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# VESTIBULAR FUNCTION AND POSTURAL CONTROL IN CHILDREN

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# ABSTRACT

**Background:** The vestibular system plays a crucial role in the ability to maintain balance. For children, balance control is reliant on multiple factors including integration of sensory information, sensorimotor mechanisms, and motor skill development. Several measures to quantify balance performance include vestibular function assessment, functional balance ability and postural control, but the relationship between these constructs has only recently been considered. Establishing the relationship between constructs for typically developing children would help to better understand balance control. Addressing this knowledge gap for children with sensorineural hearing loss or autism would also help to identify underlying mechanisms contributing to balance challenges and support optimal intervention approaches.

**Aims:** This PhD aimed to describe peripheral vestibular function and its contributions to functional balance and postural control via: (1) comparison between typically developing children 5-12 years and adults; and (2) longitudinal comparisons in typically developing children across a twelve-month period. Peripheral vestibular function, functional balance and postural control were also explored in (3) children with sensorineural hearing loss and (4) children with autism.

**Methods:** Participants were recruited from organisations across metropolitan Melbourne. Clinical vestibular assessments included the video head impulse test to measure semicircular canal (SCC) function and vestibular evoked myogenic potentials to measure otolith function. Postural control strategies were evaluated using static posturography with modified sensory inputs utilising novel approaches to analyse postural sway. Bruininks-Oseretsky Test of Motor Proficiency and Paediatric Balance Scale measured functional balance. Aim 1 compared typically developing children to adult cohorts for otolith function and postural control. Aim 2 documented normative data for children 5-12 years across all clinical vestibular assessments, functional balance, and postural control, with longitudinal comparisons for a smaller subset. These same assessments were performed for children with sensorineural hearing loss (Aim 3) and children with autism (Aim 4).

**Results:** When compared to adults, children had smaller and earlier otolith responses and increased postural sway across all static posturography conditions, with differences in sensory integration strategies observed. Normative and longitudinal comparisons in typically developing children demonstrated that some balance measures change with age, including SCC function, saccule function, and postural control.

For children with sensorineural hearing loss, vestibular impairment predicted motor performance, with greater degrees of vestibular impairment associated with reduced functional balance performance and larger amounts of postural sway for conditions requiring vestibular system reliance.

Despite normal vestibular function, children with autism showed reduced functional balance performance and greater amounts of postural sway in conditions where visual input was eliminated.

**Conclusions:** Elements of peripheral vestibular function and postural control in children change over time and differ from adults. Postural control strategies can also differ between children, depending on age, vestibular function, and functional balance performance. These findings demonstrate the need for paediatric focused normative data across clinical assessments of balance control. Utilising a range of assessments to quantify balance performance can inform optimal intervention approaches for children with vestibular impairment, as observed in children with sensorineural hearing loss, or balance concerns, as observed in children with autism. Longitudinal comparisons may also guide management.

# DECLARATION

This is to certify that:

(i) the thesis comprises only my original work towards the PhD except where indicated in the Preface;

(ii) due acknowledgement has been made in the text to all other material used;

(iii) the thesis is fewer than 100,000 words in length, exclusive of tables, maps, bibliographies, and appendices.

July 2023

Donella Rebecca Chisari

# PREFACE

This thesis is my original work and contains no material previously published or written by another person, except where due acknowledgement has been made.

I was responsible for the development, preparation and completion of the thesis, however several people have made significant contributions to the thesis and submitted manuscripts. My supervisors Prof Gary Rance and Dr Jessica Vitkovic contributed to the research plan and design and data analysis. They also critically reviewed the whole thesis and submitted manuscripts. Prof Ross Clark extracted and processed postural sway data, assisted with postural sway analysis, and critically reviewed submitted manuscripts. I have provided a declaration for submitted publications with this thesis.

I was responsible for data collection of all children. Chapter 5 of the thesis includes adult datasets from the Department of Audiology and Speech Pathology. This data was collected by Dr Jessica Vitkovic prior to the enrolment of my research higher degree candidature. I performed all statistical analyses under the guidance of my supervisory team and statistician Mr Cameron Patrick from the Statistical Consulting Centre at the University of Melbourne.

The author acknowledges the financial support of the Department of Audiology and Speech Pathology, The University of Melbourne.

