DEMYSTIFYING THE DIAGNOSTIC POTENTIALS OF AIR-CONDUCTED OCULAR AND CERVICAL VESTIBULAR EVOKED MYOGENIC POTENTIAL TEST ELICITED BY A CUSTOM-BUILT CHIRP STIMULUS AMONG PATIENTS WITH VESTIBULAR DISORDERS

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by

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LIST OF SYMBOLS

ms	Millisecond
%	Percent
n	Number
µV	Microvolt
°	Degree

LIST OF ABBREVIATIONS

BPPV	Benign Paroxysmal Positional Vertigo
SCDS	Superior Canal Dehiscence Syndrome
VM	Vestibular Migraine
ENG	Electro Nystagmography
VNG	Video Nystagmography
vHIT	video Head Impulse Test
cVEMP	Cervical Vestibular Evoked Myogenic Potential
oVEMP	Ocular Vestibular Evoked Myogenic Potential
VEMP	Vestibular Evoked Myogenic Potential
SCM	Sternocleidomastoid Muscle
ACS	Air Conducted Stimulation
BCV	Bone Conducted Vibration
ABR	Auditory Brainstem Response
VD group	Vestibular Disorder group
ASSR	Auditory Steady State Response
USM	Universiti Sains Malaysia
VOR	Vestibulo-Ocular Reflex
VSR	Vestibulo-Spinal Reflex
VCR	Vestibulo-Collic Reflex
dB	Decibels
dB nHL	Decibels above Normal Hearing Level
dB SPL	Decibel Sound Pressure LeveL
Hz	Hertz
PTA	Pure Tone Audiometry
EMG	Electro-MyoGraphy
ROC	Receiver Operating Characteristics

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DEMISTIFIKASI POTENSI DIAGNOSTIK UJIAN *OCULAR AND CERVICAL VESTIBULAR EVOKED MYOGENIC POTENTIAL TEST* MELALUI KONDUKSI UDARA YANG DIRANGSANGKAN OLEH *CHIRP* STIMULUS DALAM KALANGAN PESAKIT BERMASALAH *VESTIBULAR*

ABSTRAK

Vestibular evoked myogenic potential (VEMP) merupakan kaedah klinikal untuk menilai fungsi organ otolith. VEMP biasanya direkod menggunakan 500 Hz *tone-burst*, walau bagaimanapun, rangsangan *chirp*, pada awalnya direka untuk respons auditori batang otak, sedang digunakan untuk meneroka potensi dalam VEMP. Kajian ini meneroka potensi diagnostik rangsangan konduksi udara *downward narrowband chirp* dalam mengesan masalah vestibular menggunakan *cervical VEMP* (cVEMP) dan *ocular VEMP* (cVEMP). Pada peringkat permulaan, dua kajian rintis melibatkan 25 orang dewasa yang sihat dijalankan untuk merekod cVEMP (Pilot 1) and 35 orang dewasa yang sihat untuk merekod oVEMP (Pilot 2) untuk mengenalpasti rangsangan *chirp* yang optimum. Rangsangan yang optimum daripada kajian rintis kemudian dibandingkan dengan rangsangan 500 Hz *tone-burst* dalam respons cVEMP dan oVEMP dalam kajian kes-kawalan. Ujian cVEMP telah dijalankan ke atas 55 dewasa yang sihat dengan purata umur 29.5 ± 9.1 tahun dan 43 pesakit bermasalah vestibular dengan purata umur 41.6 ± 8.9 tahun. Sebaliknya, ujian oVEMP dijalankan ke atas 60 orang dewasa yang sihat dengan purata umur 28.0 ±7.3 tahun dan 28 pesakit bermasalah vestibular dengan purata umur 41.5 ±8.5 tahun. Dua kajian rintis telah mendedahkan ransangan (1000-100) Hz *chirp* menghasilkan amplitud yang signifikan tinggi dan latensi yang signifikan pendek bagi P1 dan N1 kedua-dua cVEMP dan oVEMP berbanding dengan rangsangan (1000-500) Hz *chirp* ($p<0.05$). Rangsangan

(1000-100) Hz *chirp* dipilih untuk digunakan dalam kajian seterusnya. Keputusan mendedahkan rangsangan (1000-100) Hz *chirp* menghasilkan latensi pendek yang signifikan dan amplitud tinggi yang signifikan berbanding dengan rangsangan 500 Hz *tone-burst* dalam ujian cVEMP ($p<0.05$). Begitu juga, rangsangan *chirp* menghasilkan latensi yang signifikan pendek bagi P1 dan N1 berbanding dengan rangsangan 500 Hz *tone-burst* dalam ujian oVEMP ($p<0.05$). Analisis lengkung operasi penerima (ROC) menunjukkan pencapaian rangsangan *chirp* terbaik untuk mengenalpasti pesakit dengan masalah vestibular. Rangsangan *chirp* mendedahkan kawasan di bawah lengkung (AUC), sensitiviti dan spesifisiti adalah lebih tinggi bagi kedua-dua ujian cVEMP dan oVEMP berbanding rangsangan *tone-burst* dalam mengenalpasti pesakit yang bermasalah vestibular. Bagi cVEMP, sensitiviti dan spesifisiti rangsangan *chirp* masing-masing berada dalam julat 60.8% hingga 88.2% dan 38.7% hingga 87.7% melebihi *tone burst* (sensitiviti 51.5% hingga 89.7%, spesifisiti 40.3% hingga 87.4%). Begitu juga, sensitiviti dan spesifisiti bagi *chirp* oVEMP, adalah 71.4% hingga 100% dan 32.0% hingga 95.2%, menonjol berbanding *tone-burst*, sensitiviti berada dalam julat 38.0% hingga 78.4% dan spesifisiti beerada dalam dalam julat 11.5% hingga 94.1%. Sebagai kesimpulan, berbanding dengan rangsangan konvensional 500 Hz *tone-burst*, rangsangan (1000-100) Hz *chirp* mempunyai kebolehan diagnostik yang lebih baik dalam mengenalpasti pesakit bermasalah vestibular. Disebabkan hasil yang dijanjikan, rangsangan ini boleh menjadi rangsangan alternatif untuk merekod cVEMP dan oVEMP dalam latihan klinikal.

