activity; 3.) presence of either nausea and vomiting or photophobia and phonophobia and; 4.) exclusion of all other causes ("Part One", 2004). Migraine without aura is the most common type of migraine ("Part One", 2004).

Migraine with aura, also referred to as classic migraine, is diagnosed as the presence of a focal neurological symptom preceding the headache, with features as described above for migraine without aura ("Part One", 2004). The focal neurological symptom, or aura, generally develops for 5 to 20 minutes before headache onset and lasts up to 60 minutes ("Part One", 2004). The IHS defines aura as exhibiting one of the following features: fully reversible visual, sensory, or dysphasic speech disturbance symptoms in combination with at least two of the following features: homonymous visual and/or unilateral sensory symptoms, a minimum of one aura symptom developing over at least 5 minutes, or aura symptoms lasting between 5 and 60 minutes ("Part One", 2004).

Basilar-type migraine, also referred to as basilar artery migraine or basilar migraine, is diagnosed as at least 2 attacks with the presence of: 1.) at least two fully reversible aura symptoms including dysarthria, vertigo, tinnitus, hypacusia, diplopia, visual symptoms, ataxia, decreased consciousness, and simultaneous bilateral paraesthesias; 2.) at least two of the following features: homonymous visual and/or unilateral sensory symptoms, a minimum of one aura symptom developing over at least 5 minutes, or aura symptoms lasting between 5 and 60 minutes; 3.) headache with features as described above for migraine without aura and; 4.) exclusion of other causes ("Part One", 2004).

The diagnosis of migraine-associated dizziness becomes difficult because duration of the dizziness symptoms are generally atypical of reported criteria for migrainous aura. The IHS classifies typical migrainous aura to occur between 5 and 60 minutes in duration. The duration of vertigo in patients with migraine-associated dizziness, in contrast, has been reported to be between a few seconds to a full day in approximately 50% of patients, and greater than 24 hours in approximately 25 - 31% of patients (Baloh, 1997; Cutrer & Baloh, 1992; Furman et al., 2003).

Treatment

Treatment for migraine headache includes dietary changes, lifestyle changes and the use of pharmacological agents. Dietary changes include avoidance of foods triggering migraine such as aspartame, chocolate, caffeine, and alcohol among others (Diamond & Wenzel, 2002; Johnson, 1998). Patients are recommended to keep a headache diary in order to determine what triggers are responsible for initiating the headache (Diamond & Wenzel, 2002). Lifestyle changes include: 1.) regular exercise

3 to 5 times per week for a minimum of 30 minutes; 2.) reduction of stress, including psychiatric therapy; 3.) avoidance of smoking and; 4.) adequate sleep (Diamond & Wenzel, 2002; Johnson, 1998; Tusa, 2000).

These treatment strategies are often combined with pharmacologic treatment. Pharmacological treatment is recommended in the following instances: 1.) when greater than 4 migraine attacks occur per month over a 3-month period; 2.) when abortive medications are ineffective; 3.) when patients are unable to use abortive medications; and 4.) when migraine attacks are disabling (Diamond & Wenzel, 2002). There are two primary types of pharmacological treatment: acute and preventative (Diamond & Wenzel, 2002).

The purposes of acute or abortive migraine therapy are to: 1.) abort the migraine attack quickly without recurrence; 2.) maintain patient functionality; 3.) avoid use of additional pharmacological therapies; and 4.) avoid disability and adverse effects (Diamond & Wenzel, 2002; Matchar, 2003). Acute migraine treatment is utilized at the onset of a migraine attack (Diamond & Wenzel, 2002). Examples of types of acute migraine therapy include: triptans, dihydroergotamine, ergotamine, phenothiazines, non-steroidal anti-inflammatory drugs (aspirin, ibuprofen, naproxen sodium, etc), lidocaine, isometheptene combinations, opiods, and barbituate hypnotics (Diamond & Wenzel, 2002; Matchar, 2003).

In contrast, preventative medications are administered on a daily basis to prevent the occurrence of a migraine attack (Diamond & Wenzel, 2002). Preventative migraine therapy is administered to reduce the frequency, severity and duration of migraine attacks which will ultimately result in improvement of responsiveness of

abortive agents and maintain functionality in the event of a migraine attack (Diamond & Wenzel, 2002). Preventative migraine therapy is recommended when abortive therapy cannot be utilized due to contraindications such as: overuse, lack of success, cost, or adverse side effects (Diamond & Wenzel, 2002). Examples of preventative migraine therapy include: beta blockers, antiepileptic agents, tricyclic antidepressants, non-steroidal anti-inflammatory drugs, calcium antagonists, methysergide, serotonin reuptake inhibitors, and natural remedies (Diamond & Wenzel, 2002).

The above treatment strategies focus primarily on treatment for migraine headaches. Specific treatment strategies for migraine-associated dizziness are unknown at this time. Traditional treatment for migraine may be effective for patients suffering from migraine related dizziness (Furman et al., 2003). Thaker et al. (2001) reported successful treatment of vertiginous symptoms in patients diagnosed with classical migraine using prophylactic anti-migraine treatment. Likewise, Reploeg and Goebel (2002) reported successfully treating migraine-associated dizziness in approximately 58 of 81 (72%) of their patients with common prophylactic therapy including tricyclic antidepressants (TCA) and beta-blockers.

Symptomatic treatments specific for dizziness associated with migraine include the use of promethazine, dimenhydrinate, meclizine, and metoclopramide (Baloh, 1997). These agents are used to control the dizziness, motion intolerance, nausea, and vomiting associated with the vertiginous episodes of migraine (Baloh, 1997). Prophylactic treatments for the dizziness associated with migraine include beta blockers, calcium-channel blockers, and trycyclic amines (Baloh, 1997). These medications are the same as those used for migraine headaches alone (Baloh, 1997).

An in-depth review of the different types of migraine treatments is outside the scope of this review. A brief review of treatment for Meniere's disease and migraine-associated dizziness was presented to demonstrate the vast difference in treatment options between these two pathophysiologies. Differential diagnosis becomes extremely important when accounting for these different treatment options.

Because treatment options for each of these pathologies is radically different, differential diagnosis is often made pending patient outcome to treatment strategies. Boismer and Disher (2001) treated and followed up on 23 patients who presented with equivocal vertigo. Their first treatment was consistent with Meniere's disease (i.e. low sodium diet, increased water consumption, and a diuretic in some instances). If after several months, the patient's symptoms persisted, they were treated with migraine prophylactic therapy. Of the 23 patients participating in the study, 60.9% reported an improvement in their symptoms with treatment consistent with Meniere's disease, 26.1% reported improvement upon prophylactic migraine treatment and the remaining 13% of patients were reportedly non-compliant with therapy and did not experience alleviation of symptoms (Boismer & Disher, 2001). The investigators concluded that when the diagnosis between Meniere's disease and migraine-associated dizziness becomes unclear, a step-wise approach to treatment may be effective. Further research is needed, however on the effectiveness of this approach for diagnosis of Meniere's.

Meniere's Disease vs Migraine-associated Dizziness: Differential Diagnosis

The differential diagnosis of Meniere's disease and migraine becomes difficult because of their similarities in symptoms, possible pathophysiologic

association, and diagnosis. Symptoms classic of Meniere's disease include the combination of vertigo, unilateral sensorineural hearing loss, aural fullness, and tinnitus. Likewise, migraine can present with a combination of any of the same symptoms. The diagnosis of migraine associated dizziness becomes more obvious when the symptoms are temporally associated with headache. However, oftentimes migrainous vertigo can result independent of a migraine headache. It is in these instances, in which the differential diagnosis of migraine-associated dizziness and Meniere's disease becomes most difficult.

A relationship between Meniere's disease and migraine has been speculated by many investigators to be due to the increased prevalence of migraine in Meniere's disease patients (Parker, 1995; Radtke, et al., 2002). Parker (1995) reported that 29 of 85 (34.1%) patients diagnosed with idiopathic Meniere's disease also evidenced migraine. Likewise, Radtke et al. (2002) found a significant difference in the prevalence of migraine headaches in Meniere's disease patients in comparison to the prevalence of migraines in a normal control group. These investigators found that 44 of 78 (56%) patients with Meniere's disease also had migraine, while only 20 of 78 (25%) controls evidenced migraine headache (Radtke et al., 2002). Lipton et al. (2001) reported the prevalence of migraine in the general population to be approximately 12.6%. The studies by Parker (1995) and Radtke et al. (2002) indicate a larger prevalence of migraine in Meniere's disease when compared to the prevalence of migraine in the general population reported by Lipton et al. (2001). Baloh (1997) suggests that this association can be attributed to the development of hydrops in response to vasospasm from migraine.

Conflicts in the differential diagnosis of these two pathologies have arisen because of the similarity in symptoms that exist between these two pathologies. A variety of clinical test batteries have been experimented with in an attempt to distinguish between these two pathologies, however considerable variation has occurred in the test outcome for both groups. Along with case history, the following clinical assessments have been utilized in diagnosing Meniere's disease and migraine: audiometric testing, electronystagmography (ENG), electrocochleography (ECochG), rotary chair, and posturography. Auditory brainstem response (ABR) testing, CT scan, MRI, and blood tests have also routinely been administered to exclude other pathologies (Gianoli, 2001).

The purpose of the present study was to generate a specific test protocol for assessing the vestibular systems of patients with Meniere's disease and migraine-associated dizziness in order to determine its accuracy in differentially diagnosing these two pathologies. The two tests evaluated in this study were electrocochleography and rotary chair testing. The following is a review of the clinical utility, test description, test protocol, and testing parameters used for electrocochleography and rotary chair testing.

Electrocochleography

Clinical Utility of Electrocochleography

Electrocochleography (ECochG) is an auditory evoked potential used to record cochlear potentials within the inner ear (Wuyts, Van De Heyning, Van Spaendonck, & Molenberghs, 1997). The two primary cochlear potentials measured in ECochG testing are the summating potential (SP) and the whole nerve or

compound action potential (CAP) (Ferraro & Durrant, 2002). These potentials are measured in response to auditory stimuli and assess the integrity of the cochlea and the eighth cranial nerve (Gianoli, 2001; Wilson & Bowker, 2002). In the past, ECochG has been used for a of variety purposes, however, currently ECochG is primarily used as a diagnostic tool for Meniere's disease (Wuyts et al., 1997).

Test Description

During ECochG testing, an active, reference and common electrode are placed on the patient (Wuyts et al., 1997). The active electrode is traditionally placed within close proximity of the cochlea, while the reference electrode is placed on either the ipsilateral or contralateral earlobe or mastoid and the common electrode is placed on the forehead (Gianoli, 2001; Wuyts et al., 1997). Auditory stimulation is then presented to the test ear via a headphone (Wuyts et al., 1997). For optimal testing, the patient should remain relaxed throughout testing (Wuyts et al., 1997).

During ECochG testing, the latencies and amplitudes of the SP and AP are recorded and measured. Because the latencies of these components are generally measured within 5 milliseconds after stimulus onset, ECochG testing is considered an early auditory evoked potential (Ferraro & Durrant, 2002). The measurement of choice with ECochG testing is the SP/AP amplitude ratio (Gianoli, 2001). Comparison of the SP and AP amplitude has gained clinical significance as ears with Meniere's disease have been found to be characterized by enlarged SP amplitudes (Ferraro & Durrant, 2002). Further explanation of this comparison will be described later in this section of the review.

Test Protocol

ECochG testing protocols can vary due to the numerous variables involved. Variables involved in ECochG testing include: electrode placement, stimulus type, stimulus intensity, stimulus polarity, stimulus rate, filter settings, number of sweeps, and time window. A brief review of each of these testing variables will be presented.

Two approaches to electrode placement are currently utilized in ECochG testing: transtympanic and extratympanic electrode placement (Ferraro & Durrant, 2002). With transtympanic electrode placement, a needle electrode is inserted through the tympanic membrane and is placed on the promontory of the cochlea (Margolis, Rieks, Fournier, & Levine, 1995). With extratympanic electrode placement, in contrast, the electrode is placed on either the tympanic membrane itself or on the canal wall (Ferraro & Durrant, 2002). The greatest difference in the ECochG response that occurs as a function of electrode placement is the amplitude of the response generated. The closer the electrode is placed in reference to the cochlea, the greater the response amplitude (Margolis et al., 1995). Margolis et al. (1995), reported response amplitudes with transtympanic electrode placement to be approximately 5 to 10 times greater in comparison to extratympanic electrode placement. While transtympanic electrode placement produces larger responses, limitations to the patient such as pain when the tympanic membrane is penetrated and physician assistance for electrode placement have resulted in increased popularity of extratympanic electrode placement (Ferraro & Durrant, 2002).