# PUBLICATIONS

The publication status for each of the results chapters are outlined below:

Chapter 5: Submitted to Gait and Posture, April 2023

Chapter 6: Unpublished material not submitted for publication

Chapter 7: Submitted revisions to International Journal of Audiology, June 2023

Chapter 8: Manuscript prepared for submission to Autism Research

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Completing a PhD is often described as a solitary process, but I would not be here without the wonderful people who have supported and encouraged me over the last several years. It has felt like a never-ending journey, but we are now there.

To begin, I would like to thank my supervisors Gary Rance and Jessica Vitkovic for their guidance and support over the course of my candidature. Gary, your encouragement, pragmatic advice, and consistent optimism has always been appreciated and you have encouraged me to let go of my perfectionism. Jess, I have appreciated your expertise, encouragement to keep going, and the many thought-provoking discussions to help me relate this all to the bigger picture.

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Finally, to Daniel. You have observed, and at times experienced the highs and lows of the PhD rollercoaster with me. Thank you for your patience, love, encouragement and support, and for always being there when things got tough.

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# ABBREVIATIONS

| ABBREVIATION | DEFINITION |
|---|---|
| **4FAHL** | Four-frequency average hearing level |
| **ASCC** | Anterior Semicircular Canal |
| **BOT-2** | Bruininks-Oseretsky Test of Motor Proficiency |
| **CoP** | Centre of Pressure |
| **CTSIB** | Clinical Test of Sensory Interaction and Balance |
| **cVEMP** | Cervical vestibular evoked myogenic potentials |
| **dB HL** | Decibels hearing level |
| **dB pFL** | Decibels peak force level |
| **dB SPL** | Decibels sound pressure level |
| **DSM-V** | Diagnostic and Statistical Manual of Mental Disorders |
| **DWT** | Discrete Wavelet Transform |
| **EC** | Eyes Closed (Firm) |
| **EMG** | Electromyographic |
| **EO** | Eyes Open (Firm) |
| **FEC** | Foam Eyes Closed (Foam) |
| **FEO** | Foam Eyes Open (Foam) |
| **HSCC** | Horizontal Semicircular Canal |
| **Hz** | Hertz |
| **LARP** | Left Anterior Right Posterior |
| **NSD** | Normal sound detection |
| **oVEMP** | Ocular vestibular evoked myogenic potentials |
| **PBS** | Paediatric Balance Scale |
| **PSCC** | Posterior Semicircular Canal |
| **PTA** | Pure tone average |
| **RALP** | Right Anterior Left Posterior |
| **SCC** | Semicircular Canal |
| **SCM** | Sternocleidomastoid |
| **SNHL** | Sensorineural hearing loss |
| **SOT** | Sensory Organization Test |
| **vHIT** | Video head impulse test |
| **VOR** | Vestibulo-ocular reflex |
| **VCR** | Vestibulo-collic reflex |
| **VSR** | Vestibulo-spinal reflex |
| **WBB** | Wii Balance Board |

# Chapter 1: INTRODUCTION

Various mechanisms play a role in the ability to maintain balance. These include sensory information received from the visual, vestibular, and somatosensory systems; central processing mechanism in the brainstem and cerebellum to control movement, and motor outputs to maintain body posture, and gaze stability. For children, these processes can work differently to adults due to age related changes and sensory integration processes for postural control. In children, numerous factors can influence functional balance ability and postural control, but the relationship between these constructs and peripheral vestibular function has only recently been considered in the literature.

This PhD project aims to describe peripheral vestibular function and its contributions to functional balance and postural control via: (1) comparison between typically developing children and adults, (2) exploration of balance function in typically developing children, including longitudinal comparisons across various balance measures, (3) children with sensorineural hearing loss and (4) children with autism.

## 1.1 Research Plan

This PhD project explored balance function in school aged children, 5-12 years old across three groups: 1) typically developing children, 2) children with bilateral, sensorineural hearing loss and 3) children with autism. All children underwent balance assessment (approximately 75 minutes); some children completed this across three time points, at six monthly intervals for longitudinal comparisons. Some of the child data was compared to two groups of normal adults who underwent postural control and otolith function measures.

## 1.2 Chapter Summary

**Chapter 2** is a literature review and begins by orienting the reader to the processes involved for maintaining balance, including balance system organisation and postural control. The role of clinical assessments for balance are then discussed, highlighting the range of clinical assessments for adults and children, and knowledge gaps in current practice.