DEMYSTIFYING THE DIAGNOSTIC POTENTIALS OF AIR-CONDUCTED OCULAR AND CERVICAL VESTIBULAR EVOKED MYOGENIC POTENTIAL TEST ELICITED BY A CUSTOM-BUILT CHIRP STIMULUS AMONG PATIENTS WITH VESTIBULAR DISORDERS

ABSTRACT

The vestibular evoked myogenic potential (VEMP) is a clinical method to assess the function of otolith organs. VEMP is typically recorded with the 500 Hz tone burst, however, a chirp stimulus, initially designed for auditory brainstem responses, is being used to explore VEMP's diagnostic potential. This study explores the diagnostic potential of an air conducted downward narrowband chirp stimulus in detecting vestibular disorders using cervical VEMP (cVEMP) and ocular VEMP (oVEMP). In the initial stage, two pilot studies involving 25 healthy adults for cVEMP (Pilot 1) and 35 healthy adults for oVEMP (Pilot 2) were conducted to identify the optimal chirp stimulus. The optimal stimulus from the pilot studies was then compared with the 500 Hz tone burst stimulus in cVEMP and oVEMP responses in the subsequent case control experiment. The cVEMP testing was conducted on 55 healthy adults with a mean age of 29.5 ± 9.1 years and 43 patients with vestibular disorders with a mean age of 41.6 ± 8.9 years. On the other hand, the oVEMP testing was performed on 60 healthy adults with a mean age of 28.0 ± 7.3 years and 28 patients with vestibular disorders with a mean age of 41.5 ± 8.5 years. The two pilot studies revealed that the (1000-100) Hz chirp stimulus produced significantly higher amplitudes and shorter latencies of P1 and N1 for both cVEMP and oVEMP compared to the (1000-500) Hz chirp stimulus ($p < 0.05$). The (1000-100) Hz chirp stimulus was chosen to be used in the subsequent study. Results revealed that the (1000-100) Hz

chirp stimulus generated significantly shorter latencies and larger amplitudes than the 500 Hz tone burst stimulus in the cVEMP testing (p <0.05). Likewise, the chirp stimulus elicited significantly shorter P1 and N1 latencies compared to the 500 Hz tone burst in the oVEMP testing (p <0.05). Receiver operating characteristic (ROC) analysis demonstrated the superior performance of the chirp stimulus for identifying patients with vestibular disorders. The chirp stimulus revealed a higher area under the curve (AUC), sensitivity, and specificity for both cVEMP and oVEMP tests compared to the tone burst. For cVEMP, the chirp's sensitivity ranged from 60.8% to 88.2%, and specificity from 38.7% to 87.7%, exceeding those of the tone burst (sensitivity: 51.5% to 89.7%, specificity: 40.3% to 87.4%). Similarly, oVEMP chirp's sensitivity and specificity were 71.4% to 100.0% and 32.0% to 95.2%, respectively, surpassing those of the tone burst with sensitivity ranged from 38.0% to 78.4%, and specificity ranged from 11.5% to 94.1%. In conclusion, compared to the conventional 500 Hz tone burst stimulus, the (1000-100) Hz chirp stimulus has better diagnostic abilities to identify patients with vestibular disorders. Due to its promising outcomes, this stimulus can be an alternative stimulus for recording cVEMP and oVEMP in clinical practice.

CHAPTER 1

INTRODUCTION

1.1 Research background

The vestibular system provides a sense of balance in addition to information about body position, allowing rapid compensatory movements in response to both self-inflicted and external forces. Despite the fact that we are usually unaware of its function, the vestibular system is an important component of both postural reflexes and eye movements. If the system is compromised, it affects balance, control of eye movements, and a sense of orientation in space. Serious symptoms, including vertigo, nausea, floating sensations, imbalance, and other types of dizziness, would occur in those with vestibular problems (Yoo & Mihaila, 2022).

1.1.1 Anatomy and physiology of the vestibular system

The inner ear is located within the petrous temporal bone. It consists of the cochlea, three semicircular canals that are sensitive to angular accelerations (head rotations), and the otolith organs (utricle and saccule), which are sensitive to linear acceleration, gravitational forces, and tilting of the head, as illustrated in Figure 1.1 (Yoo & Mihaila, 2022).

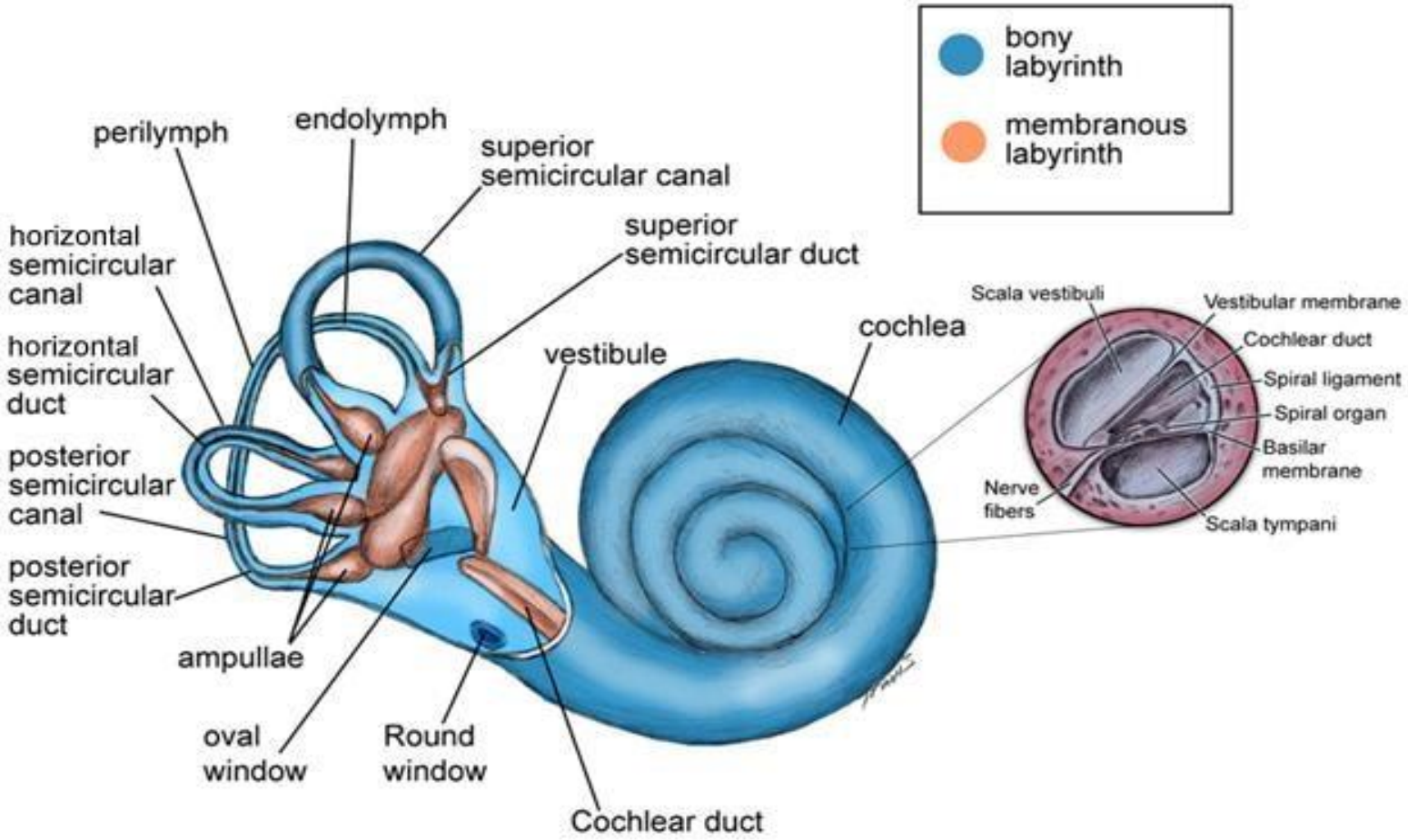

Figure 1.1 Anatomy of the vestibular system. The figure was adapted from the website of Medscape (Lee et al., 2016).