Wuyts et al. (1997) reported that the two most common stimuli used with ECochG testing are broadband clicks and toneburst stimuli. Broadband click stimuli

are frequently used since click stimuli contain energy across a broad range of frequencies and therefore stimulate a wide range of cochlear hair cells resulting in a more synchronous response (Ferraro & Durrant, 2002). In contrast, tone burst stimuli allow the examiner to assess potentials in frequency specific areas of the cochlea (Ferraro & Durrant, 2002; Wyuts et al., 1997). Because tone burst stimuli are longer in duration, with a 2-5 ms ramp and a 4-12 ms plateau, in comparison to the typical 100 microsecond duration of click stimuli, tone burst stimuli generate a more discernable SP (Ferraro & Durrant, 2002; Wyuts et al., 1997).

High stimulus intensities are generally used for ECochG testing because the SP is only generated in response to high intensity levels (Wuyts et al., 1997). Most ECochG protocols generally employ stimulus intensities of approximately 90 dBnHL for both tone burst and click stimuli (Devaiah, Dawson, Ferraro, & Ator, 2003; Ferraro & Tibbils, 1999; Margolis et al., 1995; Sass, 1998; Wilson & Bowker, 2002; Wuyts et al., 1997).

Stimulus polarity (i.e. rarefaction, condensation, or alternating stimuli) used during ECochG testing has been found to vary. The most commonly used stimulus polarity is alternating because the potential contributions from stimulus artifact and the cochlear microphonic, both of which can degrade the ECochG tracing, are diminished with this stimulus (Ferraro & Durrant, 2002; Wuyts et al., 1997). Stimulus artifact often obscures the ECochG tracing, while measurement of the CM can overshadow both the AP and CAP (Ferraro & Durrant, 2002).

Stimulus rates, filter settings, number of sweeps, and time window utilized are generally uniform among testing protocols. For click-evoked ECochG testing,

stimulus rates between 8 - 11.5 clicks per second are generally used, while higher stimulus rates between 30 - 40 per second are used for tone burst testing (Devaiah et al., 2003; Ferraro & Tibbils, 1999; Sass, 1998; & Wuyts et al., 1997). The bandpass analogue filter settings used for ECochG testing generally range from 3 - 3000 Hz to capture the energy present in the response (Ferraro & Tibbils, 1999; Margolis et al., 1995; Sass, 1998; Wuyts et al., 1997). Most ECochG studies report obtaining an identifiable SP/AP response using approximately 1000 sweeps per average for extratympanic recordings and approximately 100 – 200 sweeps for transtympanic recordings (Devaiah et al., 2003; Ghosh et al., 2002; Ferraro & Tibbils, 1999; Margolis et al., 1995). Lastly, an analysis window of 10 ms is most commonly reported for recording ECochGs to click stimuli (Devaiah et al., 2003; Ghosh et al., 2002; Ferraro & Tibbils, 1999; Margolis et al., 1995; Sass, 1998). In contrast, a longer time window of 20 ms is commonly reported for tone burst stimuli, to account for the longer duration of tone burst stimuli (Margolis et al., 1995; Sass, 1998).

Testing Parameters

In human ECochG testing, two primary electrical potentials (i.e., SP and CAP) are recorded and measured (Wilson & Bowker, 2002). These electrical potentials were briefly introduced within the cochlear potentials section earlier in this review however their role in ECochG testing will be addressed within this current section.

The summating potential is a complex response made up of several components. It is stimulus driven and originates at the level of the hair cells in the organ of Corti. The SP reflects the displacement pattern of the cochlear partition. This

potential is measured as a dc shift in the cochlear microphonic baseline (Ferraro & Durrant, 2002). The direction of this shift is determined by the interaction between the polarity of the stimulus and the location of the recording electrodes (Ferraro & Durrant, 2002).

The role of the summating potential in the cochlea's hearing function is unknown, however, it is speculated that the summating potential supplies information regarding the cochlea's functionality by revealing representations of non-linearities within the cochlea (Ferraro & Durrant, 2002; Wilson & Bowker, 2002). The non-linear characteristic of the SP has made ECochG testing a valuable tool for monitoring certain clinical pathologies, such as Meniere's disease. Specifically, patients with Meniere's disease have been found to have enlarged SP's in comparison to normal ears or ears with cochlear disorders due to pathologies other than Meniere's disease or endolymphatic hydrops (Ferraro & Durrant, 2002). It is currently unknown if this enhanced or enlarged SP is the product of excessive endolymph or if other factors such as biochemical and/or vascular changes are responsible (Ferraro & Durrant, 2002).

Two theories exist which attempt to explain how the pathophysiology of Meniere's disease's affects on ECochG results. First, it is speculated that this excessive production of endolypmph fluid seen in Meniere's disease causes a downward deflection of the basilar membrane, resulting in an irregular pattern of hair cell stimulation (Gibson, Moffat, & Ramsden, 1977; Sass, 1998). This downward deflection pushes the basilar membrane toward the scala tympani (Ryan, 1999). With intact hair cells, this deflection is speculated to enhance non-linearities in the cochlea,

thus enhancing the amplitude of the SP (Ryan, 1999). A second theory speculates that the resting potential of the endolymph fluid changes due to a spasm within the stria vascularis, which is then responsible for enhancement of the SP amplitude seen in Meniere's patients (Gibson et al., 1977).

The second primary electrical potential recorded in ECochG testing is the compound action potential (CAP). The CAP is not a true cochlear potential as it represents the synchronous firing of a group of auditory neurons in response to stimulation. Depending upon the type of stimulus utilized, different groups of afferent neurons are stimulated. For example, with click stimulation, the entire basilar membrane is theoretically stimulated resulting in a CAP which represents neural synchrony across approximately the entire basilar membrane (Ferraro & Durrant, 2002). Due to transducer properties, ear canal resonance, and the middle ear response, however, CAPs measured from click stimuli are generally more representative of synchrony in specific areas of the basilar membrane (Ferraro & Durant, 2002). Tone burst stimuli responses are representative of the synchrony of a group of neurons in a specific area of the basilar membrane (Ferraro & Durrant, 2002). Regardless of stimuli used these groups of neurons discharge at stimulus locked intervals (Margolis et al., 1995).

For clinical purposes, the CAP is measured in terms of amplitude and latency. The amplitude of the AP represents the number of nerve fibers responding to stimulation as well as the afferent output of the inner hair cells (Ferraro & Durrant, 2002). In contrast, the AP latency represents the time delay between stimulus onset

and the occurrence of peak N1 (Ferraro & Durrant, 2002). The AP latency is generally measured between 1.3 to 1.7 ms (Ferraro & Durrant, 2002).

In order to interpret the electrocochleogram, the latency and amplitude of the SP and CAP are measured. As shown in figure 15, the SP is measured as a downward deflection from the stimulus onset to the first negative trough (Devaiah et al., 2003). The SP should persist throughout the duration of the stimulus (Ferraro & Durrant, 2002). In contrast, the CAP is measured as the first maximum negative deflection from the pre-stimulus baseline, also shown in figure 15 (Margolis et al., 1995). Latencies of both the SP and CAP are measured as the time delay between stimulus onset and their subsequent occurrence.

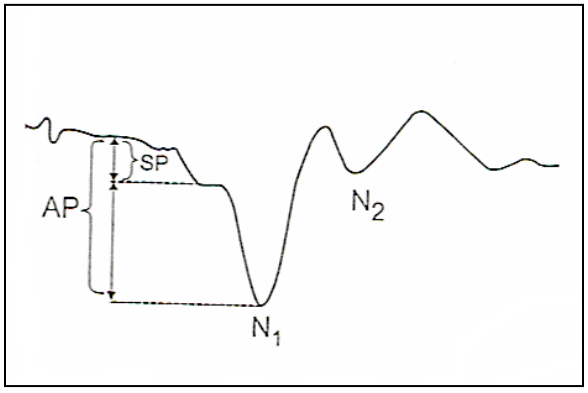

Figure 15. Depiction of electrocochleogram measurements of amplitude from Ferraro & Durrant, 1999.

ECochG recordings are generally interpreted according to the SP/AP amplitude ratio. In subjects with normal functioning inner ears, the mean SP/AP ratios vary over a relatively small range (0.16 to 0.31) despite the fact that various

recording techniques have been used across studies (Ferraro & Durrant, 2002). Patients with Meniere's disease, in contrast, are characterized by enlarged SP/AP amplitude ratios. Figure 16a illustrates a normal SP/AP amplitude ratio of 13%, while Figure 16b illustrates an abnormally large SP/AP amplitude ratio of 75%, which is consistent with Meniere's disease (Hall, 1992). Electrocochleograms are considered positive for Meniere's disease when the SP/AP amplitude ratio exceeds a specified ratio cutoff. Numerous studies of patients with Meniere's disease have reported a wide variation in cutoffs for SP/AP ratios that indicate abnormality, such as 0.26 (Margolis et al., 1995), 0.29 (Ghosh et al., 2002), 0.30 (Selmani, Martilla, Pyykko, & Ishizaki, 2002), 0.41 (Ferraro & Tibbils, 1999), and 0.53 (Devaiah et al., 2003).

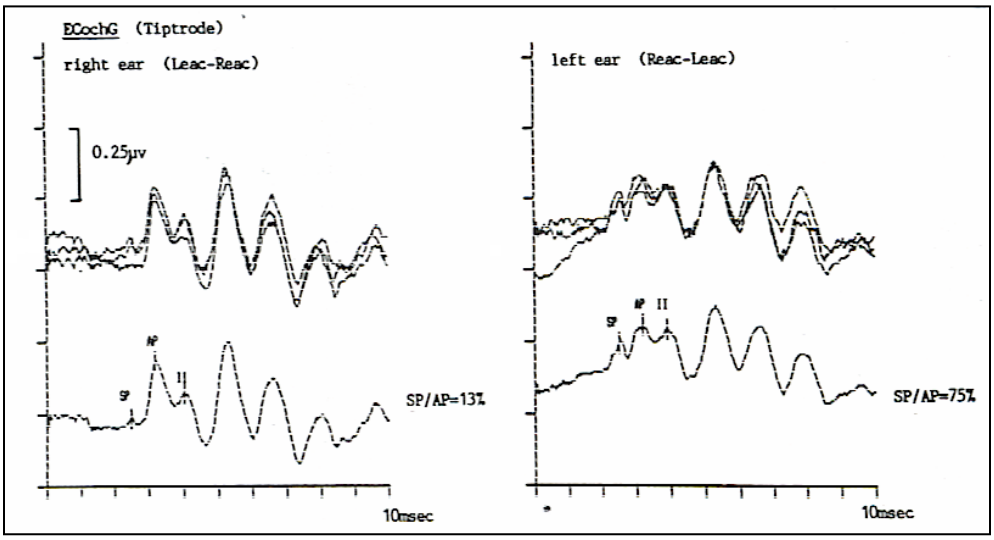

Figure 16a & 16b. Illustrations of waveforms for both a.) normal EcochG (SP/AP = 13%) and b.) abnormal EcochG (SP/AP = 75%). In both illustrations replications of waveforms are located in the top half of the figure, while the sums of the replicable waveforms are located in the bottom haf of the figure. Figure taken from Hall, 1992.

Rotary Chair Testing

Clinical Utility of Rotary Chair Testing

The purpose of rotational testing is to investigate the presence of a peripheral vestibular lesion via study of the VOR over a range of rotational frequencies (Honrubia, 2000; Wuyts, Furman, & Van de Heyning, 2003). In many instances, rotational testing is performed in conjunction with electronystagmography (ENG) testing. The ENG is a series of tests of vestibular function (Yellin, 2000). As discussed previously, a nystagmus is generated as the result of the relationship between the VOR and horizontal semicircular canal function. During ENG testing,

this nystagmus is measured via electro-oculography, in which the corneoretinal potentials are measured during various eye movements (Yellin, 2000).

The ENG consists of the following subtests: ocular motor testing, positional testing, and caloric testing (Wuyts et al., 2003). The ocular motor subtest is responsible for the evaluation of eye movements in the absence of vestibular stimuli, while both the positional test and the caloric test involve the evaluation of eye movements in the presence of vestibular stimulation (Wuyts et al., 2003). Positional testing includes both positioning and positional testing (Wuyts et al., 2003). Positioning testing assesses for the presence of benign paroxysmal positional vertigo while positional testing evaluates positionally induced nystagmus (Wuyts et al., 2003). Lastly, caloric testing assesses the presence of vestibular lesions through the use of both warm and cool water or air irrigations in the ear canal (Wuyts et al., 2003). These caloric irrigations stimulate the endoloymph fluid within the horizontal semicircular canals individually. Therefore, caloric testing has the ability to lateralize peripheral vestibular lesions (Wuyts et al., 2003).

The use of rotational testing supplements caloric information by further assessing the peripheral vestibular apparatus. Traditional caloric stimulation assesses vestibular function of the horizontal semicircular canals in a limited frequency range between 0.002 and 0.004 Hz and accelerations of less than 10 degrees/ sec2 (Shepard, 2001). Normal head movement generally occurs from approximately 1-4 Hz (Goebel et al., 2000). Because the caloric tests assesses the VOR in a limited range well below the general function of the VOR, a caloric weakness cannot be interpreted as absent peripheral vestibular function and similarly normal caloric responses cannot be

interpreted as normal peripheral vestibular function (Shepard, 2001). Vestibular tests, which assess the VOR at high frequencies such as rotary chair testing, have higher test retest reliability over caloric testing (Kingma, Meulenbroeks, & De Jong, 2000).