**Chapter 3** provides a rationale for the PhD project and includes aims and hypotheses for each study.

**Chapter 4** outlines the study methodology. This begins by introducing participants for each of the four studies, and outlines recruitment processes including inclusion and exclusion criteria. Procedures and measures used in the PhD project are outlined in detail. The chapter concludes with statistical methods and analyses for each of the four studies.

**Chapter 5** is a cross sectional, comparative study exploring postural control and otolith function in typically developing children and adults, and reports on Aim 1 of the PhD project. The chapter explores whether children use similar postural control strategies to adults across different standing measures, by utilising a range of clinical tests across both groups. The relationship between postural control and otolith function in children is also explored.

**Chapter 6** is a comparison of vestibular function postural control and functional balance in typically developing children aged between 5 to 12 years. In this chapter normative data comparisons are explored across each of the measures, followed by longitudinal comparison of constructs used for balance in a smaller subset of children. The chapter concludes by exploring the relationship between peripheral vestibular function and functional balance including standardised measures.

**Chapter 7** explores balance function in children with sensorineural hearing loss via vestibular function, functional balance and postural control measures. The relationship between degree of vestibular impairment and balance outcomes are explored. Background, methods, results and discussion are provided in this chapter to address PhD Aim 3.

**Chapter 8** explores balance function in children with autism via measures of functional balance, vestibular function, and postural control. Background, methods, results and discussion are provided in this chapter to address PhD Aim 4.

**Chapter 9** is the final chapter of the PhD project and critically evaluates the project findings. It begins by providing the reader an overview of the four research aims and principal findings from each study and synthesises study findings in the context of insights provided by previous literature. Clinical implications are discussed, followed by strengths and weakness of the current PhD project. The chapter concludes with clinical applications of PhD findings and future directions for research.

# Chapter 2: LITERATURE REVIEW

## PART I: What is balance and why is it important?

The sense of balance is intrinsically complex and reliant on several different sensory processes within the body as well as central processing to maintain a steady position or posture. Synchronous information to the brain from the visual, somatosensory and vestibular systems enables one to maintain balance when moving or changing body position and is also relied upon in instances of quiet stance.

The sensory processes required for balance control are varied and complex. To sense or execute movement, multiple sensory systems are synchronously engaged to provide afferent information to the central nervous system, in turn initiating reflexes and relevant muscles to initiate or sustain a particular head or body position.

## 2.1 Defining balance

Balance can be described as the organised response to sensory information (Woollacott & Shumway-Cook, 1990), with sensory information typically referring to information from the visual, vestibular and somatosensory systems.

Several terms describe the concept of balance, including stability, functional balance, and equilibrium. Descriptors related to balance typically refer to the ability to maintain a sustained spatial position, which is reliant on equal weight distribution in relation to the centre of gravity. Although some terms are used interchangeably across literature and disciplines, there is no mutually agreed upon term to define balance.

Balance can broadly be described by two parameters; static balance, which is the maintenance of posture when stationary, and dynamic balance, referring to the maintenance of upright posture with movement (Williams, 1983). Both parameters are reliant on sensory system integration which vary in their relative contributions dependent on context (Forssberg & Nashner).

Throughout this thesis, the term “balance function” will be used to describe a collective of processes related to achieving and maintaining balance control. The terms “static balance” and “postural control” will be used to describe the concept of maintaining an upright, sustained spatial position, through integration of sensory systems used for balance. “Functional balance” will be used to describe the requirements of static and dynamic balance function for daily activity.

## 2.2 Balance system organisation

Balance is crucial to human function. It enables us to maintain visual focus when moving, maintain an upright posture and to correct for any errors in processing that may result in a fall or loss of balance. Furthermore, we rely on balance to navigate complex sensory environments and maintain an upright posture for most physical activities such as walking to the mailbox, hanging out the washing, or taking the dog for a walk. Often, we tend to be most aware of balance ability when we are in jeopardy of losing it. In order to understand how balance is achieved, it is important to first consider the different components required for optimal balance control.

Three main elements define how the balance system is organised, as can be seen in Figure 2.1 (Herdman & Clendaniel, 2014). Sensory inputs, central processing and motor outputs are fundamental for generating eye and body movement and maintaining upright posture when still or during motor activities. The delicate interplay between these elements is achieved via multiple adaptive systems and sensory re-weighting which is a process of adjusting sensory contributions for balance control (Forssberg & Nashner, 1982; Woollacott & Shumway-Cook, 1990). Sensory inputs provide continuous information regarding location and position in the spatial environment to the central processing mechanisms, which comprise several nuclei in the brainstem related to sensory information, and the cerebellum. The central processing mechanisms provide fast motor outputs that can be reflexive or more refined depending on the individual’s body position and environmental context. Typically, these motor outputs relate to eye, body or head position and are used to achieve or maintain visual focus, upright head position and upright postural control.