The crista ampullaris is the sensory neuroepithelium of the semicircular canals, whereas the macula is the sensory neuroepithelium of the utricle and saccule. Both neuroepithelial structures contain sensory cells known as hair cells. Each hair cell has numerous stereocilia on its apical ends, which are arranged in rows according to their length, and a single kinocilium on the lateral most end of the apical surface. When the head is turned, the endolymph moves, which causes the stereocilia to bend. This can cause either depolarization or hyperpolarization, depending on how the stereocilia bend (see Figure 1.2).

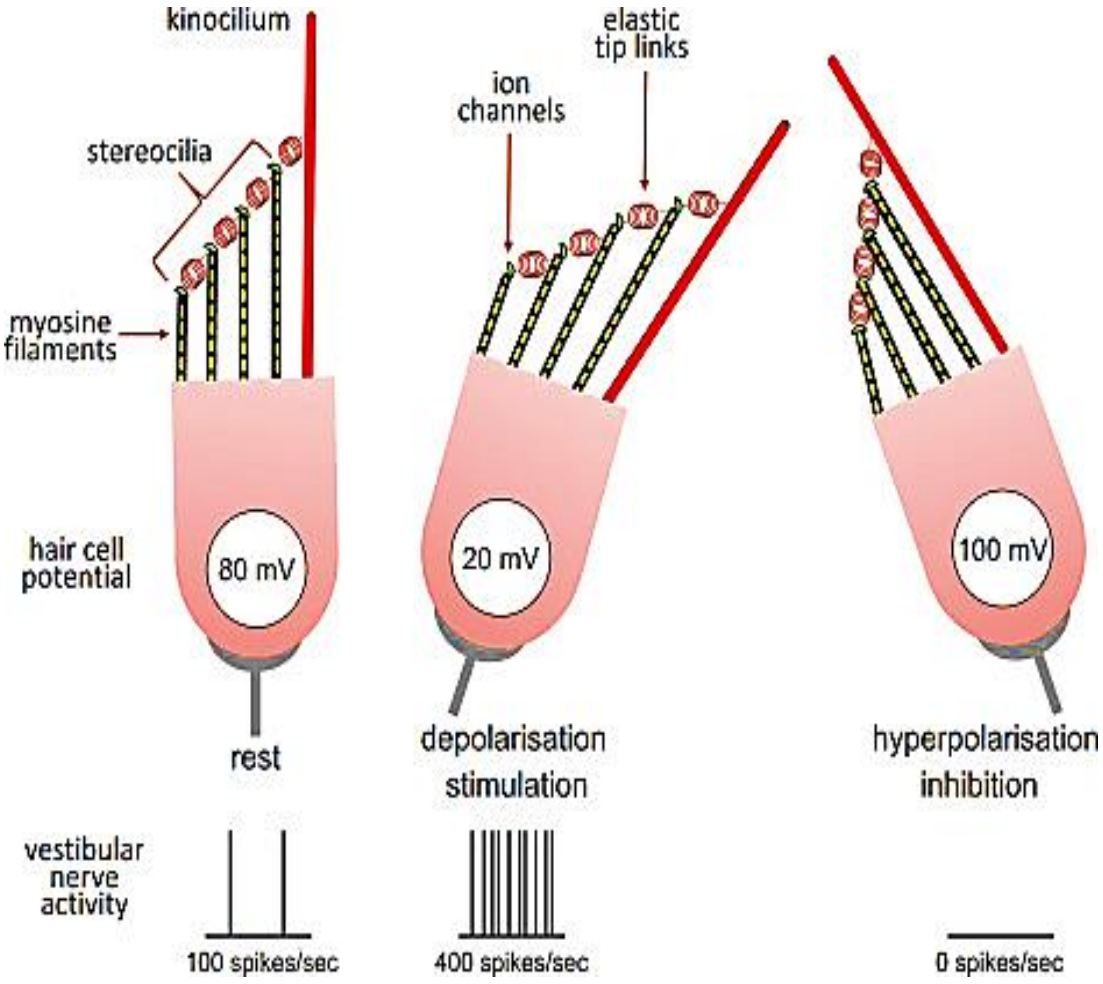

Figure 1.2 The hair cell of the vestibular system. Adapted from (Kingma & van de Berg, 2016).

The vestibular nerve is formed when the Scarpa ganglion's afferent axons connect. Following that, the vestibular nerve and the cochlear nerve fuse to form the vestibulocochlear nerve (8th cranial nerve). Which, in turn, transmits the neural impulses to the vestibular nucleus complex in the brainstem, where they are processed. After that, the central system unifies all the nerve signals coming from the ear, eye, head, and body to send them to either the thalamus, cortex, or cerebellum to control balance and orientation (Casale et al., 2020).

1.1.2 Vestibular assessment

Previous research has revealed a wide range of reported vestibular disorders, ranging from 6.1 percent to 35.4 percent (Nakashima et al., 2016). Vestibular dysfunctions may impair postural control, balance, and visual stability in this population. Vestibular disorders can be classified as peripheral, central, or mixed vestibular disorders. The most common peripheral vestibular disorders that affect the balance organs in the inner ear include benign paroxysmal positioning vertigo (BPPV), Meniere's disease, vestibular neuritis, and superior canal dehiscence syndrome (SCDS). Central problems, on the other hand, affect the parts of the central nervous system that communicate with one another to maintain balance, such as brainstem vascular disease, acoustic neuromas, tumors of the brainstem or cerebellum, multiple sclerosis, and vestibular migraine (VM) (Balance & Dizziness Canada, 2021).

Assessment and diagnosis of vestibular disorders are made through clinical examinations (such as the dix hallpike test, side lying test (Semont Diagnostic Maneuver), head thrust test, etc.), objective tests (electro/video-nystagmography [ENG or VNG], rotary chair, video head impulse testing [vHIT], cervical/ocular vestibular evoked myogenic potential [cVEMP/oVEMP], etc.), and subjective tests (dizziness handicap inventory [DHI], vertigo symptom scale [VSS], and so on). These

tests are conducted to pinpoint the site of lesions so that proper treatments can take place to minimise the negative consequences of vestibular disorders.

1.1.2(a) Vestibular evoked myogenic potential (VEMP)

In clinical settings, the functions of semicircular canals are conveniently measured by established clinical assessments such as VNG, rotary chair, and vHIT tests. On the other hand, limited clinical assessments are available to measure the function of the otolith organs (saccule and utricle), which can also be compromised due to specific lesions affecting the vestibular system. The VEMP tests are the only assessments that can measure the function of the otolith organs objectively. The cVEMP is one of the major subtypes of VEMP used to measure the function of the ipsilateral saccule and inferior vestibular nerve from the sternocleidomastoid muscle (SCM). The cVEMP waveform consists of two prominent peaks: a positive peak (P1) with a latency of around 13 ms, followed by a negative peak (N1) with a latency of around 23 ms. Another subtype is oVEMP, which is obtained from the inferior oblique eye muscle to reflect the function of the contralateral utricle and superior vestibular nerve. The N1 or N10 response should be around 10 ms and the P1 around 13 ms (Hain & Cherchi, 2021; Dlugaiczyk et al., 2020).