Due to these limitations in caloric testing, many patients exhibiting symptoms of vestibular system involvement can elicit normal ENG studies. In these cases, rotational testing can be utilized to help further assess the extent of peripheral involvement. For example, Shepard (2001) studied 2266 patients who presented with vestibular symptoms over a 32 month period in his clinical practice. Among this group of patients, 16% had normal ENG studies. Rotary chair testing performed on these individuals with normal ENG findings revealed however, that 80% had abnormalities suggesting peripheral vestibular system pathology. The primary rotary chair abnormalities revealed in these cases were phase abnormalities (35%) and asymmetry abnormalities (45%). Each of these rotary chair test parameters will be discussed in further detail later in this section.

Rotational testing is often recommended with the following ENG results: the presence of a unilateral weakness that has been centrally compensated, the presence of a bilateral peripheral vestibular weakness, or in instances when caloric testing cannot be completed (i.e. narrow ear canals, middle ear effusion, and tympanic membrane perforation) (Shepard, 2002). Rotational testing is also utilized when monitoring the progression of certain pathologies, such as Meniere's disease and is utilized in measuring the effectiveness of specific treatments, such as chemical ablation of either peripheral vestibular system for treatment of Meniere's disease (Shepard, 2001). When caloric testing suggests a bilateral weakness, rotational testing

can be used to confirm and further define the extent of the peripheral vestibular lesion (Shepard & Telian, 1996). Overall, rotational testing supplies information regarding the verification, extent, and compensation of peripheral vestibular lesions (Shepard, 2002).

Test Description

There are currently two forms of rotational testing: passive and active. Passive rotational testing involves movement of the patient's entire body, while active rotational testing requires the patient to physically rotate his or her own head back and forth (Stockwell & Bojrab, 1997). The rotary chair testing utilized for the current study is a form of passive rotational testing because the stimulus is being delivered to the head as a means of total body movement. Rotary chair testing, as shown in Figure 17, is performed using a chair driven by an electric torque motor enclosed within a lightproof booth (Shepard & Telian, 1996). This testing is performed with eyes open in complete darkness (Stockwell & Bojrab, 1997). In order to maintain alertness, the patient is asked to perform mental tasks, such as simple arithmetic throughout the testing (Stockwell & Bojrab, 1997). During this test, the patient's head is secured to the chair with restraints (Shepard, 2002). It is assumed that whenever the chair moves, the patient's head is also making the same movements (Shepard, 2002). The patient's eye movements are then recorded with electro-oculographic methods, an infrared camera or with scleral coil eye movement recording techniques (Shepard & Telian, 1996).

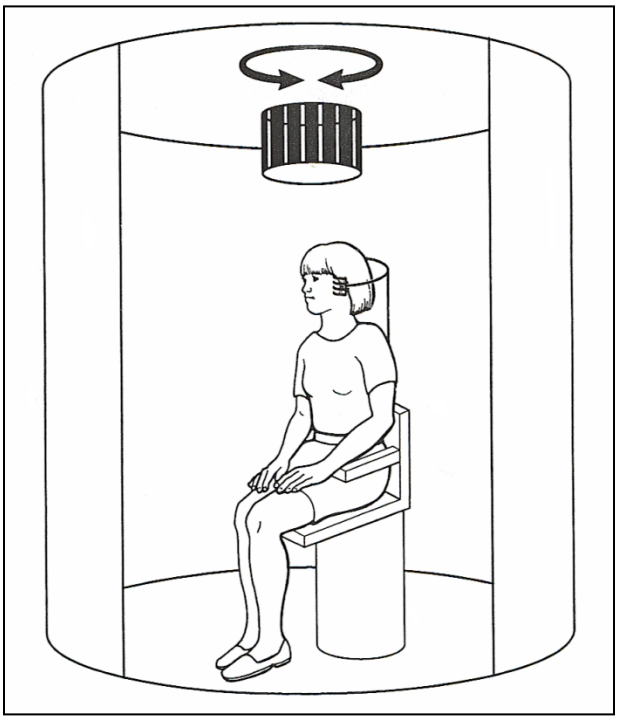

Figure 17. Picture of typical setup for rotary chair testing from Shepard & Telian, 1996.

Test Protocol

Currently, the most widely used testing protocol for rotary chair testing is the slow harmonic acceleration (SHA) test (Stockwell & Bojrab, 1997). Because this SHA testing protocol was utilized for the current study, this is the only testing protocol that will be discussed within this review. With SHA, the chair is rotated with sinusoidal waveforms at frequencies ranging from 0.01 to 1.28 Hz, while the peak chair velocity remains constant at 50-60 degrees/second regardless of test frequency (Shepard, 2001; Shepard & Telian, 1996). The patient's head is restrained securely during the entire test and it is assumed that stimulation received by the body is likewise received by the head (Shepard & Telian, 1996). This assumption becomes

faulty at frequencies greater than 1.0 Hz because skin movement relative to the skull may occur resulting in artifacts (Shepard, 2002).

When performing the SHA testing, the horizontal semicircular canals are placed within their plane of rotation and the patient undergoes rotations of varying frequencies (Stockwell & Bojrab, 1997). The frequencies generally assessed include octave intervals above .01 Hz including 0.01, 0.02, 0.04, 0.08, 0.16, 0.32 and 0.64 Hz (Shepard, 2001; Stockwell & Bojrab, 1997). The patient is rotated for numerous cycles at each test frequency (Stockwell & Bojrab, 1997). The slow component eye velocity response from each cycle of stimulation is added to subsequent responses and divided by the total amount of cycles recorded to yield an average response per test frequency (Shepard & Telian, 1996). Once this is completed, the test frequency is doubled and the process repeats (Shepard, 2002). As with ENG testing, the responses measured and averaged during rotary chair testing are only the slow component eye velocities, while the fast corrective saccade components as well as other artifacts such as eye blinks, are removed (Goebel et al., 2000; Shepard & Telian, 1996). The reliability of the SHA response depends on the number of cycles averaged. Reliability can therefore, be increased by increasing the number of cycles averaged (Shepard & Telian, 1996). The only exception to this rule occurs at very low frequencies, such as 0.01 Hz, where performing more than 3 cycles is prohibitive because it produces unpleasant neurovegatative symptoms for the patient (Shepard & Telian, 1996). Because of the possible unpleasant symptoms experienced at low test frequencies, Shepard recommends the test protocol begins at 0.08 Hz, then the test frequency is

decreased in octave intervals until reaching 0.01 Hz, and lastly testing should proceed at octave intervals above .08 Hz (Shepard, 2002).

Testing Parameters

When performing rotary chair testing, three testing parameters (gain, phase, and asymmetry) are measured to assess the function of the VOR and to evaluate the function of the peripheral vestibular system. Prior to discussing each of these parameters, the underlying physiology of the VOR will be briefly reviewed. During any particular head movement, the VOR is responsible for generating eye movements, which are equal and opposite in direction to the movement of the head (Stockwell & Bojrab, 1997). Head rotation to the right inhibits the left semicircular canal while exciting the right semicircular canal and vice versa. This occurs because of the push/pull arrangement of the horizontal semicircular canals. Nystagmus beats in the direction of the head turn. Therefore rightward chair excursions will elicit right-beating nystagmus, while leftward chair excursions will elicit left-beating nystagmus. Because each horizontal semicircular canal is affected by each chair excursion, most rotary chair testing protocols cannot be used to lateralize vestibular lesions as with caloric testing (Shepard, 2002). However, the measurement of these 3 test parameters (gain, phase, and symmetry) can be used to assess the integrity of the horizontal semicircular canals, eighth cranial nerves, and central vestibular pathways (Wuyts et al., 2003).

The first parameter to be discussed is gain. Gain is calculated by dividing the slow component velocity of eye movement by the slow component velocity of head movement, which can be assumed to be the same as the slow component velocity of

chair movement (Shepard & Telian, 1996). Gain is an indication of response magnitude and the overall responsiveness of the system (Honrubia, 2000). A principal clinical use of gain measurements is to define the presence of a bilateral vestibular weakness (Shepard & Telian, 1996). In cases of bilateral vestibular weakness, the gain value verifies that a severely reduced or absent bilateral caloric response does accurately reflect a bilateral weakness and is not due to a stimulus or subject-related artifact (Shepard & Telian, 1996). Variables such as alertness and mechanical or neurological restrictions of eye movement can cause gain measurements to be reduced therefore, the patient should be carefully observed throughout testing (Shepard, 2001).

Figure 18 is an example of normal rotary chair results (Shepard & Telian, 1996). The un-shaded areas indicate mean normal gain values plus or minus two standard deviations (Shepard & Telian, 1996). As can be seen in figure 18, average normal gain values are somewhat lower at lower test frequencies and increase as the stimulus test frequency increases (Goebel et al., 2000).

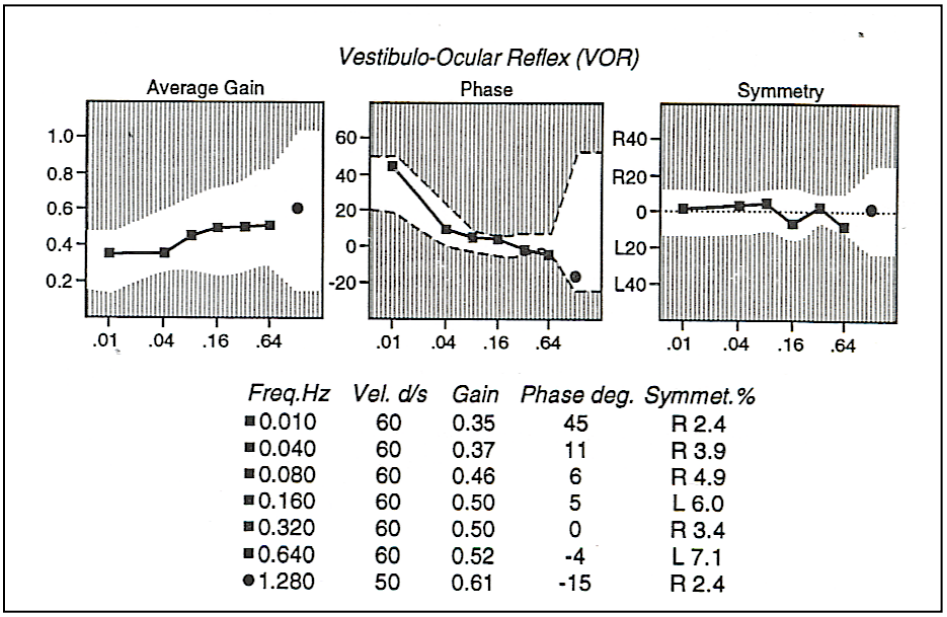

Figure 18. Normal mean rotary chair test results for gain, phase, and symmetry from Shepard & Telian, 1996.

The second parameter in rotational testing is phase. Phase measurements are a comparison of the timing relationship between head movement and reflexive eye movement elicited from the VOR (Shepard & Telian, 1996). As discussed previously, the VOR is responsible for eliciting eye movement in an equal and opposite direction of head movement. This would infer that eye movements and head movements would be exactly 180º out of phase. As shown in figure 18, normal phase values only ranged from 45 degrees to -15 degrees. When a low stimulus frequency rotation (e.g., 0.01 and 0.04 Hz) is employed, it is assumed that the stimulus has been ongoing for some time before a sampling of eye movements has begun (Shepard, 2001; Stockwell & Bojrab, 1997). In this case, the compensatory eye movement generated by the VOR will “lead” the head movement and generally result in positive gain values (Shepard

& Telian, 1996). The amount of phase "lead" that occurs is called the phase angle and is measured in degrees (Shepard & Telian, 1996). In contrast, for a sudden, single head movement, the reflexive eye movement would "lag" behind the unanticipated head movement (Shepard, 2001).

Mean phase values for normal subjects are shown in figure 18. At the lower test frequencies, the average phase values in normal subjects should show phase leads reflected in positive phase values. As the test frequency slowly increases the phase values decrease and become negative values (Goebel et al., 2000). Similar to the gain portion of the figure, the un-shaded region depicts the average phase values for normal subjects plus or minus two standard deviations.

Phase measurements are used to document the presence of peripheral vestibular dysfunction (Shepard, 2001; Shepard & Telian, 1996). In cases of peripheral vestibular dysfunction, more specifically when lesions occur in the vestibular labyrinth or the vestibular VIII nerve, an increase in the phase angle, or phase lead, is generally present (Shepard, 2001).