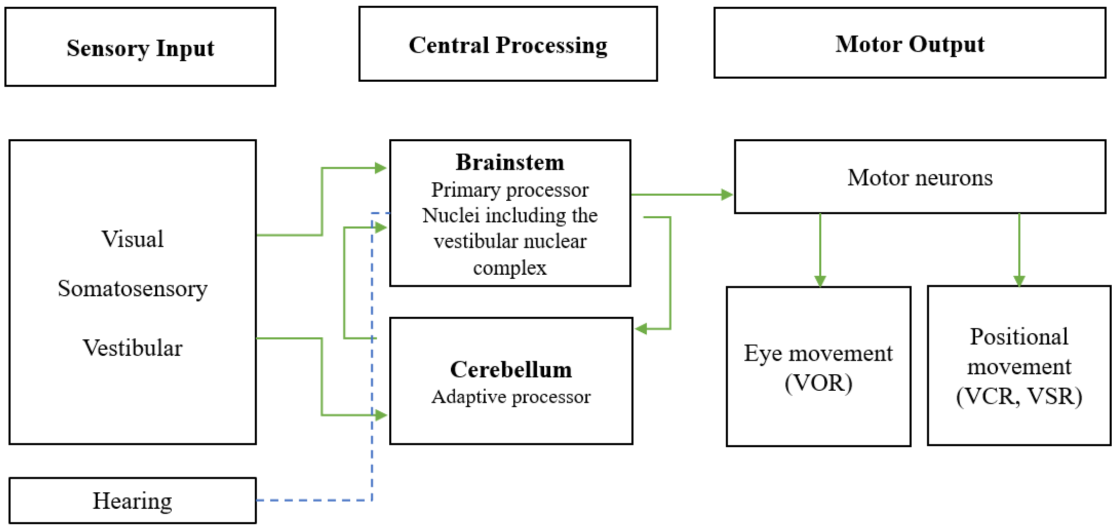



**Figure 2.1.** Balance system organisation comprising sensory inputs, central processing and motor outputs. VOR corresponds to the vestibulo-ocular reflex, VCR corresponds to the vestibulo-collic reflex, and VSR corresponds to the vestibulo-spinal reflex. Overall figure adapted from Herdman (Herdman & Clendaniel, 2014).

## 2.3 Sensory inputs

Visual, somatosensory and vestibular systems provide sensory input regarding location, sensation and motion, and feed this into the central processing mechanisms to generate motor outputs related to eye, head or body position (Figure 2.1). These three main sensory systems contribute to overall balance function, with variable contributions depending on context, task and age of the individual.

Whilst it is possible for a single sensory input to dominate in certain conditions, equal reliance on all three is, theoretically, not a fundamental requirement to maintain balance. It is possible to maintain balance with only two of three sensory systems inputting information. Successful use of only two of three sensory systems requires appropriate sensory integration and intact motor outputs. If the latter are impaired, balance will be affected.

The three main sensory inputs for balance, namely the visual, somatosensory and vestibular systems, are outlined across Sections 2.4.1-2.4.3. Other sensory processes, such as hearing, can influence balance control (Vitkovic et al., 2016) but the focus of this literature review remains on visual, somatosensory and vestibular systems. Information from these three systems (visual, somatosensory, and vestibular) provides sensory information that can be weighted differently, depending on context. For example, when moving in low light, greater reliance on somatosensory and vestibular information is needed as visual information is not as useful, leading to an increase in the weighting of somatosensory and vestibular information, and decrease in weighting of visual information. The vestibular system is the predominant sensory input related to motion and is the primary sensory system of focus in the PhD project. Therefore, it will be discussed in greater detail compared to the other sensory systems.

### 2.3.1 The visual system

Vision is not an essential requirement for balance control, yet it is known that vision can improve balance stability (Guerraz & Bronstein, 2008). Visual information within the environment assists with navigation, and ocular movements mediated by the vestibular system enable one to maintain a stable visual image when moving (Casselbrant et al., 2007; Wade & Jones, 1997). The visual system takes longer to adapt to conflicting visual stimuli or changes in environmental context than the other sensory systems (Forssberg & Nashner, 1982).