VEMP can be elicited through the use of air conducted stimulation (ACS) via insert earphones or bone conducted vibration (BCV) with a vibrating transducer, similar to the auditory portion of the ear. When exposed to a specific sound or vibration intensity, a brief stimulus has the ability to stimulate a muscle reflex, which originates from the vestibular organ (Fredén Jansson et al., 2021).

1.1.2(a)(i) Sensitivity and specificity of VEMP

Sensitivity and specificity values can be used as guidelines to identify the accuracy of the VEMP test. The proportion of persons who are true positive for the

disease in the entire population of people who have the disease is determined by sensitivity, which is expressed as a percentage, whereas specificity represents the probability of a negative test result in those who do not have the disease (Šimundić, 2009).

The percentage of abnormal VEMP results in vestibular neuritis varied from 36.6 to 80 percent. Whereas in Meniere's disease studies, there was a significant link between the existence of VEMP abnormalities and the presence of Meniere's disease, with amplitude reduction being the most common finding. In patients with BPPV, cVEMP abnormalities ranged from 30–50 % (Godha et al., 2020; Scarpa et al., 2019). The VEMP responses were also found to be abnormal in SCDS, and the reported sensitivity and specificity were 86.5% and 87.8%, respectively (Tran et al., 2020).

1.1.2(a)(ii) Stimulus issues in VEMP recording

Normative data for the specified population is required prior to implementing the VEMP test in clinical settings. Even so, the type of stimulus has a substantial impact on the VEMP normative data. This is due to the fact that responses change based on the nature of the stimulus (Choi, 2020).

Whether in a clinical situation or for scientific investigation, a 500 Hz tone burst is typically utilised to record VEMP because it reliably elicits responses with large amplitudes, making it applicable to the testing of both healthy individuals and patients suffering from vestibular disorders (Özgür et al., 2015). Although VEMP recordings may be made with tone bursts of different frequencies (250 Hz, 1 kHz, 2 kHz, etc.), their amplitudes are significantly lower than those of the 500 Hz tone burst (Cebulla & Walther, 2019).

Click stimulus offer the advantage of shorter latencies compared to the 500 Hz tone burst stimulus (Cheng et al., 2003; Wu et al., 2007). However, click stimulus produces significantly smaller VEMP amplitudes (Viciana & Lopez-Escamez, 2012).

Initially, upward chirp stimulus was created and studied to enhance the waveforms of the auditory brainstem response (ABR) testing. Mathematically devised chirp stimulus can overcome the cochlear travelling wave delay, resulting in larger ABR amplitudes and shorter latencies compared to the traditional click stimuli (Zakaria et al., 2017). The diagnostic utility of VEMP when evoked by CE chirp stimulus has attracted increasing attention in recent years (Aydın et al., 2021; Ocal et al., 2021; Moinudeen et al., 2020).

Early studies compared cVEMP responses elicited by click, tone burst, and upward chirp stimuli (Özgür et al., 2015; Wang et al., 2013). These studies employed wide frequency range upward chirp stimuli, finding shorter latencies and comparable amplitudes to tone bursts.

Recent research explored the use of narrowband upward chirp stimuli. Walther & Cebulla (2016) observed the largest cVEMP amplitudes with a 250-1000 Hz chirp in healthy subjects. Interestingly, this stimulus also yielded the longest latencies, a finding corroborated by their subsequent study (Cebulla & Walther, 2019).

Similar to cVEMP, the chirp stimulus is gaining interest for oVEMP testing. Early research indicates that chirp stimuli can elicit larger oVEMP amplitudes compared to tone burst (Bas et al., 2020; Aydın et al., 2021). However, further investigation is needed to determine the optimal chirp parameters for oVEMP testing and to compare its performance to other stimulus types across various clinical applications.

It is worth mentioning that all published studies on chirp-evoked VEMP were carried out using an upward chirp stimulus, i.e., the frequencies are arranged from low to high (e.g., 250–1000 Hz). In 2016, Syahirah and Mohd Normani developed a novel custom-built downward chirp stimulus (1000–100 Hz, i.e., arranged from high to low frequencies), and its usefulness was studied accordingly. Interestingly, the custom-built downward narrowband chirp stimulus was found to produce the most optimal cVEMP responses (i.e., the largest amplitudes and shorter latencies) compared to the upward narrowband chirp stimulus (100–1000) Hz and the 500 Hz tone burst among healthy subjects (KH & Zakaria, 2016). Figure 1.3 illustrates the waveform of the upward and downward chirp. It can be seen that the arrangement of frequencies from low to high in the upward chirp leads to a longer rise time compared to the downward chirp, which has a frequency arrangement from high to low, which leads to a faster rise time as the full amplitude is reached more quickly.

These findings highlight the complex interplay between stimulus type and VEMP responses. Further investigation is needed to optimize stimulus parameters for improved diagnostic accuracy and utility in diverse clinical scenarios. This will allow clinicians to select the most appropriate stimulus for each individual patient, ensuring reliable and accurate VEMP testing for vestibular disorders.