The third parameter measured in rotational testing is asymmetry. Calculating asymmetry values involves a comparison of rightward versus leftward slow phase velocities (Stockwell & Bojrab, 1997). Symmetry values are expressed in percentages and are helpful when analyzing results from patients who have had abnormal directional preponderance findings on their ENG. It is the calculations of symmetry for rotary chair testing, however, are reversed in comparison to those utilized for ENG. When calculating directional preponderances in ENG testing, the speed of slow component of nystagmus is measured, but the directional preponderance is named

according to the fast phase of the nystagmus (Shepard & Telian, 1996). With rotational testing, asymmetry is calculated using the slow component velocities and named according to the slow phase (Shepard & Telian, 1996). Therefore, in the event of a left directional preponderance with ENG testing, rotational testing should evidence a right asymmetry, which is indicative of greater right slow component velocity than left slow component velocity (Shepard & Telian, 1996).

In contrast to gain and phase values, asymmetry values should remain relatively constant across the test frequencies. This pattern is also shown in figure 18. An asymmetry of greater than 20 percent is considered abnormal at any test frequency (Honrubia, 2000).

When interpreting asymmetries in rotational testing, these findings may be due to an abnormality in either peripheral system, such as a peripheral weakness on the side which has the stronger slow component velocity response, or an irritative lesion on the opposite side of the asymmetry (Shepard & Telian, 1996). In a small number of cases, the asymmetry may be due to an uncompensated lesion in the central pathways (Rubin & Brookler, 1991). Lastly, an infrequent pattern that is seen is a right asymmetry at one or more stimulus test frequencies and a left asymmetry noted at other test frequencies. This finding suggests that the peripheral system may be behaving in a paretic fashion at some frequencies and an irritative fashion at others (Shepard, 2002). This pattern may be associated with Meniere's disease (Shepard, 2002).

Concluding this review a clear understanding of the need for differential diagnosis of these two pathologic groups is evident. Each pathologic group displays

similar symptoms however each differs radically in terms of hypothesized underlying pathophysiology, treatment strategies, and testing outcomes. For this reason, differential diagnosis between Meniere's disease and migraine-associated dizziness becomes crucial.

The purpose of the current study was to determine if a clinical vestibular test battery exists which could be used as an effective diagnostic tool for the accurate diagnosis of Meniere's disease versus migraine-associated dizziness. The two tests evaluated in this study were the rotary chair test and electrocochleography. The specific parameters evaluated in the rotary chair test were rotary chair gain values at test speeds ranging from 0.01 to 0.64 Hz (0.01, 0.02, 0.04, 0.08, 0.16, 0.32, & 0.64). In contrast, the SP/AP amplitude ratio is the test parameter that was evaluated for electrocochleography. The specific aims of the study were to determine:

1.) If significant differences existed between these two pathophysiologic groups in terms of their rotary chair gain values at each of the test speeds.
2.) If significant differences existed between these two pathophysiologic groups in terms of their ECochG SP/AP amplitude ratios.

CHAPTER 3:

METHODS

Patient Selection and Demographics

A retrospective chart review of patients seen at the University of Maryland Medical System: Division of Otolaryngology Head and Neck Surgery in Baltimore, MD was performed for this study. Participants were selected if they had been diagnosed as having had either Meniere's disease or migraine-associated dizziness. Patient diagnosis was based upon case history, presenting symptoms, and response to treatment. A diagnosis of Meniere's disease was based on the criteria set forth by the American Academy of Otolaryngology Head and Neck Surgery Committee on Hearing and Equilibrium. Likewise, a diagnosis of migraine was based on the International Headache Society diagnostic classifications of migraine.

Twenty patients were included in this study. Of the 20 patients, 10 patients were diagnosed as having Meniere's disease and 10 patients were diagnosed as having migraine-associated dizziness. All patients were adults between the ages of 18 to 58 years with a mean age of 37.7 $\pm$ 10.3 years. Patients in the Meniere's disease group were between the ages of 18 to 50 years with a mean age of 34.9 $\pm$ 9.2 years. Patients in the migraine-associated dizziness group were between the ages of 22 to 58 years with a mean age of 40.5 $\pm$ 11.0 years. All of the patients had presenting symptoms for a minimum of one year. Each of the participants was a patient from the University of Maryland Medical System who had received an otolaryngologic

examination by one of the co-investigators (H.S.). All ECochG and rotary chair testing were performed by the audiology staff at this facility. Patients were off of all medications for at least 72 hours prior to testing.

Patients were excluded from the study if they met any one of the following criteria: (1) either ECochG or rotary chair testing had not been administered, (2) their diagnosis was questionable, or (3) if a patient could not perform rotary chair testing due to claustrophobia.

The following test protocols were utilized during ECochG and rotary chair testing.

ECochG Methodology

All ECochG testing was performed using the Nicolet SPIRIT evoked potential system. All ECochG recordings were obtained via an extratympanic Nicolet Biomedical gold tiptrode and Nicolet Biomedical disposable electrodes. For the ECochG recordings, the tiptrode was used as the active, or positive, electrode; the forehead (Fpz) was used as the ground electrode; and the reference, or negative, electrode was placed either on the contralateral earlobe or mastoid. In some cases, a tiptrode was used in the contralateral ear as the reference electrode.

The ECochGs were recorded to a click stimulus (duration of 100μs) of alternating polarity presented at an intensity level of 95 dBnHL. These stimuli were presented at a rate of 7.1 clicks per second. Stimuli were presented with Nicolet Biomedical model TIP-300 (300 ohm) transducers. The amplifier gain was set to 50,000 and an EEG bandpass filter of 500 – 1500 Hz was employed. The post-stimulus analysis time was 10 msec. A minimum of two trials were obtained, each

containing 500 sweeps. The two trials were summed and all response measurements were taken on the summed response.

For each subject's responses, the following amplitude and latency measurements were taken: the baseline, the summating potential, and the action potential. The baseline was measured as a reference point at the pre-stimulus baseline. The latency of the summating potential was measured as the first negative deflection after stimulus onset and the amplitude was measured as the difference in amplitude between the baseline and this first negative deflection. The latency of the action potential was measured as the maximum negative deflection, or N_1, after stimulus onset and the amplitude was measured as the difference in amplitude between the baseline and this maximum negative deflection. The SP/AP amplitude ratio was then automatically calculated by the SPIRIT software system based on these measurements. An example of the amplitude measurements are shown in Figure 15. The SP/AP amplitude ratio was the only ECochG parameter evaluated in the present study. An SP/AP amplitude ratio greater than 50% was considered positive for Meneire's disease / endolymphatic hydrops.

Rotary Chair Methodology

Rotary chair testing was performed using Micromedical Technologies, Inc. software version 6.0 and the System 2000 booth. Eye movements were recorded using an infrared camera system that was calibrated at the beginning of the test for each subject. Patients were seated in the rotary chair located within the System 2000 booth with constraints placed across the forehead, which kept the head confined in place. A seat belt was worn across the lap to insure the patient's safety.

All subjects were rotated via a sinusoidal harmonic acceleration paradigm at a constant velocity of 60 degrees/second. Patients were tested at the following test frequencies: 0.01, 0.02, 0.04, 0.08, 0.16, 0.32, and 0.64 Hz. Rotations began at 0.08 Hz and decreased in octave intervals to 0.01 Hz, and then proceeded in octave intervals from 0.16 to 0.64 Hz rotations, as per Shepard's (2002) suggested protocol. A rate sensor was located as part of the chair control system. Calibration was performed prior to each rotary chair test. This was done by asking the subject to follow a series of dots with their eyes which were projected on the inside wall of the booth. During rotary chair testing, subjects were asked to perform various mental tasks, such as naming objects and counting. Each rotary chair test took approximately 24 minutes. Gain, phase, and symmetry values were then automatically calculated by the Micromedical Technologies, Inc. software system at each test speed. These values were then plotted for comparison to normalized data for rotary chair testing. Gain values at each of the test speeds was the only test parameter evaluated for the current study.

Statistical Analysis

Descriptive statistics, independent t-tests and two-way repeated measure ANOVAs were calculated on the data to determine if there were any statistically significant differences between these two groups. The variables analyzed were the ECochG SP/AP ratio and rotary chair gain values at each of the test speeds. An alpha level of $p < 0.05$ was used to indicate statistical significance. If statistically significant differences did exist, then Newman-Kuels post hoc testing was conducted to

determine the pattern of these differences. All statistics were completed using the SPSS program.

CHAPTER 4:

RESULTS

Results for Electrocochleography Testing

Table 3 displays the SP/AP ratios for each subject tested in the migraine-associated dizziness group and in the Meniere's disease group. Depending upon the ear tested, only 6 – 7 subjects in the migraine-associated dizziness group and 9 – 10 subjects in the Meniere's disease group were seen for electrocochleography testing. The mean and standard deviation SP/AP ratio values in the migraine-associated dizziness group were 0.32 (± 0.13) for the right ear and 0.32 (± 0.9) for the left ear, indicating no obvious differences between the ears. The mean and standard deviation SP/AP ratio values for the right and left ears in the Meniere's disease group were 0.35 (± .16) and 0.37 (± .14) respectively, again suggesting no clear differences between the ears.

Comparisons of the mean and standard deviation SP/AP ratio values for the right and left ears of the Meniere's disease group versus the migraine-associated dizziness group are shown in figure 19. This figure demonstrates two trends. First, the Meniere's disease group had slightly higher mean SP/AP amplitude ratios in comparison to the migraine-associated dizziness group regardless of ear tested. Secondly, the Meniere's disease group also had higher standard deviation values regardless of ear tested, thus indicating larger variability in ECochG SP/AP amplitude ratio values.

Subject # Migraine	Right Ear	Left Ear	Subject # Meniere's	Right Ear	Left Ear
1	0.1	0.33	1	0.69	0.3
2	0.22	dnt*	2	0.43	0.45
3	0.31	0.18	3	0.28	0.18
4	dnt*	dnt*	4	0.34	0.55
5	dnt*	dnt*	5	0.23	0.57
6	0.4	0.34	6	0.3	0.29
7	0.38	0.29	7	0.29	0.44
8	dnt*	dnt*	8	0.5	0.28
9	0.5	0.47	9	0.1	dnt*
10	0.33	0.28	10	0.3	0.27
Mean	0.32	0.32		0.35	0.37
(SD)	(0.13)	(0.09)		(0.16)	(0.14)
n =	7	6		10	9

*dnt = did not test

Table 3. Individual subjects' electrocochleography SP/AP amplitude ratios as well as mean and standard deviation values for the SP/AP amplitude ratios for the right and left ears of each group. There were 7 right ears and 6 left ears tested in the migraine-associated dizziness group, and 10 right ears and 9 left ears in the Meniere's disease group.

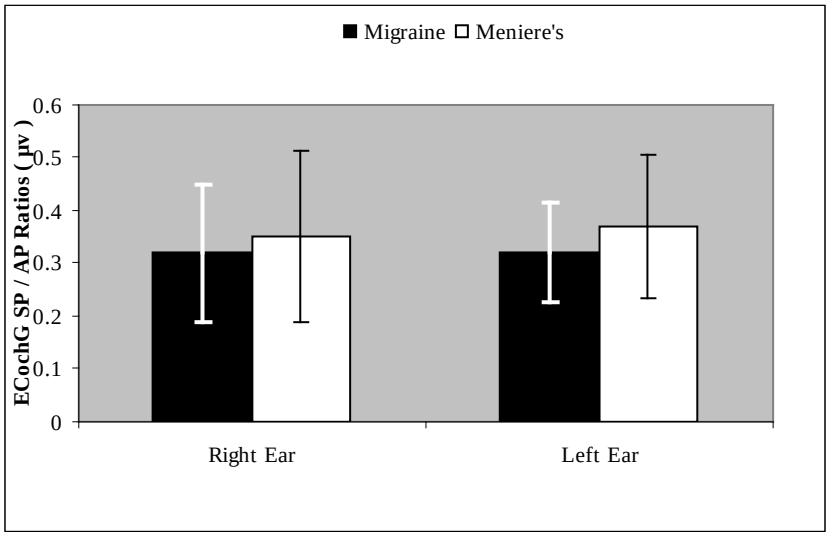

Figure 19. Mean and standard deviation values for ECochG SP/AP ratios for the Meniere's disease group (white bars) and the migraine-associated dizziness group (black bars). Results for the right ear are on the left side of the figure, and results for the left ear are on the right side of the figure.

Even though the Meniere's disease group demonstrated higher SP/AP amplitude ratios in comparison to the migraine-associated dizziness group, results of the independent t-test analyses indicated that there were no statistically significant differences in the SP/AP amplitude ratio values for these two subject groups for either the right ear ($t = -0.353$, $df = 15$, $p = .729$) or the left ear ($t = -0.854$, $df = 13$, $p = .409$).

Results for Rotary Chair Testing

The rotary chair gain values for each subject as well as the mean and standard deviation rotary chair gain values at each test speed are shown in table 4. The top half of the table contains the values for the subjects with migraine-associated dizziness and the lower half of the table contains the values for subjects with Meniere's disease.