The role of vision in overall balance function is to provide both context regarding the external environment and depth perception for navigating. Three vision components are considered for balance control: ambient (peripheral) vision, central vision and retinal slip. The ambient visual system relates to peripheral vision that ties in with perception of self-motion and perception of postural control. The central (or focal) visual system relates to recognition and motion perception of objects. The third, retinal slip, relates to when spontaneous body oscillations cause a shift of the environmental visual imagery on the retina (Guerraz & Bronstein, 2008). Central and peripheral vision are important for static balance and can be dependent on the age of the individual. In children >6 years and adults, peripheral vision is important for static balance (Grace Gaerlan et al., 2012; Nougier et al., 1998), but in children <6 years, central vision also has a role in balance control (Nougier et al., 1998).

Two main models of visual contribution to balance have been considered by Held (Held, 1970) and Gibson (Gibson, 2014). Held described the traditional "two-mode" theory of vision, based on the premise that visual information received is categorised as focal or ambient vision (Held, 1970; Wade & Jones, 1997). Based on this theory, ambient vision is the main determinant of postural stability. Focal vision is relevant to visual acuity and includes object recognition and identification, utilising information from the central visual field. On the other hand, ambient vision utilises visual information received in relation to spatial orientation and locomotion (Held, 1970). Ambient vision utilises both central and peripheral retinal information (Schmidt & Lee, 2005), thereby more reliant on retinal stimulation to contribute to the perception of self-motion (Wade & Jones, 1997).

From an ecological perspective, Gibson (Gibson, 2014) postulates that the visual system is sensitive to various optical inputs during self-motion. In this model, visual perception is dependent on the information received from multiple areas of the optic array to determine locomotion. Optical flow fields are generated as an individual navigates their surrounding environment. For any given position, optical flow fields comprise lamellar flow, which is the flow structure of the peripheral visual field; and radial flow, which is the central point of the optical flow field (Gibson, 2014). As an individual navigates towards a central point, the optical array flows outward from the radial point and is transformed to lamellar flow. As such, postural control is not only determined by retinal sensitivity (centre and periphery), but also information from the light structures within the optical flow field (radial and lamellar), which is dependent on motion (Stoffregen, 1985). Stoffregen (1985) found that lamellar flow is a greater determinant of postural sway, rather than radial flow. This theory contrasts Held's 'two mode' theory of vision, however when comparing the two theories of Held and Gibson, Gibson's ecological perspective is more encompassing in relation to postural control for dynamic movement.

The visual system is integrated into the postural control system in two different ways, impacting on different sensorimotor mechanisms during standing balance (Collins & De Luca, 1995a); visual input can decrease the activity of more reflexive sensorimotor mechanisms, thereby decreasing musculoskeletal activity in the lower limbs. On the other hand, it can alter the refined feedback mechanisms required for standing balance, which in turn alters the role of vestibular and proprioceptive information in these instances.

### 2.3.2 The somatosensory system

The somatosensory system is a complex network of neural structures throughout the body and brain involved in the perception of touch, pressure, vibration and movement (Kaas, 2011). Through this information, subtle adjustments to muscles, tendons and joints within the body occur to generate or alter body position related to internal and external stimuli. Proprioception is the term given to the body's position in relation to the surrounding environment. The percept of somatosensation utilises motor responses to refine a spatial position. Biomechanics and sensory inputs from muscles, joints, and reflexes also contribute to maintaining posture and spatial awareness.

Somatosensory system function involves sensors in the motor pathways (including those from the joints, muscles and tendons) and information processing in the nervous system within the body and brain. Receptors in the skin, muscles and joints feed information to the peripheral nerve afferents which synapse with neurons in the spinal cord and brainstem (Kaas, 2011). This information is then transmitted to the somatosensory structures within the central nervous system including the medial lemniscus column, ventroposterior complex of the thalamus, and somatosensory thalamus (Kaas, 2011).