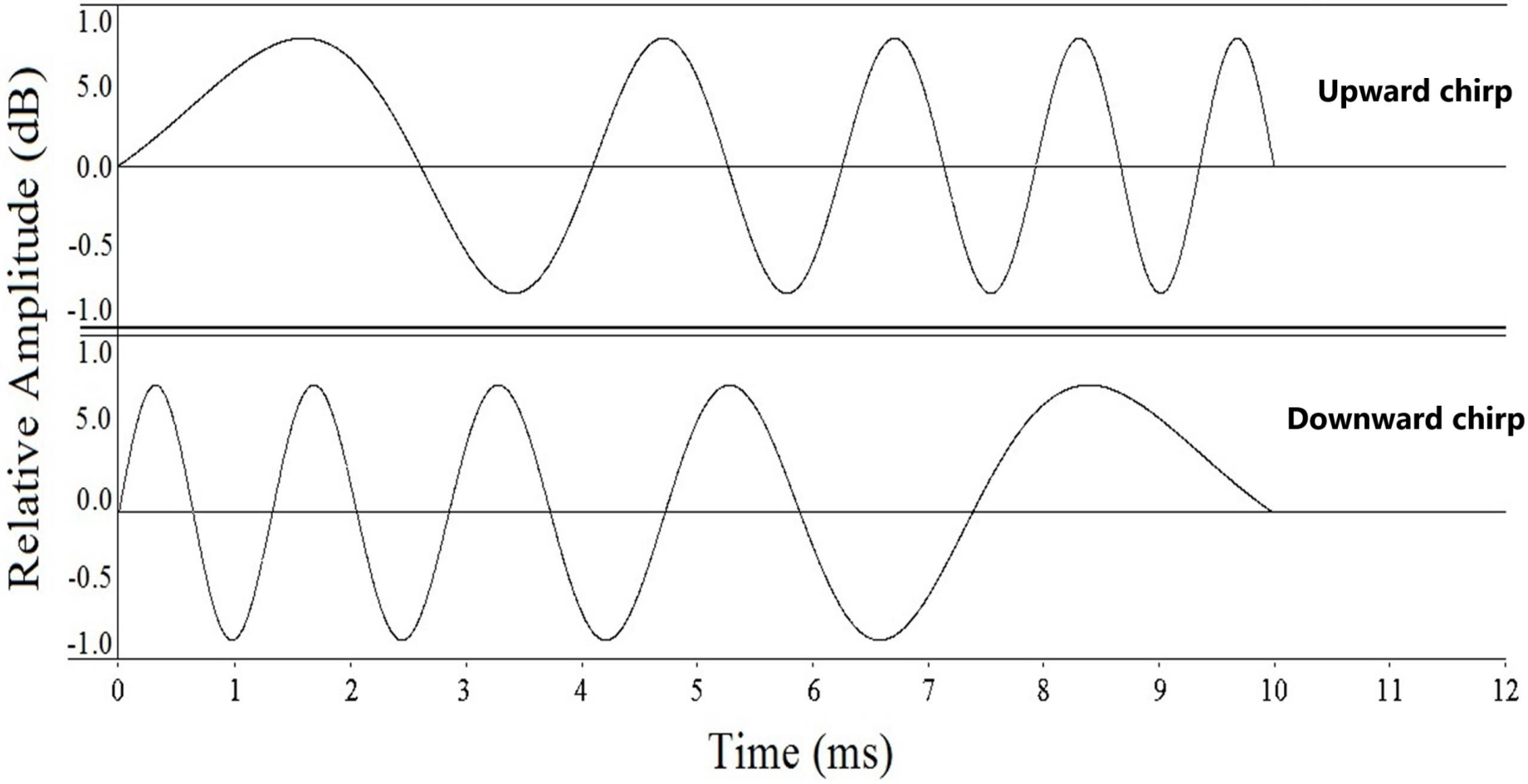

Figure 1.3 Waveform of the upward and downward chirp.

1.2 Problem statement

Vestibular disorders occur in a relatively wide range of adults, significantly impacting daily life and quality of life (Agrawal et al., 2018). Historically, many of the common vestibular tests in clinical settings only assess the functions of the semicircular canals through VOR evaluation. With the advancement of research in cVEMP and oVEMP, it is now possible to objectively assess the status of the otolith organs in clinical practice. It is worth mentioning that despite the VEMP test holding promise as a diagnostic tool for the vestibular disorder, its accuracy for vestibular disorders remains inconsistent, with sensitivity and specificity ranging from 16.7%–90% and 36%–100%, respectively (Egami et al., 2013; Lamounier et al., 2017; Kim-Lee et al., 2009; Chen et al., 2016; Salviz et al., 2016; Lee et al., 2013; Singh & Apeksha, 2015; Kim et al., 2015).

This inconsistency highlights the need for further research to improve the diagnostic accuracy of VEMP testing. Contributing factors include the type of vestibular disorders, variations in recording parameters, and the potential for different stimuli to elicit varying responses (Scarpa et al., 2019).

While the 500 Hz tone burst remains the gold standard in clinical settings to record VEMP due to its consistent and robust response characteristics, particularly its large amplitude, the upward chirp stimulus has emerged as a promising alternative. Its ability to produce larger ABR amplitudes in auditory tests raises the possibility of similar benefits for VEMP recording.

Some studies found larger VEMP amplitudes and shorter VEMP latencies when tested with the chirp stimulus, while contradictory outcomes were reported by others. The disagreements between the studies might be contributed by different types

of upward chirp used in the respective studies. In this regard, further investigation is crucial to determine the optimal chirp stimulus parameters for VEMP recording. Furthermore, the literature on the performance of chirp-evoked VEMP test when testing patients with vestibular disorders is notably lacking. It is intriguing to mention that, apart from its robust and large amplitude, the sensitivity and specificity of the stimulus are important in ensuring a better diagnosis.

Encouraged by Syahirah and Mohd Normani's (2016) finding that downward chirps elicit larger VEMP responses, this study investigates the diagnostic value of downward narrowband chirp in patients with vestibular disorders. Additionally, it is also unknown which type of downward narrowband chirp stimulus is the most optimal to record VEMP. In this respect, conducting a pilot study would be beneficial to compare two different downward chirp stimuli with different frequency content (1000–100 Hz versus 1000–500 Hz). The chirp stimulus that produces the optimum VEMP responses (i.e., larger amplitudes) will be chosen and used in the subsequent phase of the study.

Our downward chirp design, starting at 1 kHz and reaching 100 Hz or 500 Hz, strategically targets the frequency range essential for both saccular and utricular function. The saccule is most sensitive to frequencies below 1 kHz, with most individuals around (250-500) Hz (Townsend & Cody, 1971). Conversely, utricular function is best reflected by stimuli around 100 Hz (Todd et al., 2008). Therefore, including 100 Hz in the wider range (1000-100) Hz ensures stimulation within the optimal range for both the saccule and utricle. This broad stimulation across the known sensitive range of these organs increases the likelihood of activating a sufficient number of hair cells, maximizing the chance of eliciting a measurable VEMP response. Additionally, the narrower range (1000-500) Hz focuses on the specific frequency (500

Hz) where previous research has shown stronger saccular VEMP responses, allowing for a more targeted exploration of saccular function within this key range (Murofushi et al., 1999).

The cVEMP and oVEMP provide complementary information about the saccular and utricular otolithic functions, as the testing of the oVEMP and cVEMP allows the crossed vestibulo-ocular reflex and ipsilateral sacculo-collic reflex to be determined. Therefore, conducting these tests together may increase the sensitivity and specificity of detecting vestibular disorders.

1.3 Objective of the study

VEMP (oVEMP and cVEMP) have a pathway that includes the saccule and utricle, vestibular nerve, vestibular nucleus, and vestibulospinal tract. Therefore, in patients with vestibular disorder, oVEMP and cVEMP may show abnormal findings. So, the study attempts to achieve the following objectives:

1.3.1 General objective

To examine the usefulness of the oVEMP and cVEMP evoked by the downward narrowband chirp stimulus in detecting vestibular disorders.

1.3.2 Specific objectives

1. To compare the cVEMP results between two different downward narrowband chirp stimuli (1000–100 Hz and 1000–500 Hz) among healthy adults (within-group comparisons) (Pilot Study 1).
2. To compare the oVEMP results between two different downward narrowband chirp stimuli (1000–100 Hz and 1000–500 Hz) among healthy adults (within-group comparisons) (Pilot Study 2).

3. To compare oVEMP and cVEMP results between the (1000–100) Hz downward narrowband chirp stimulus and the 500 Hz tone burst in healthy individuals (within-group comparisons).
4. To compare oVEMP and cVEMP results between the (1000–100) Hz downward narrowband chirp stimulus and the 500 Hz tone burst in vestibular disorder (VD) group (within-group comparisons).
5. To compare oVEMP and cVEMP results between healthy and VD groups for each stimulus (between-group comparisons).
6. To determine the sensitivity and specificity of the oVEMP and cVEMP in detecting vestibular disorders for each stimulus.
7. To determine the overall sensitivity and specificity of the combined oVEMP and cVEMP findings in detecting vestibular disorders for each stimulus.