All ten subjects from each group were seen for rotary chair testing. There are several trends clearly evident in this data. First, the Meniere's disease group demonstrated higher mean rotary chair gain values at each of the test speeds in comparison to the migraine-associated dizziness group, as shown in figure 20. Secondly, the Meniere's disease group had slightly smaller standard deviation values across the majority of test speeds in comparison to the migraine-associated dizziness group. Thus, indicating less variability in the data for this clinical population. Lastly, the mean rotary chair gain values increased as the test speed increased for both subject groups. The only exceptions to this third pattern of findings occurred at 0.04 Hz and 0.32 Hz for the Meniere's disease group and at 0.32 Hz for the migraine-associated dizziness group.

Subject Group and # Migraine	Test Frequencies 0.01 Hz	0.02 Hz	0.04 Hz	0.08 Hz	0.16 Hz	0.32 Hz	0.64 Hz
1	0.17	0.21	0.33	0.38	0.38	0.27	0.45
2	0.22	0.30	0.35	0.38	0.40	0.31	0.38
3	0.40	0.51	0.44	0.58	0.60	0.58	0.55
4	0.30	0.33	0.40	0.38	0.30	0.40	0.42
5	0.23	0.29	0.31	0.35	0.30	0.42	0.45
6	0.33	0.29	0.40	0.35	0.38	0.43	0.40
7	0.40	0.37	0.33	0.48	0.40	0.39	0.35
8	0.25	0.35	0.39	0.40	0.45	0.48	0.38
9	0.40	0.51	0.44	0.50	0.55	0.58	0.59
10	0.30	0.33	0.40	0.35	0.38	0.27	0.35
Mean (SD)	0.30 (0.08)	0.35 (0.10)	0.38 (0.05)	0.42 (0.08)	0.41 (0.10)	0.41 (0.11)	0.43 (0.08)
n =	10	10	10	10	10	10	10
Subject Group and # Meniere's	**Test Frequencies 0.01 Hz**	**0.02 Hz**	**0.04 Hz**	**0.08 Hz**	**0.16 Hz**	**0.32 Hz**	**0.64 Hz**
1	0.38	0.48	0.51	0.55	0.67	0.68	0.63
2	0.40	0.50	0.49	0.60	0.59	0.23	0.68
3	0.42	0.55	0.39	0.42	0.58	0.49	0.66
4	0.39	0.52	0.51	0.62	0.68	0.61	0.55
5	0.38	0.48	0.55	0.51	0.60	0.55	0.60
6	0.40	0.50	0.50	0.49	0.60	0.53	0.68
7	0.42	0.55	0.55	0.39	0.42	0.49	0.61
8	0.50	0.48	0.44	0.50	0.59	0.23	0.68
9	0.38	0.48	0.51	0.55	0.58	0.49	0.66
10	0.40	0.50	0.49	0.60	0.68	0.61	0.55
Mean (SD)	0.41 (0.04)	0.50 (0.03)	0.49 (0.05)	0.52 (0.08)	0.60 (0.08)	0.49 (0.15)	0.63 (0.05)
n =	10	10	10	10	10	10	10

Table 4. Individual subjects' rotary chair gain values as well as mean and standard deviation gain values are shown for each of the test speeds. Results for the migraine-associated dizziness group are displayed in the top half of the table, and results for the Meniere's disease group are displayed in the lower half of the table.

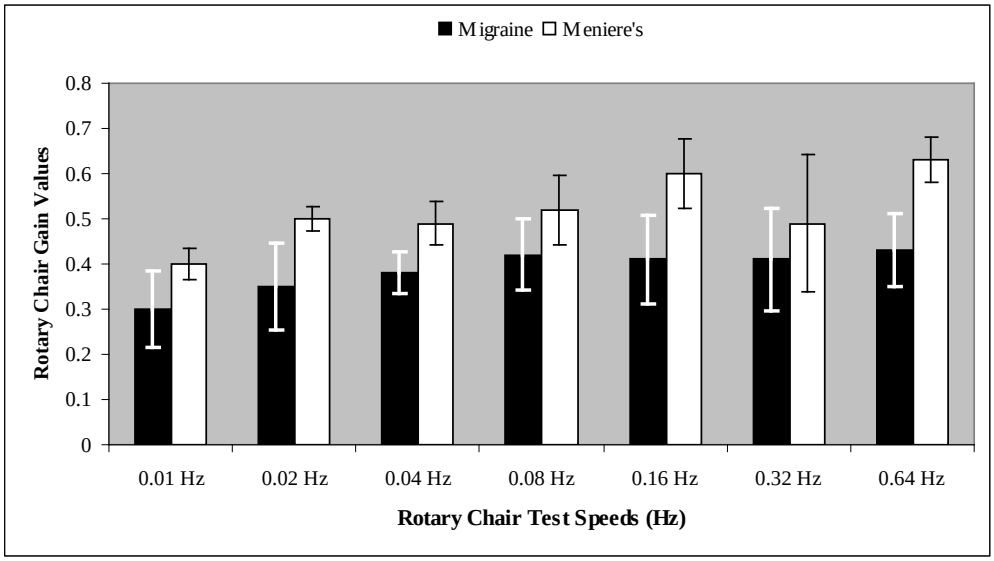

Figure 20. Comparisons of mean and standard deviation rotary chair gain values as a function of test speed for the Meniere's disease group (white bars) versus the migraine-associated dizziness group (black bars).

Results of the independent t-test analyses revealed that there were statistically significant differences in the mean rotary chair gain values between the migraine-associated dizziness group and the Meniere's disease group at each of the following test speeds: 0.01 Hz ($t = -3.752$, $df = 18$, $p = 0.001$), 0.02 Hz ($t = -4.942$, $df = 18$, $p = 0.000$), 0.04 Hz ($t = -5.446$, $df = 18$, $p = 0.000$), 0.08 Hz ($t = -3.117$, $df = 18$, $p = 0.006$), 0.16 Hz ($t = -4.771$, $df = 18$, $p = 0.000$), and 0.64 Hz ($t = -6.522$, $df = 18$, $p = 0.000$). The only test speed that did not produce a statistically significant difference in mean gain values between these two subject groups was at 0.32 Hz ($t = -1.312$, $df = 18$, $p = 0.206$).

In order to further explore the pattern of the significant differences in the rotary chair gain values between these 2 subject groups, a two-way repeated measure

ANOVA and Neuman-Keuls' post-hoc testing were conducted. For the ANOVA, the between subject variable was subject group (i.e., migraine-associated dizziness versus Meniere's disease) and the within subject variable was rotary chair test speed (i.e., 0.01, 0.02, 0.04, 0.08, .16, 0.32, and 0.64 Hz).

As expected, the results of the ANOVA revealed a statistically significant effect for subject group [F (1,18) = 30.58, p = .000], such that the overall mean rotary chair gain value for the Meniere's disease group was significantly higher than the overall mean gain value for the migraine-associated dizziness group as shown in Figure 21.

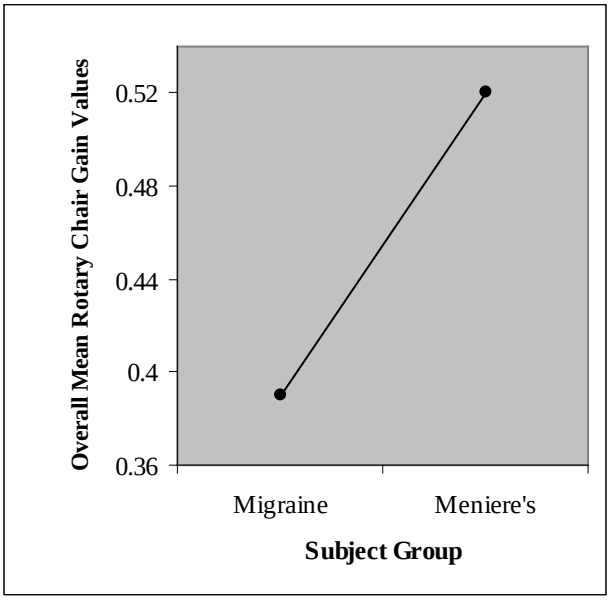

Figure 21. Comparison of overall mean rotary chair gain values between the migraine-associated dizziness group and the Meniere's disease group.

A statistically significant effect for rotary chair test speed was also found [F (6, 108) = 15.38, p = .000]. A Newman-Keuls post hoc analysis was conducted in order to explore the pattern of these significant differences in gain values as a function of test speed. The results of this post hoc testing revealed that: 1.) the overall mean gain value at 0.01 Hz was significantly smaller than the overall mean gain value at the remaining testing speeds; 2.) the overall mean gain value at 0.64 Hz was significantly larger than the overall mean gain values at all of the remaining test speeds with the exception of 0.16 Hz; 3.) the overall mean gain value at 0.32 Hz was significantly smaller than the overall mean gain value at 0.16; and 4.) the overall mean gain value at 0.16 Hz was significantly larger than the overall mean gain values at 0.02 and 0.04 Hz. The overall mean gain values as a function of test speed are shown in Table 5.

	Test Frequencies						
	0.01 Hz	**0.02 Hz**	**0.04 Hz**	**0.08 Hz**	**0.16 Hz**	**0.32 Hz**	**0.64 Hz**
Overall group	0.35	0.43	0.44	0.47	0.51	0.45	0.53

Table 5. Overall mean rotary chair gain values as a function of test speed collapsed across subject group.

Lastly, the results of the ANOVA revealed a significant interaction between subject group and rotary chair gain values [F (6, 108) = 2.30, p = 0.039]. Specifically, the mean rotary chair gain values are significantly higher in the Meniere's disease group when compared to the migraine-associated dizziness group regardless of test speed as shown in figure 22.

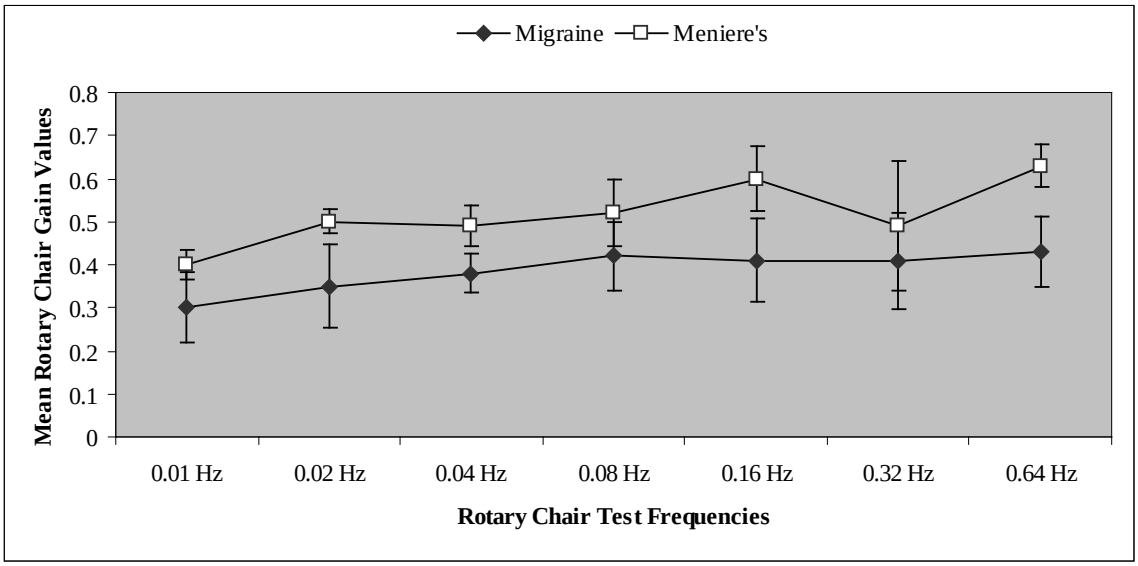

Figure 22. Relationship between subject group (i.e., Meniere's disease group versus the migraine-associated dizziness group) and mean rotary chair gain values. Standard deviation values for each subject group at each test speed are also indicated. The mean data for the Meniere's disease group are indicated in the white squares; the mean data for the migraine-associated dizziness group are shown in the black diamonds.

Summary of the Results

The objective of the current study was to determine if a specific testing protocol consisting of electrocochleography and rotary chair testing could effectively differentially diagnose Meniere's disease and migraine-associated dizziness. Results indicated that no statistically significant differences existed in the ECochG SP/AP amplitude ratios of the migraine-associated dizziness group in comparison to the Meniere's disease group. Statistically significant differences did however exist in the

rotary chair gain values of the migraine-associated dizziness group when compared to the Meniere's disease group at all of the test speeds with the exception of 0.32 Hz.

CHAPTER 5:

DISCUSSION

This study was a retrospective chart review, which investigated whether a clinical vestibular test battery consisting of rotary chair and ECochG testing could differentially diagnose between Meniere's disease and migraine-associated dizziness. The aim of the current study was to determine if significant differences existed between these two pathophysiologic groups in terms of: 1.) their ECochG SP/AP amplitude ratios; and 2.) their rotary chair gain values at test speeds ranging from 0.01 to 0.64 Hz (i.e., 0.01, 0.02, 0.04, 0.08, 0.16, 0.32, & 0.64). The patient population was made up of 10 patients with a diagnosis of Meniere's disease and 10 patients with a diagnosis of migraine-associated dizziness.