The somatosensory system also utilises a range of open and closed-loop feedback systems to maintain posture. Open-loop strategies are fast corrective responses to maintain postural control but may be less precise for motor control, as they are based entirely on the intended input of the system: the output has no effect on the motor control. On the other hand, closed-loop strategies look at the current output and alters it to the desired condition via feedback. For balance control, closed-loop strategies typically enable controlled and subtle corrections using feedback from sensory mechanisms (Peterka, 2002), sensory transduction processing and muscle activation. Collins and De Luca postulated that during quiet stance, a combination of closed-loop feedback and open-loop feedback strategies are used to maintain posture (Collins & De Luca, 1993). Additionally, reflexive outputs that relate to descending commands for different muscles involved in postural control and also relate to mechanical fluctuations of joints within the body (Collins & De Luca, 1993).

### 2.3.3 The vestibular system

The vestibular system provides an estimate of self-motion and plays a role in gaze stabilization and balance control for static and dynamic activity. Vestibular stimulation occurs during motion, the peripheral vestibular organs project primary afferent information to the vestibular nuclei in the brainstem. Information processed here is projected to neural structures involved in gaze stabilisation and body position, and further to cortical structures for perception of self-motion (Cullen, 2012).

The peripheral vestibular system is a membranous labyrinth surrounded by perilymph fluid and encased within the petrous portion of each temporal bone (Schubert & Minor, 2004). It develops in utero and is structurally complete by 25 weeks gestation (Fife, 2010; Jones & Jones, 2011; Nandi & Luxon, 2008) although vestibular contributions to postural control continue to develop throughout childhood and adolescence (Hirabayashi & Iwasaki, 1995; Sinno et al., 2021).

Five specialised sensory organs make up the vestibular labyrinth; three semicircular canals (SCC) filled with endolymph, and two membranous sacs forming the otolith organs (Rabbitt et al., 2004) (Figure 2.2). Each sensory organ has highly specialised sensory neuroepithelium and collectively, respond to head movement in all planes of motion.

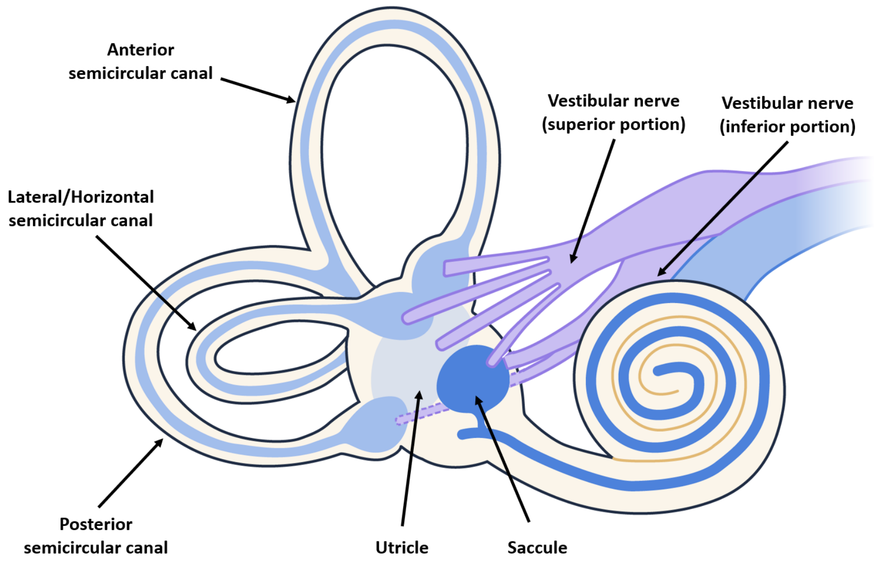



**Figure 2.2.** Vestibular anatomy. The peripheral vestibular system comprises three semicircular canals: lateral/horizontal, anterior and posterior, and two otolith organs: utricle and saccule. These structures are innervated by the superior and inferior portions of the vestibular nerve. Image adapted from Dingman (Dingman, 2020).

### 2.3.3.1 Semicircular canals

Three semicircular canals (SCC); horizontal, anterior and posterior are orthogonally orientated within the head and work in three co-planar pairs: left and right horizontal SCC, left anterior and right posterior SCC (LARP); and right anterior and left posterior SCC (RALP) (Schubert & Minor, 2004). The primary purpose of the SCC's are to detect rotatory or angular acceleration. Within each SCC lies the ampulla and cupula. The ampulla encases the cupula, a gelatinous, flexible structure that partitions the canal but deflects with endolymph movement. The cupula protects the crista ampullaris, a sensory structure comprising sensory hair cells which deflect in response to endolymph movement within the SCC, causing a change to the membrane potential. Collectively, the cristae from all SCC's sense angular acceleration (Chang et al., 2004).