1.4 Research questions

Based on the objectives, the present study aimed to answer the following research questions:

1. Are the cVEMP results in the healthy group better when it is evoked by the (1000–100) Hz narrowband chirp or the (1000–500) Hz narrowband chirp? (Pilot Study 1)
2. Are the oVEMP results in the healthy group better when it is evoked by the (1000–100) Hz narrowband chirp or the (1000–500) Hz narrowband chirp? (Pilot Study 2)
3. Do the VEMP results in the healthy group differ when evoked by the downward narrowband chirp compared to the 500 Hz tone burst?

4. Do the VEMP results in the VD group differ when evoked by the downward narrowband chirp compared to the 500 Hz tone burst?
5. Is there a significant difference in oVEMP and cVEMP results between the healthy and the VD groups for each stimulus?
6. Which of the two stimuli has the higher sensitivity and specificity of oVEMP and cVEMP in diagnosing vestibular disorders?
7. Is the overall sensitivity and specificity of the downward narrowband chirp stimulus for combined oVEMP and cVEMP higher than that of the 500 Hz tone burst stimulus in diagnosing vestibular disorders?

1.5 Study hypothesis

The research hypotheses of the studies are as follows:

1.5.1 Null hypothesis, Ho

1. There is no significant difference in the cVEMP results when using the (1000–100) Hz narrowband chirp stimulus compared to the (1000–500) Hz narrowband chirp in healthy individuals (Pilot Study 1).
2. There is no significant difference in the oVEMP results when using the (1000–100) Hz narrowband chirp stimulus compared to the (1000–500) Hz narrowband chirp in healthy individuals (Pilot Study 2).
3. There is no significant difference in the VEMP results when using the downward narrowband chirp stimulus compared to the 500 Hz tone burst in the healthy group.
4. There is no significant difference in the VEMP results when using the downward narrowband chirp stimulus compared to the 500 Hz tone burst in the VD group.

5. There is no significant difference in the VEMP results between the healthy and VD groups when using the downward narrowband chirp stimulus compared to the 500 Hz tone burst.
6. The sensitivity and specificity of the oVEMP and cVEMP for diagnosing vestibular disorders evoked by the downward narrowband chirp are not higher than those for the 500 Hz tone burst.
7. The downward narrowband chirp has not had a higher overall sensitivity and specificity of the combined oVEMP and cVEMP findings than the 500 Hz tone burst in detecting vestibular disorders.

1.5.2 Alternative hypothesis, Ha

1. There is a significant difference in the cVEMP results when using the (1000–100) Hz narrowband chirp stimulus compared to the (1000–500) Hz narrowband chirp in healthy individuals (Pilot Study 1).
2. There is a significant difference in the oVEMP results when using the (1000–100) Hz narrowband chirp stimulus compared to the (1000–500) Hz narrowband chirp in healthy individuals (Pilot Study 1).
3. There is a significant difference in the VEMP results when using the downward narrowband chirp stimulus compared to the 500 Hz tone burst in the healthy group.
4. There is a significant difference in the VEMP results when using the downward narrowband chirp stimulus compared to the 500 Hz tone burst in the VD group.
5. There is a significant difference in the VEMP results between healthy and VD groups when using the downward narrowband chirp stimulus.

6. The sensitivity and specificity of the oVEMP and cVEMP for diagnosing vestibular disorders evoked by the downward narrowband chirp are higher than those of the 500 Hz tone burst.
7. The overall sensitivity and specificity of the combined oVEMP and cVEMP findings in detecting vestibular disorders for the downward narrowband chirp is higher than that for the 500 Hz tone burst.

1.6 Significance of the study

It has been found that the prevalence of reported vestibular disorders is not small (Nakashima et al., 2016; Agrawal et al., 2009). Instability in vision, balance, and the capacity to maintain proper posture may all be affected by vestibular dysfunction. Although vestibular disorder occurs in a relatively wide range of adults, the available data on the sensitivity and specificity of VEMP in discriminating vestibular disorder in adults is inconsistent, ranging from 30%–90% and 40%–100%, respectively.

The type of stimulus may have an effect on the VEMP's sensitivity and specificity. Whereby having VEMP responses with larger amplitudes and shorter latencies would be beneficial in clinical settings as the testing time can be reduced and the response variability is minimised (increased test reliability). Although the 500 Hz tone burst is frequently used in the VEMP tests, some studies found larger VEMP amplitudes and shorter latencies when tested with the chirp stimulus, while contradictory outcomes were reported by others. The disagreements between the studies might be contributed by the different types of chirp stimulus used in the respective studies, in addition to other stimulus and recording parameter factors.

There is little research to clearly depict the clinical applicability of the narrowband chirp stimulus in VEMP recordings, even though several studies have

been conducted using the chirp stimulus in ABR and ASSR recordings with favorable outcomes. Furthermore, the available literature on chirp-evoked VEMP lacks consensus on which type of chirp stimulus should be used, and previous research has not clearly mentioned standard values that are acceptable to all. Thus, in this research, standard values of oVEMP and cVEMP will be determined using the downward narrowband chirp stimulus. Moreover, the studies investigating the performance of narrowband chirp-evoked VEMP tests in patients with vestibular disorders are limited, so the sensitivity and specificity of the oVEMP and cVEMP evoked by the downward narrowband chirp in detecting vestibular disorders will be determined.

Initially, this study aimed to focus exclusively on peripheral vestibular disorders and not include central disorders. In addition to assessing the effectiveness of both cVEMP and oVEMP in each specific subtype of peripheral vestibular disorders, such as Meniere's disease, BPPV, and labyrinthitis/vestibular neuritis. However, unfortunately, we could not apply this plan due to challenges in recruiting a sufficient number of participants for each specific subtype of peripheral vestibular disorder at the Universiti Sains Malaysia (USM) hospital. Consequently, after having thorough discussions with my supervisors, the study direction shifted to pool all types of vestibular disorders into a single group.

CHAPTER 2

LITERATURE REVIEW

2.1 Introduction

To provide an overview of the vestibular system, section 2.2 of this chapter begins by describing the anatomy and physiology of the human ear structures. The balance system (section 2.3), the vestibular system (section 2.4) (including three semicircular canals) (section 2.4.1), the otolith organs (i.e., the utricle and saccule) (section 2.4.2), the sensory cells (section 2.4.3), and the vestibular nerve (section 2.4.4)) are elaborated upon. In section 2.5, the mechanism of the vestibular system is explained. In section 2.6, vestibular disorders are covered. Following this, in section 2.7, methods of assessment for vestibular disorders are detailed. Section 2.7.3 describes VEMP tests that include both cVEMP and oVEMP, along with the factors that influence VEMP, stimulus issues in VEMP, and the outcomes of VEMP studies. Section 2.8, which concludes this chapter, summarises the literature gaps.

2.2 Anatomy and Physiology of the Ear

In the context of physiological research, the ear can be categorised into three primary components (as shown in Figure 2.1):

1. The outer ear consists of the auricle (or pinna) and the external acoustic meatus, which ends at the tympanic membrane (Nava & Lasrado, 2023).
2. The middle ear is a cavity filled with air. It is made up of three ossicles: the malleus, incus, and stapes, as well as the eustachian tube, which connects the middle ear to the back of the nose. The eustachian tube helps equalise the middle ear's pressure. Pressure equality is a necessary condition for the proper transmission of sound vibrations (Nava & Lasrado, 2023).