Electrocochleography Testing

In the current study, no significant differences were found to exist when ECochG SP/AP amplitude ratios were compared between patients with Meniere's disease and patients with migraine-associated dizziness. To date, no other studies in the literature have made a direct comparison of the SP/AP amplitude ratios between these two same subject groups.

A variety of investigators, however, have claimed that enlarged ECochG SP/AP amplitude ratios are a diagnostic indicator for Meniere's disease (e.g., Conlon & Gibson, 2000; Sass, 1998). Specifically, Conlon and Gibson (2000) compared ECochG SP/AP amplitude ratios of patients diagnosed with Meniere's disease to a

normal control group and found the mean SP/AP amplitude ratio of the Meniere's disease group to be approximately 40% while the control group had a mean SP/AP ratio of approximately 25%. Sass (1998) also compared ECochG SP/AP ratios of Meniere's disease patients to a control group with cochlear hearing and no history of otologic disease. The pure-tone average (PTA) of the cochlear hearing loss group ranged between 30 to 60 dB. The mean SP/AP amplitude ratios for the Meniere's disease and cochlear hearing loss groups were found to be approximately 45% and 20%, respectively. One study recently completed ECochG testing on 4 patients diagnosed with migraine-associated dizziness (Reploeg & Goebel, 2002). These investigators reported that no individual in this group exhibited abnormally enlarged SP/AP amplitude ratios.

In the current study, enlarged SP/AP amplitude ratios were expected for the Meniere's disease group because this pathology has been attributed to the overproduction or underabsorption of endolymph fluid due to either obstruction of the endolymphatic duct or endolymphatic sac dysfunction (Gibson and Arenburg, 1997; Schuknecht, 1974). In contrast, normal SP/AP amplitude ratios were expected for the migraine-associated dizziness group because this pathology is hypothesized to be due to a central pathology involving either a vascular, metabolic, ion channel, neuropeptide, or calibration origin and therefore normal SP/AP amplitude ratios were expected (Baloh, 1997; Cutrer & Baloh, 1992; Kuritzky et al., 1981; Thakar et al., 2001). The lack of significant differences in the SP/AP amplitude ratios between the two subject groups in the current study may have been the result of several factors including: 1.) whether the patient was symptomatic at the time of testing; 2.) the

effects of hearing loss on ECochG testing outcomes; 3.) the duration of Meniere's disease and; 4.) the sensitivity and specificity of the SP/AP ECochG amplitude ratio in ECochG testing. The role of each one of these factors will be discussed below.

Patient Symptoms at Time of Testing

Because the nature of Meniere's disease is transient, enlarged SP/AP amplitude ratios cannot be anticipated in all patients with Meniere's disease. Enlarged SPs and SP/AP amplitude ratios are more likely to occur when the patient is experiencing symptoms of Meniere's disease (i.e., tinnitus, fluctuating hearing loss, vertigo, and aural fullness) at the time of ECochG testing (Ferraro & Tibbils, 1999; Ryan, 1999). Therefore, in periods of remission, ECochG SP/AP amplitude ratios may be within normal limits.

For the present study, it is unknown how close in proximity the ECochG testing was conducted in the Meniere's disease group in relation to the onset of symptoms for the patient. Even though the Meniere's patients did show a slightly higher mean SP/AP amplitude ratio value (0.36 μV) in comparison to the migraine-associated dizziness group (0.31 μV), the lack of statistically significant differences between the SP/AP amplitude ratios for these two subject groups may be attributed, at least in part, to the patient's symptoms at the time of testing.

Duration of Meniere's Disease

In the early stages of Meniere's disease, the increase in endolymphatic fluid pressure typically results in an enlarged SP/AP amplitude ratio due to an enlarged SP measurement and a stable AP measurement (Margolis et al., 1995). In later stages of the disease, after the loss of cochlear neurons and hair cells has occurred, the

amplitude of both the SP and the AP are often affected (Margolis et al., 1995). When the amplitude of the AP is decreased due to neuron and hair cell loss, an artificially enlarged SP/AP amplitude ratio may result (Margolis et al., 1995). This enlarged SP/AP amplitude is not indicative of Meniere's disease (Margolis et al., 1995). The sensitivity of ECochG testing in the later stages of the disease becomes somewhat questionable (Margolis et al., 1995).

In the present study, chart reviews were performed on patients who had exhibited symptoms for greater than one year. It is not known whether ECochG testing was completed within the beginning or later stages of the disease process.

Effects of Hearing Loss on ECochG Recordings

In order to accurately record ECochG potentials, relatively normal function of the outer and inner hair cells is necessary (Margolis et al., 1995). Ferraro and Durrant (2002) have reported that ECochGs can be reliably recorded in individuals with sensorineural hearing loss less than or equal to 50 to 60 dB HL. When hearing losses exceed these levels, however, the reliability of ECochG testing becomes questionable (Ferraro & Durrant, 2002).

In the current study, the degree of hearing loss in all 20 patients was not known. Therefore, we cannot state whether the SP or AP amplitude measurements in either subject group were affected by the presence of hearing loss.

Variability in Sensitivity and Specificity of the SP/AP Amplitude Ratio in ECochG Testing

Another factor that can influence the accuracy of the traditional SP/AP amplitude ratio in diagnosing Meniere's disease is its variability in sensitivity (i.e., the amount of subjects with Meniere's disease who exhibit enlarged SP/AP amplitude

ratios) and specificity (i.e., the amount of non-Meniere's disease subjects who exhibit normal SP/AP amplitude ratios). Sensitivity values of SP/AP amplitude ratio in diagnosing Meniere's disease have been reported to range from as low as 60% to as high as 92% in cases where the patients were symptomatic (Devaiah et al., 2003). Additional studies have also indicated sensitivity values of the SP/AP amplitude ratios ranging between 64% and 82% (Wilson & Bowker, 2002) and as high as 100% (Ghosh et al., 2002). In these 2 latter studies, high specificity values of 95% (Wilson & Bowker, 2002), and 80% to 90% (Ghosh et al., 2002) were reported. The specificity values reported suggest that ECochG testing accurately identifies non-Meniere's disease patients, however, the sensitivity values indicate that ECochG testing is somewhat variable in the correct identification of Meniere's disease. These investigators speculated that the variability in sensitivity and specificity values of ECochG testing might be attributed to a variety of factors such as stage of disease, amount of hearing loss present, placement of electrode, equipment, method of recording and SP/AP ratio cutoff criteria (Devaiah et al., 2003; Sass, 1998).

Because of the variability in the sensitivity values associated with traditional SP/AP amplitude ratio calculations, attempts have been made to improve the sensitivity of ECochG testing. One suggestion has been to calculate the SP/AP area ratio in addition to the traditional SP/AP amplitude ratio (Ferraro & Durrant, 2002). The SP/AP area ratio is calculated by first measuring the area of the SP from the response onset to the point where the waveform returns to baseline following N1 as shown in figure 17 (Devaiah et al., 2003). Secondly, the area of the CAP is measured from the beginning of its deflection to the end of its deflection as shown in figure 17

(Devaiah et al., 2003). An SP/AP area ratio is then calculated using the area of the SP and the area of the AP (Ferraro & Tibbils, 1999). Recently, Devaiah et al. (2003) conducted a study in which both the SP/AP amplitude ratio and the SP/AP area ratio were calculated for 8 patients with possible Meniere's disease. Out of these 8 patients, 4 patients had significantly large SP/AP amplitude ratios, while 7 patients had significantly large SP/AP area ratios (Devaiah et al., 2003). Likewise, Ferraro & Tibbils (1999) measured both the SP/AP area ratio and SP/AP amplitude ratio of 20 patients with true Meniere's disease and 25 patients with probable Meniere's disease. They found that 90% of patients with true Meniere's disease had both elevated SP/AP area and amplitude ratios, while almost half of patients with probable Meniere's disease had elevated SP/AP area ratios and normal SP/AP amplitude ratios. The preliminary results from these two studies suggest that the SP/AP area ratio calculation may increase the likelihood of detection of Meniere's disease, thus improving test sensitivity.

In the present study, only the traditional SP/AP amplitude ratio was calculated for each subject group due to limitations of the ECochG software. The use of SP/AP area ratios in combination with the traditional SP/AP amplitude ratio for the differential diagnosis of Meniere's disease and migraine-associated dizziness might however be an area for future research.

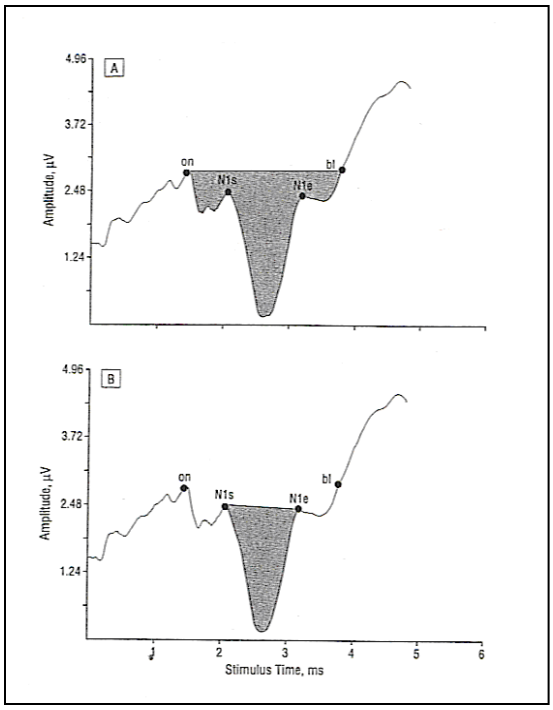

Figure 23. Representation of SP/AP area measurements from Devaiah et al., 2003.

Rotary Chair Testing

In the current study, statistically significant differences in rotary chair gain values were found between the Meniere's disease group and the migraine-associated dizziness group at most test speeds. Specifically, the migraine-associated dizziness group demonstrated significantly lower rotary chair gain values when compared to the Meniere's disease group at the following test speeds: 0.01, 0.02, 0.04, 0.08, 0.16, and 0.64 Hz. The only exception to this pattern occurred at the test speed of 0.32 Hz, where the differences in rotary chair gain values between these two subject groups did not reach statistical significance. In 2001, Dimitri and colleagues also performed

rotary chair testing on patients diagnosed with either migraine-associated dizziness or Meniere's disease (Dimitri, Wall, Oas & Rauch, 2001). These investigators found significantly lower mean rotary chair gain values in the migraine-associated dizziness group in comparison to the Meniere's disease group, similar to that shown in the present study. The mean and standard deviation rotary chair gain values reported by Dimitri et al. (2001) for the Meniere's disease group and the migraine-associated dizziness group (0.809 $\pm$ 0.111 and 0.719 $\pm$ 0.96 respectively) were somewhat larger for both groups when compared to the overall mean and standard deviation rotary chair values calculated in the present study for the Meniere's disease group and migraine-associated dizziness group (0.52 $\pm$.074 and 0.39 $\pm$.047respectively). Dimitri et al. (2001) utilized a two parameter vestibulo-ocular reflex frequency response model to calculate these gain values, which may have contributed to the differences seen across studies. Dimitri and colleagues also demonstrated that the Meniere's disease group had significantly lower age adjusted time constants in comparison to the migraine-associated dizziness group, a factor not evaluated in the present study.

Several studies have investigated all three parameters of rotary chair testing (i.e., gain, phase, and symmetry) in individuals presenting with basilar artery migraine, classic migraine, or Meniere's disease (e.g., Olsson, 1991; Kingma et al., 2000; Kuritzky et al., 1981). Olsson (1991) completed rotary chair testing on approximately 50 patients diagnosed with basilar artery migraines and reported that 56.2% of patients evidenced asymmetry, 41.7% evidenced abnormal gain, and 29.2% evidenced abnormal phase. Similarly, Kuritzky et al. (1981) performed rotary chair testing on 20 patients with a diagnosis of either common migraine or classical

migraine and reported that 15 patients evidenced asymmetry with no evidence of abnormalities in gain or phase. Lastly, Kingma et al. (2000) investigated vestibular function in 25 patients diagnosed with Meniere's disease via high frequency head rotation trial. Eighteen of these subjects had been diagnosed with "unilateral definite Meniere's disease" and seven subjects had been diagnosed with "unilateral possible Meniere's disease). These investigators found that 13/18 or 72.2% of the "unilateral definite Meniere's disease" subjects and 4/7 or 57% of the "unilateral possible Meniere's disease" subjects showed a significant phase lag during sinusoidal head rotation from 4 - 6Hz with normal gain values at these test speeds (Kingma et al., 2000). Based upon the results from these three studies, inclusion of phase and symmetry variables in rotary chair testing might be a fruitful area for future research in the differential diagnosis of Meniere's disease and migraine-associated dizziness.