The SCC's work in conjugate pairs, so an increase in neural firing rate in the ipsilateral SCC is coupled with a decrease in neural firing rate in the contralateral, conjugate SCC (Halmagyi & Curthoys, 1988). The orientation of the kinocilium within the crista ampullaris is dependent on the SCC: for horizontal canals, excitation occurs when there is ampullopetal flow: the endolymph moves towards the ampulla; in the anterior and posterior SCC, excitation occurs when there is ampullofugal flow: the endolymph moves away from the ampulla (Schubert & Minor, 2004). This pattern of responses is also described by Ewald's second and third laws (Halmagyi & Curthoys, 1988; Kingma & van de Berg, 2016).

### 2.3.3.2 Otolith organs: Utricle and saccule

Two membranous sacs within the labyrinth form two otolith organs, the utricle and saccule, both of which contain sensory neuroepithelial structures, the maculae. The relative orientation of the otolith organs in an upright individual is similar to the planes they detect; the utricle, orientated in a relatively horizontal position, detects linear acceleration, and the saccule, in a relatively vertical position, detects vertical forces and gravity.

Within the maculae, the otolithic membrane is a gelatinous structure embedded with calcium carbonate crystals (otoconia or otoliths) which provides an inertial mass to the membrane (Schubert & Minor, 2004). Sensory hair cells project into the otolithic membrane. Each otolith organ is divided by a central region, the striola, with the kinocilium of the sensory hair cells either oriented towards the striola in the case of the utricular macula, or away from the striola in the case of the saccular macula (Khan & Chang, 2013; Schubert & Minor, 2004). Given the different orientation of the sensory hair cells, the otoliths can also detect tilt or linear acceleration in multiple directions.

### 2.3.3.3 Vestibular physiology and vestibular projections

The cristae ampullaris in the SCC and maculae in the otolith organs contain sensory mechanoreceptors called hair cells (Khan & Chang, 2013). Each hair cell includes a single kinocilium, and approximately 40-200 stereocilia arranged in order of decreasing size away from the kinocilium (Fife, 2010). Shorter stereocilia are connected to the taller stereocilia via tip links. The hair cells within the sensory organs deflect with gravity or head motion. Stereocilia deflection towards the kinocilium causes depolarization, or an increase in neural firing; deflection away from the kinocilium causes hyperpolarization, leading to a decrease in neural firing from the sensory afferents (Khan & Chang, 2013). The vestibular afferents are broadly classified into two groups based on their relative discharging properties, regular or irregular. Irregular vestibular afferents have a greater role in the rapid detection of head movement and initiation of the vestibulo-ocular reflex (Lysakowski et al., 1995). Regular vestibular afferents provide a signal which is proportional to head velocity over a large range of rotations. It has been well established that the resting firing rate of vestibular afferents in primates is between 70-100 spikes per second (Goldberg & Fernandez, 1971; Lysakowski et al., 1995).

Primary vestibular afferents from the crista ampullaris and the maculae project to Scarpa's Ganglion located in the internal auditory meatus. Scarpa's ganglion is divided into two portions, the superior portion, innervated by the cristae ampullaris from the horizontal and anterior SCC, utricular macula, and the "hook" region of the saccular macula; and inferior portion, innervated by the crista ampullaris of the posterior SCC and saccular macula (Fife, 2010; Khan & Chang, 2013). These divisions within Scarpa's ganglia form the superior and inferior branches of the vestibular nerve respectively.

The vestibular nerve merges with the cochlear nerve bundle to form the vestibulo-cochlear nerve, coursing through the internal auditory meatus, and entering the brainstem at the pontomedullary junction. Most of the afferent vestibular nerve fibres project to the vestibular nuclear complex ipsilaterally (Khan & Chang, 2013), with a smaller proportion projecting to the flocculus of the cerebellum; these projections do not cross the midline. Vestibular afferents also project to the autonomic nervous system, spinal cord and visual system.

## 2.4 Central processing

There are two main central processing structures involved in balance control: the vestibular nuclear complex (VNC) in the brainstem, and the cerebellum (Figure 2.1). The VNC is the primary processor that quickly processes afferent information from the vestibular, visual and somatosensory systems, and projects to motor neuron outputs that are typically reflexive to correct positional movement to prevent falling (Hain &

Helminski, 2014). The cerebellum is an adaptive processor or central gatekeeper for volitional movement, through integration of incoming information from the vestibular nuclei, and primary sensory system afferents. Importantly it modulates vestibular performance (Herdman & Clendaniel, 2014; Khan & Chang, 2013).