3. Inner ear: The inner ear resides within the petrous temporal bone. It is composed of two primary components: the bony labyrinth, filled with perilymph fluid, and the membranous labyrinth, which is endolymph-filled and situated in the middle of the bony labyrinth, mimicking the shape of its small cavities. It is worth mentioning that the inner ear comprises two distinct systems: the hearing system and the balance system (Zabolotnyi & Mishchanchuk, 2020). I will explain the balance system in section 2.3.

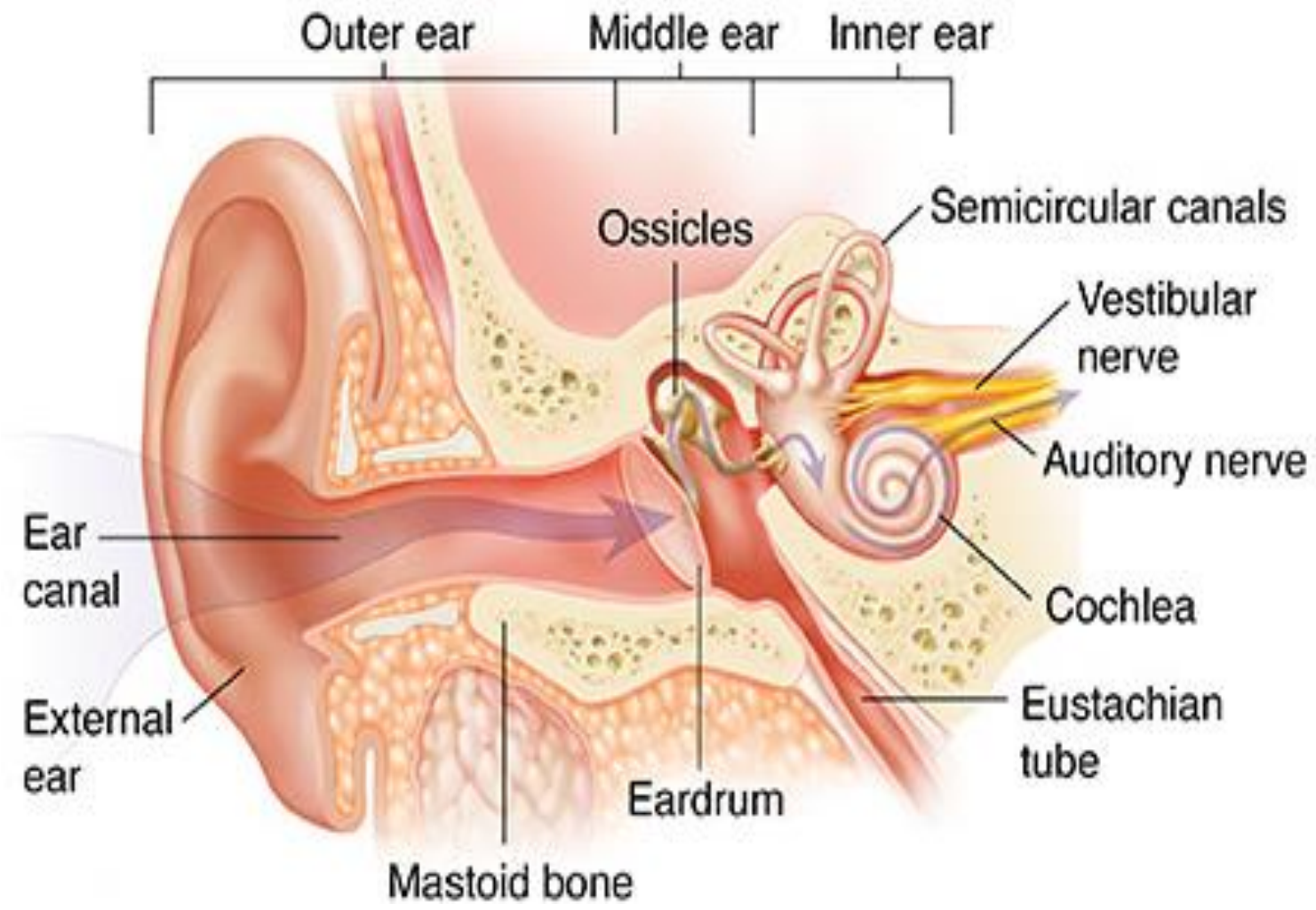

Figure 2.1 Anatomy of the Ear. The figure was adapted from Mary Ann Zapalac (2023).

Hearing is initiated by the outer ear. Sound vibrations, which originate from sources external to the outer ear, propagate through the external auditory canal before impacting the tympanic membrane (eardrum). Eardrum vibrations occur. Following this, the vibrations traverse the ossicles. Sound is amplified by the ossicles and then transmitted by them to the cochlea. Upon arrival at the inner ear, sound waves undergo a transformation into electrical impulses. These impulses are transmitted by the auditory nerve to the brain. Next, the brain converts these electrical impulses into sound (Nava & Lasrado, 2023).

2.3 The balance system

Balance is a person's ability to maintain their centre of gravity over their base of support (BOS). A well-functioning balance system lets humans preserve a clear visual image both in static and dynamic conditions, figure out where they are relative to gravity, detect the direction and speed of their movement, and make automatic postural adjustments to keep their posture and stability in different situations and activities (Watson et al., 2016).

Balance is achieved and maintained through a complex combination of sensorimotor control systems, including the visual, vestibular, and predominately proprioceptive somatosensory systems. All three of these information sources convey messages to the brain in the form of nerve impulses from sensory receptors, which are subsequently sorted and integrated with learned knowledge from the cerebellum (the brain's coordination centre) and cerebral cortex (the thinking and memory centres). As sensory integration occurs, the brain stem transfers impulses to the muscles that control the movements of the eyes, head and neck, trunk, and legs, allowing a person to maintain balance and see clearly while moving (Watson et al., 2022). These

components may be impacted by trauma, illness, particular medications, or ageing. Moreover, psychological variables can significantly damage our sense of balance (Bronstein, 2016). Figure 2.2 demonstrates a general overview of the human balance system.