Differences in rotary chair gain values between the two subject groups (Meniere's disease versus migraine-associated dizziness) are speculated to be the result of two different underlying pathophysiologies. The pathophysiology underlying migraine has been speculated to be of central vestibular origin, while the pathophysiology of Meniere's disease has been speculated to be of peripheral vestibular origin. Because the presence of low rotary chair gain values are an indication of a bilateral peripheral vestibular weakness (Shepard & Telian, 1996), we did not anticipate finding low rotary chair gain values in the migraine-associated dizziness group. Results from the current study as well as those reported by Dimitri et al. (2001) found lower rotary chair gain values in the migraine-associated dizziness group in comparison to the Meniere's disease group. Dimitri et al. (2001) speculated

that the lower gain values in the migraine population might be the result of a possible central mechanism responsible for both reduced gain as well as the symptom of motion sickness, which is often associated with migraine. The higher, or normal gain findings within the Meniere's disease group, in contrast are speculated to be the result of fluctuations in gain compensation following unilateral peripheral vestibular loss (Dimitri et al., 2001).

It should also be noted that reductions and/or variability in gain values have been reported to occur as the result of lack of alertness, stress, fatigue and neurological restrictions (Honrubia, 2000; Shepard, 2001). Careful observation of the patient during rotary chair testing is recommended to ensure that decreases in gain values are not due to subject-related artifact (Shepard, 2001).

In individuals with normal function vestibular systems, rotary chair gain values should be lower at low frequencies and increase with increases in the test speed (Goebel et al., 2000; Stockwell & Bojrab, 1997). This pattern of increasing rotary chair gain values as a function of test speed was demonstrated for the vast majority of test speeds for both subject groups (as shown in table 5).

Future Research

Electrocochleography Testing

In spite of the numerous factors affecting its accuracy, calculating the traditional SP/AP amplitude ratio for ECochG testing is still routinely used in the diagnosis of Meniere's disease. Preliminary investigations using both SP/AP area ratios and the traditional SP/AP amplitude ratio appears to substantially increase the sensitivity and specificity of the ECochG, especially in patients with Meniere's

disease. As recommended by Ferraro and Tibbils (1999), however, this new approach needs to be investigated with a larger population of Meniere's disease patients. If in fact this new combined ECochG protocol (SP/AP amplitude ratio and SP/AP area ratio) does prove to be beneficial in the accurate diagnosis of Meniere's disease, than future investigations should also explore whether this combined ECochG protocol would be of benefit in the differential diagnosis of Meniere's disease and migraine-associated dizziness.

Rotary Chair Testing

Several investigators have reported abnormalities in test parameters of rotary chair testing other than gain values in patients with both Meniere's disease and migraine-associated dizziness (Kingma et al., 2000; Kuritzky et al., 1981; Olsson, 1991). Specifically, Kingma et al. (2000) reported the presence of abnormal rotary chair phase lags in conjunction with normal gain values in patients with Meniere's disease. Kuritzky et al. (1981) and Olsson (1991) have also reported directional preponderances, abnormal gain, and abnormal phase values during rotary chair testing in patients with migraine. In the current study, neither phase nor symmetry information were evaluated for either subject group. Given the aforementioned findings, future research in the differential diagnosis of Meniere's disease versus migraine-associated dizziness should include a comparison of not only rotary chair gain values but also phase and symmetry values to determine if one or more of these test parameters is most sensitive in differentiating between these two subject groups.

Future Utility of Rotary Chair Testing

In many clinical practices ENG is frequently the only test utilized in vestibular assessment. Advantages of including rotary chair testing in the assessment of vestibular function are that it: 1.) supplements caloric information by further assessing the peripheral vestibular apparatus over a wider range of frequencies; 2.) confirms clinical findings; 3.) is useful in counseling patients; 4.) evaluates the effectiveness of certain treatments; 5.) expands vestibular assessment and; 6.) has higher test-retest reliability in comparison to caloric testing (Honrubia, 2000; Kingma et al., 2000; Shepard, 2001). The addition of rotary chair testing to vestibular assessment has limitations, however, including cost and knowledge among audiologists and physicians regarding correct interpretation of the results. The cost of purchasing a rotary chair and the appropriate test booth range between approximately $60,000 to $100,000 (Medical Technologies, personal communication, January 11, 2005). Many ENT and audiology practices, however, have the option of sending the patient to an outside facility for rotary chair testing. Many practicing audiologists, however, have little or no experience in correctly administering and interpreting roary chair test results.

Results from the current study indicate that rotary chair testing provides valuable information which is helpful in the assessment and diagnosis of Meniere's disease and migraine-associated dizziness. Since the role of the audiologist is continuing to grow in the area of vestibular assessment and rehabilitation, it is important that the future audiology students receive adequate course work and training in the area of rotary chair testing. Similarly, for audiologists that are currently

practicing in various clinical setting, there is a need for hands-on courses and seminars on this topic, which would enhance their knowledge base in this area.

Bibliography

Anniko, M., & Takumida, M. (2001). Functional morphology of the normal peripheral vestibular system. In A. F. Jahn, & J. Santos-Sacchi (Eds.), *Physiology of the ear* (2nd ed., pp. 481-513). San Diego, CA: Singular.

Anzai, Y., & Lufkin, R. (1996). Laboratory evaluation: III. Imaging. In R. W. Baloh, & G. M. Halmagyi, (Eds.), *Disorders of the vestibular system* (pp. 223-242). New York: Oxford University Press.

Arenburg, I. K. (1993). Meniere's disease: Diagnosis and management of vertigo and endolymphatic hydrops. In I. K. Arenburg (Ed.), *Dizziness and balance disorders* (pp. 503-509). Amsterdam: Kugler.

Baloh, R. W. (1997). Neurotology of migraine. *Headache, 37*, 615-621.

Bamiou, D. E., & Luxon, L. (2003). Medical management of balance disorders and vestibular rehabilitation. In L. Luxon, J. M. Furman, A. Martini, & D. Stephens (Eds.), *Textbook of audiological medicine: Clinical aspects of hearing and balance* (pp. 889-916). London: Martin Dunitz.

Barber, H. O., & Stockwell, C. W. (1980). *Manual of electronystagmography* (2nd ed.). St. Louis, MO: Mosby.

Bear, M. F., Connors, B. W., & Paradiso, M. A. (2001). *Neuroscience: Exploring the brain* (2nd ed.). Baltimore: Lippincott, Williams & Wilkins.

Bear, M. F., Connors, B. W., & Paradiso, M. A. (1996). *Neuroscience: Exploring the brain*. Baltimore: Lippincott, Williams & Wilkins.

Bellis, T. J. (1996). *Central auditory processing disorders: In the educational setting*. San Diego, CA: Singular.

Bellis, T. J. (2003). *Assessment and management of central auditory processing disorders: In the educational setting. From science to practice* (2nd ed.). Canada: Thomson Delmar Learning.

Bhatnagar, S. C., & Andy, O. J. (1995). *Neuroscience: For the study of communicative disorders*. Baltimore: Williams & Wilkins.

Boismier, T. E., & Disher, M. J. (2001). Spontaneous vertigo and headache: Endolymphatic hydrops or migraine? *Ear, Nose & Throat Journal, 80* (12), 881-885.

Brodal, P. (2004). *The central nervous system: Structure and function* (3rd ed.). New York: Oxford University Press.

Bruegel, C. (2003). Staying a step ahead of migraines. *Nursing, 33* (11), 56-58.

Carlson, N. R. (1980). *Physiology of behavior*. Boston: Allyn and Bacon.

Chermak, G. D., & Musiek, F. E. (1997). *Central auditory processing disorders: New perspectives*. San Diego, CA: Singular.

Cohen, B., & Gizzi, M. (2003). The physiology of the vestibulo-ocular reflex. In L. Luxon, J. M. Furman, A. Martini, & D. Stephens (Eds.), *Textbook of audiological medicine: Clinical aspects of hearing and balance* (pp. 701-715). London: Martin Dunitz.

Committee on Hearing and Equilibrium (1995). Committee on Hearing and Equilibrium guidelines for the diagnosis and evaluation of therapy in Meniere's disease. *Otolaryngology Head and Neck Surgery, 113* (3), 181-185.

Conlon, B.J., & Gibson, W.P.R. (2000). Electrocochleography in the diagnosis of Meniere's disease. *Acta Otolaryngologica, 120*, 480-483.

Costa, S. S., Sousa, L. C., & Piza, M. R. (2002). Meniere's disease: Overview, epidemiology, and natural history. *Otolaryngologic Clinics of North America, 35* (3), 455-495.

Cutrer, F. M., & Baloh, R. W. (1992). Migraine-associated dizziness. *Headache, 32*, 300-304.

Dallos, P. (1974). *The auditory periphery: Biophysics and physiology*. New York: Academic Press.

Dallos, P., & Fakler, B. (2002). Prestin, a new type of motor protein. *Molecular Cell Biology, 3*, 104-111.

Devaiah, A. K., Dawson, K. L., Ferraro, J. A., & Ator, A. (2003). Utility of area curve ratio electrocochleography in early Meniere's disease. *Archives of Otolaryngology Head and Neck Surgery, 129*, 547-551.

Diamond, S., & Wenzel, R. (2002). Practical approaches to migraine management. *Drugs, 16* (6), 385-403.

Dieterich, M. D., & Brandt, T. (1999). Episodic vertigo related to migraine (90 cases): Vestibular migraine? *Journal of Neurology, 246*, 883-892.

Dimitri, P. S., Wall C., III, Oas, J. G., & Rauch, S. D. (2001). Application of multivariate statistics to vestibular testing: Discriminating between Meniere's disease and migraine associated dizziness. *Journal of Vestibular Research, 11*, 53-65.

Evans, R. W., & Olesen, J. (2003). Migraine classification, diagnostic, criteria, and testing. *Neurology, 80* (Suppl 2), S24-S30.

Ferraro, J. A., & Durrant, J. D. (2002). Electrocochleography. In J. Katz (Ed.), *Handbook of clinical audiology* (5th ed., pp. 249-273). Philadelphia: Lippincott, Williams & Wilkins.

Ferraro, J. A., & Tibbils, R. P. (1999). SP/AP area ratio in the diagnosis of Meniere's disease. *American Journal of Audiology, 8*, 21-28.

Fetter, M. (2000). Vestibular system disorders. In S. J. Herdman (Ed.), *Vestibular rehabiliation* (2nd ed., pp. 91-102). Philadelphia: F.A. Davis.

Furman, J. M., Marcus, D. A., & Balaban, C. D. (2003). Migrainous vertigo: Development of a pathogenic model and structured diagnostic interview. *Neuro-Opthalmology and Neuro-Otology, 16*, 5-13.

Furman, J. M., & Whitney, S. L. (2000). Central causes of dizziness. *Physical Therapy, 80* (2), 179-187.

Furman, J. M., & Wuyts, F. L. (2003). Clinical application of vestibular laboratory testing. In L. Luxon, J. M. Furman, A. Martini, & D. Stephens (Eds.), *Textbook of audiological medicine: Clinical aspects of hearing and balance* (pp. 735-746). London: Martin Dunitz.

Gelfand, S. A. (1997). *Essentials of audiology*. New York: Thieme.

Gelfand, S. A. (1998). *Hearing: An introduction to psychological and physiological acoustics.* New York: Marcel Dekker.

Ghosh, S., Gupta, A. K., & Mann, S. S. (2002). Can electrocochleography in Meniere's disease be noninvasive? *The Journal of Otolaryngology, 31* (6), 371-375.

Gianoli, G. J. (2001). Fluctuating vestibular disease. In J. A. Goebel (Ed.), *Practical management of the dizzy patient* (pp. 211-224). Philadelphia: Lippincott, Williams & Wilkins.

Gibson, W. P. R., & Arenburg, I. K. (1997). Pathophysiologic theories in the etiology of Meniere's disease. *Otolaryngologic Clinics of North America, 30* (6), 961-967.

Gibson, W. P. R., Moffat, D. A., & Ramsden, R. T. (1977). Clinical electrocochleography in the diagnosis and management of Meniere's disease. *Audiology, 16*, 389-401.

Goebel, J. A. (1993). Understanding eye movements in balance disorders. In I. K. Arenburg (Ed.), *Dizziness and balance disorders: An interdisciplinary approach to diagnosis, treatment and rehabilitation* (pp. 49-55). Amsterdam: Kugler.

Goebel, J. A. (2001). Practical anatomy and physiology. In J. A. Goebel (Ed.), *Practical management of the dizzy patient* (pp. 3-16). Philadelphia: Lippincott, Williams & Wilkins.

Goebel, J. A., Isipradit, P., & Hanson, J. M. (2000). Manual rotation testing of the vestibulo-ocular reflex. *Laryngoscope, 110*, 517-535.

Hain, T. C., Ramaswamy, T. S., & Hillman, M. A. (2000). Anatomy and physiology of the normal vestibular system. In S. J. Herdman (Ed.), *Vestibular rehabilitation* (2nd ed., pp. 3-24). Philadelphia: F.A. Davis.

Hall, J. W., III. (1992). *Handbook of auditory evoked responses*. Boston: Allyn and Bacon.

Halmagyi, G. M., Cremer, P. D., & Curthoys, I. S. (2003). Peripheral vestibular disorders and diseases in adults. In L. Luxon, J. M. Furman, A. Martini, & D. Stephens (Eds.), *Textbook of audiological medicine: Clinical aspects of hearing and balance* (pp. 797-818). London: Martin Dunitz.

Hamid, M. A. (1993). Overview of clinical anatomy and physiology of the vestibular system. In I. K. Arenburg (Ed.), *Dizziness and balance disorders: An interdisciplinary approach to diagnosis, treatment and rehabilitation* (pp. 41-43). Amsterdam: Kugler Publications.

Herdman, S. J., & Tusa, R. J. (1999). *Diagnosis and treatment of benign paroxysmal positional vertigo*. Schaumburg, IL: ICS Medical Corporation.

Highstein, S. M. (1996). How does the vestibular part of the inner ear work? In R. W. Baloh, & G. M. Halmagyi (Eds.), *Disorders of the vestibular system* (pp. 3-11). New York: Oxford University Press.

Honrubia, V. (2000). Quantitative vestibular function tests and the clinical examination. In S. J. Herdman (Ed.), *Vestibular rehabiliation* (2nd ed., pp. 105-165). Philadelphia: F.A. Davis.

Honrubia, V., & Goodhill, V. (1979). Clinical anatomy and physiology of the peripheral ear. In V. Goodhill (Ed.), *Diseases, deafness, and dizziness* (pp. 4-63). Hagerstown, MD: Harper & Row.

Honrubia, V., & Hoffman, L. F. (1997). Practical anatomy and physiology of the vestibular system. In G. P. Jacobson, C. W. Newman, & J. M. Kartush (Eds.), *Handbook of balance function testing* (pp. 9-52). San Diego, CA: Singular.

Johnson, G. D. (1998). Medical management of migraine-related dizziness and vertigo. *Laryngoscope, 108,* 1-28.

Kayan, A., & Hood, J. D. (1984). Neuro-otological manifestations of migraine. *Brain, 107*, 1123-1142.

Keshner, E. A. (2000). Postural abnormalities in vestibular disorders. In S. J. Herdman (Ed.), *Vestibular Rehabiliation* (2nd ed., pp. 52-76). Philadelphia: F.A. Davis.

Kingma, H. (2003). Function and dysfunction of the vestibular system. In L. Luxon, J. M. Furman, A. Martini, & D. Stephens (Eds.), *Textbook of audiological medicine: Clinical aspects of hearing and balance* (pp. 665-670). London: Martin Dunitz.

Kingma, H., Meulenbroeks, A., & De Jong, I. (2000). Vestibular ocular reflexes in Meniere's disease patients evaluated by passive high frequency head rotation (yaw) and sidewards acceleration. *Acta Otolaryngologica, Suppl 544,* 19-26.

Kuritzky, A., Toglia, U. J., & Thomas, D. (1981). Vestibular function in migraine. *Headache, 21*, 110-112.

LaRouere, M. J., Seidman, M. D., & Kartush, J. M. (1997). Medical and surgical treatment of vertigo. In G. P. Jacobson, C. W. Newman, & J. M. Kartush (Eds.), *Handbook of balance function testing* (pp. 337-357). San Diego, CA: Singular.

Lee, H., Lopez, I., Ishiyama, A., & Baloh, R. W. (2000). Can migraine damage the inner ear? *Archives of Neurology, 57,* 1631-1634.

Lipton, R. B., Stewart, W. F., Diamond, S., Diamond, M. L., Reed, M. (2001). Prevalence and burden of migraine in the United States: Data from the american migraine study II. *Headache, 41*, 646-657.

Margolis, R. H., Rieks, D., Fournier, E. M., & Levine, S. E. (1995). Tympanic electrocochleography for diagnosis of Meniere's disease. *Archives of Otolaryngology Head & Neck Surgery, 121*, 44-55.

Martin, J. (1996). *Neuroanatomy: Text and atlas*. Stamford, CT: Appleton & Lange.

Matchar, D. B. (2003). Acute management of migraine: Highlights of the US Headache Consortium. *Neurology, 60* (Suppl 2), S21-S23.

Mattox, D. E. (2000). Surgical management of vestibular disorders. In S. J. Herdman (Ed.), *Vestibular Rehabilitation* (2nd ed. , pp. 251-263). Philadelphia: F.A. Davis.

Merchant, S. N. (1999). A Method for quantitative assessment of vestibular otopathology. *Laryngoscope, 109*, 1560-1569.

Olsson, J. E. (1991). Neurotologic findings in basilar migraine. *Laryngoscope, 101*: 1-42.

Parker, W. (1995). Meniere's disease: Etiological considerations. *Archives of Otolaryngology Head & Neck Surgery, 12*, 377-382.

Part one: The primary headaches (2004). *Cephalalgia, 24* (Suppl 1), 23-136.

Phillips, D. P. (2001). Introduction to the central auditory nervous system. In A. F. Jahn, & J. Santos-Sacchi (Eds.), *Physiology of the Ear (*2nd ed., pp. 613-638). San Diego, CA: Singular.

Paparella, M. M., & Djalilian, H. R. (2002). Etiology, pathophysiology of symptoms, and pathogenesis of Meneire's disease. *Otolaryngology Clinics of North America, 35* (3), 529-545.

Pickles, J. O. (1988). *An Introduction to the physiology of hearing*. San Diego, CA: Academic Press.

Radtke, A., Lempert, T., Gresty, M. A., Brookes, G. B., Bronstein, A. M., & Neuhauser, H. (2002). Migraine and Meniere's disease: Is there a link? *Neurology, 59*, 1700-1704.

Rappaport, J. M., & Provencal, C. (2002). Neuro-otology for audiologists. In J. Katz (Ed.), *Handbook of clinical audiology* (5th ed., pp. 9-32). Philadelphia: Lippincott, Williams & Wilkins.

Reploeg, M. D. & Goebel, J. A. (2002). Migraine-associated dizziness: Patient characteristics and management options. *Otology & Neurotology, 23*, 364-371.

Rubin, W. (1993). Differential diagnosis of disorders causing dizziness. *The American Journal of Otology, 14* (3), 309-312.

Rubin, W., & Brookler, K. H. (1991). *Dizziness: Etiologic approach to management*. New York: Thieme.

Ryan, A. F. (1999). The pathophysiology of Meniere's disease. In J. P. Harris (Ed.), *Meniere's Disease* (pp. 169-174). New York: Kugler.

Ryan, A. F. (2002). New views of cochlear function. In M. S. Robinette, & T. J. Glattke (Eds.), *Otoacoustic emissions: Clinical applications* (pp. 48-73). New York: Thieme.

Sass, K. (1998). Sensitivity and specificity of transtympanic electrocochleography in Meniere's disease. *Acta Otolaryngologica, 118*, 150-156.

Scaravilli, F. (2003). The pathology of the vestibular system. In L. Luxon, J. M. Furman, A. Martini, & D. Stephens (Eds.), *Textbook of audiological medicine: Clinical aspects of hearing and balance* (pp. 641-664). London: Martin Dunitz.

Schubert, M. C., & Minor, L. B. (2004). Vestibulo-ocular physiology underlying vestibular hypofunction. *Physical Therapy, 84* (4), 373-385.

Schuknecht, H. (1974). *Pathology of the ear*. Cambridge, MA: Harvard University Press.

Schuknecht, H. (1981). The pathophysiology of Meniere's disease. In K. H. Vosteen, H. Schuknecht, C. R. Pfaltz, J. Wersall, R. S. Kimura, C. Morgenstern, & S. K. Juhn (Eds.), *Meniere's disease: Pathogenesis, diagnosis, and treatment* (pp. 10-15). New York: Thieme-Stratton Inc.

Selmani, Z., Marttilla, T. I., Pyykko, I., & Ishizaki, H. (2002). Evaluation of cochlear outer hair cell function by evoked otoacoustic emission and electrocochleography in patients with Meneire's disease and other cochlear disorders. *Journal of Audiological Medicine, 11*(1), 35-45.

Shepard, N. T. (2001). Rotational chair testing. In J. A. Goebel (Ed.), *Practical management of the dizzy patient* (pp. 129-141). Philadelphia: Lippincott, Williams & Wilkins.

Shepard, N. T. (2002). Evaluation and management of balance system disorders. In J. Katz (Ed.), *Handbook of clinical audiology* (5th ed., pp. 407-439). Philadelphia: Lippincott, Williams & Wilkins.

Shepard, N. T., & Telian, S. A. (1996). *Practical management of the balance disorder patient*. San Diego, CA: Singular.

Stockwell, C. W., & Bojrab, D. I. (1997). Background and technique of rotational testing. In G. P. Jacobson, C. W. Newman, & J. M. Kartush (Eds.), *Handbook of balance function testing* (pp. 237-248). San Diego, CA: Singular.

Thakar, A., Anjaneyelu, C., & Deka, C. (2001). Vertigo symptoms and mechanisms in migraine. *The Journal of Otolaryngology & Otology, 115*, 782-787.

Thai-Van, H., Bounaix, M. J., & Fraysse, B. (2001). Meniere's disease: Pathophysiology and treatment. *Drugs, 61* (8), 1089-1102.

Tusa, R. J. (2000). Diagnosis and management of neuro-otological disorders due to migraine. In S. J. Herdman (Ed.), *Vestibular Rehabiliation* (2nd ed., pp. 298-313). Philadelphia: F.A. Davis.

Viirre, E. S. & Baloh, R. W. (1996). Migraine as a cause of sudden hearing loss. *Headache, 36*, 24-28.

Welch, K. M., Cutrer, M., & Goadsby, P. J. (2003). Migraine pathogenesis: Neural and vascular mechanisms. *Neurology, 60* (Suppl 2), S9-S14.

Wilson, W. J., & Bowker, C. A. (2002). The effects of high stimulus rate on the electrocochleogram in normal hearing subjects. *International Journal of Audiology, 41*, 509-517.

Wright, C. G., & Schwade, N. D. (2000). Anatomy and physiology of the vestibular system. In R. J. Roesser, M. Valente, & H. Hosford-Dunn (Eds.), *Audiology diagnosis* (pp. 73-84). New York: Thieme.

Wuyts, F. L., Furman, J. M., & Van de Heyning, P. (2003). Instrumentation and principles of vestibular testing. In L. Luxon, J. M. Furman, A. Martini, & D. Stephens (Eds.), *Textbook of audiological medicine: Clinical aspects of hearing and balance* (pp.717-734). London: Martin Dunitz.

Wuyts, F. L., Van De Heyning, P. H., Van Spaendonck, M. P., & Molenberghs, G. (1997). A review of electrocochleography: Instrumentation settings and meta-analysis of criteria for diagnosis of endolymphatic hydrops. *Acta Otolaryngologica, Suppl 526*, 14-20.

Yellin, M. W. (2000). Assessment of vestibular function. In R. J. Roeser, M. Valente, & H. Hosford-Dunn (Eds.), *Audiology diagnosis* (pp. 571-589). New York: Thieme.

Yost, W. A. (2000). *Fundamentals of Hearing*. San Diego, CA: Academic Press.

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Educational Background:

Graduate	Au.D.	Towson University Doctor of Audiology Program GPA 3.77/4.0	May 2005, expected
Undergraduate	B.S.	Towson University Speech Language Pathology and Audiology Program GPA 3.87/4.0 overall; 3.93/4.0 major	2001

Academic Honors:

- Maryland Academy of Audiology Doctoral Scholarship 2001
- Dean's List Central Missouri State University 1997-2000
- Dean's List Towson University 2000-2001

Clinical Experience:

Towson University (January 2002 – December 2002)
Basic audiological evaluation, hearing aid selection and fitting, electrophysiologic testing, and hearing conservation of adults, children and special populations.

Towson ENT (January 2003 – May 2003)
Skills utilized include basic audiological evaluation, hearing aid selection and use, electrophysiologic testing, and testing and management of vestibular function of adults, children, and special populations. Located in Good Samaritan and Union Memorial Hospital, Baltimore, MD.

Anne Arundel County Department of Health (May 2003 – July 2003)
Skills utilized include basic audiological evaluation, hearing aid selection and fitting, and OAE testing of the pediatric population.

University of Maryland Medical System (September – December 2003)
Skills utilized include basic audiological evaluation, hearing aid selection and fitting, newborn hearing Screening (ABR and OAE), electrophysiologic testing including ABR, ECoG and OAE, and testing and management of vestibular function including ENG, posturography, and rotary chair of adults, children, and special populations.

Au.D. Externship:

ENT Specialties, P.C. (January 2004 – January 2005)
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Research Experience:

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Research in the differential diagnosis of Meniere's disease and migraine associated dizziness through analysis of ECoG and rotary chair testing results.