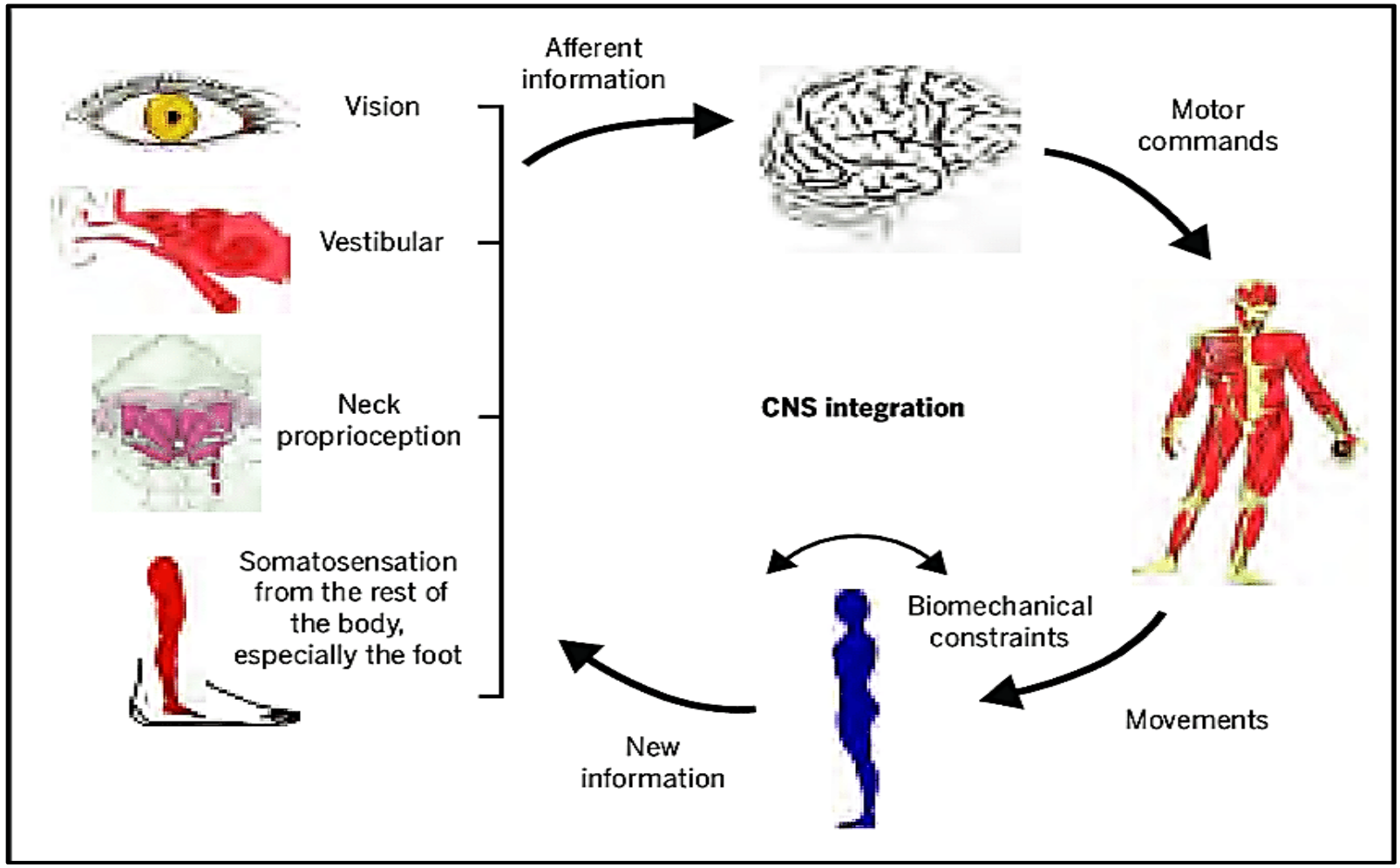

Figure 2.2 The human balance system. This figure was adapted from Kristjansson & Treleaven (2009).

2.4 Vestibular system

The peripheral component of the vestibular system consists of three semicircular canals, the vestibulum, which contains spherical (saccule) and elliptical (utricle) sacs that comprise the receptor otolith organ, and the 8th (vestibulocochlear) cranial nerve (Figure 2.3) (Zabolotnyi & Mishchanchuk, 2020).

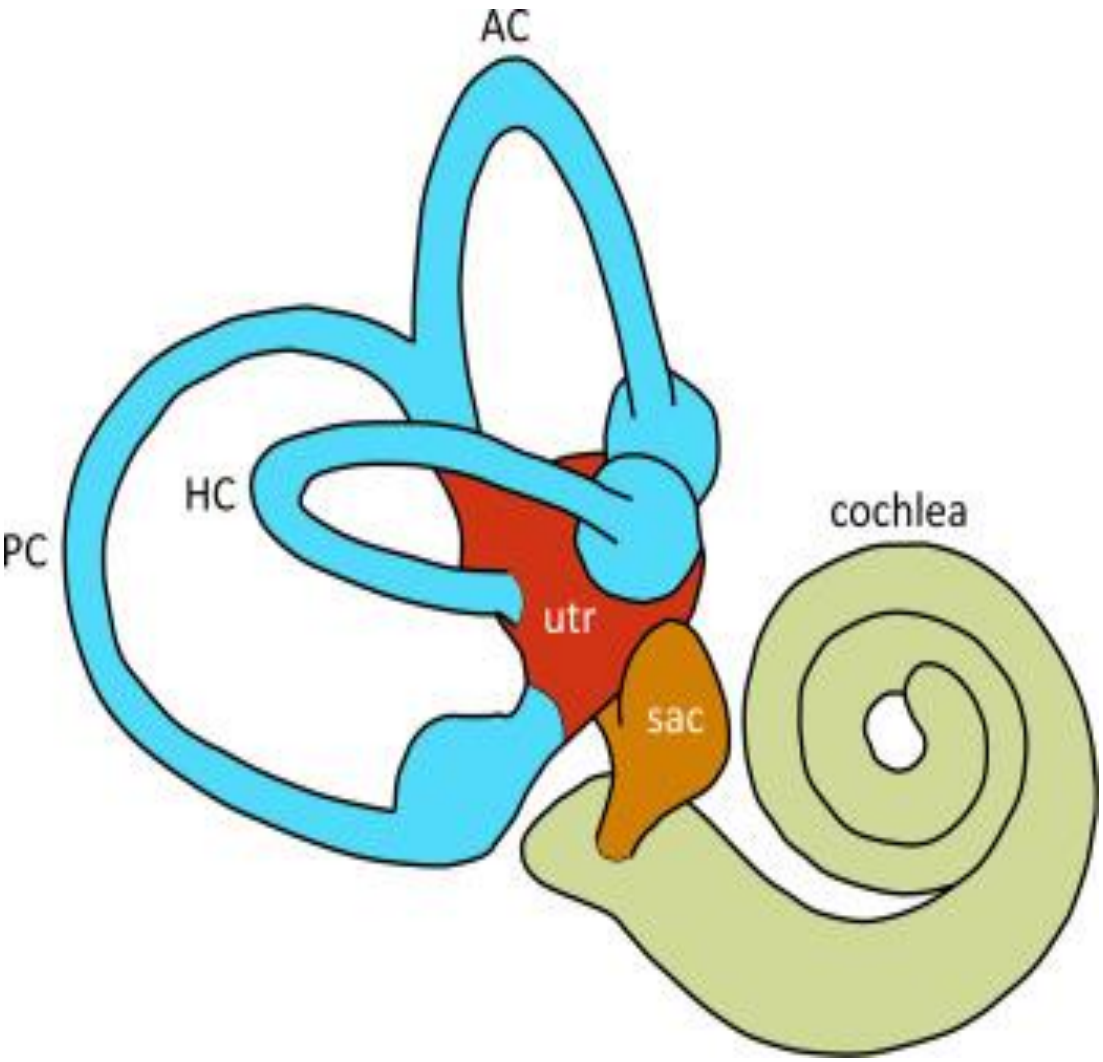

Figure 2.3 Components of the right vestibular system. Adapted from Kingma & van de Berg (2016).