### 2.4.1 Brainstem nuclei

Multimodal integration of vestibular and non-vestibular cues occurs in the vestibular nuclei. The nuclei receive afferent information from the peripheral vestibular system, spinal cord and reticular formation. Four major nuclei make up the vestibular nuclear complex in the brainstem: medial, lateral, superior and inferior (spinal). The medial vestibular nuclei are housed in the medial column, with the other nuclei (superior, lateral and inferior vestibular nuclei) housed in the lateral column (Khan & Chang, 2013). These nuclei integrate information from sensory afferents including the somatosensory and vestibular systems, and central structures including the contralateral nuclei and cerebellum. The medial vestibular nuclei use vestibular signals to mediate the vestibulo-ocular reflex and vestibulo-spinal reflexes. The superior vestibular nuclei predominately receive and process information from the SCC to mediate the vestibulo-ocular reflex. The lateral vestibular nuclei, or Dieters' nucleus, predominately receives input from the utricle and vestibulo-cerebellum, projecting to the vestibulo-spinal tracts (predominately lateral vestibulo-spinal tract) and other vestibular nuclei (Fife, 2010). The inferior (spinal) vestibular nuclei receives and processes information from the otoliths, and feeds into the other vestibular nuclei and cerebellum (Khan & Chang, 2013). Lateral vestibulo-spinal tracts course from the lateral vestibular nucleus down the entire spinal cord, whereas the medial vestibulo-spinal tracts originate from the medial and lateral nuclei and descend to the level of the thoracic spine (Colebatch, 2002). All vestibular nuclei project to the medial longitudinal fasciculus.

The vestibular nuclei can be differentiated by their overall afferent fibre projections, related to those that 1) mediate the vestibulo-ocular reflex (VOR), and 2) mediate self-motion and posture (Cullen, 2012). Specifically, the VOR neurons project to central neurons within the vestibular nuclei (predominantly superior and medial VN), and then to the extraocular motor neurons, enabling gaze stability during head motion. These neurons are largely the position-vestibular-pause (PVP) neurons, and floccular target neurons (FTN), the latter of which receives input from both the vestibular nerve and flocculus of the cerebellum (Cullen, 2012). On the other hand, neurons that control postural stability and self-motion project to higher order structures, including the cerebellar nodulus, thalamus and cortex, as well as the spinal cord (Cullen, 2012). These are considered to be vestibular only neurons (VO), as they do not contribute to the VOR, but instead are thought to contribute to the vestibular spinal reflexes (Cullen, 2012; Goldberg & Cullen, 2011).

The reticular formation also serves a role in some of the vestibular and non-vestibular mediated reflexes. The medial tegmental field is one of three longitudinal zones of the reticular formation and is involved in controlling eye, head and postural muscles through reticular spinal pathways (Horn & Adamczyk, 2012).

### 2.4.2 Cerebellum

The cerebellum is fundamental for coordination, motor function precision and motor learning. It is also involved in the adaptive process for postural control. Afferent information entering the cerebellum arise from sensory inputs including sensory systems and the spinal cord. Different areas of the cerebellum correspond to afferent and efferent connectivity and are largely divided into four main functional zones: the vermis, intermediate and lateral zones, and flocculonodular nodule (Morton & Bastian, 2004). The vermis is the most medial part of the cerebellum and receives input from vestibular, reticular, and pontine nuclei as well as primary vestibular afferents and spinocerebellar tracts (Morton & Bastian, 2004). Specifically, the vermis is important for integrating vestibular and spinal inputs and influences the vestibulo-spinal tract (Morton & Bastian, 2004). The intermediate zone of the cerebellum is involved in integrating cortical and spinal inputs and projects to motor cortical areas (Morton & Bastian, 2004). The lateral zone integrates information from several cortices (including primary motor and primary somatosensory cortices) and is primarily involved in voluntary modifications to locomotion (Morton & Bastian, 2004). The flocculonodular lobe receives inputs from primary vestibular afferents as well as various nuclei (reticular, vestibular, pontine) and projects information via Purkinje cells for eye movement control and balance. In particular, the central vestibular system generates motor outputs to the ocular muscles and spinal column, generating numerous reflexive pathways. Of these, three main reflexes are mediated by the vestibular system: the vestibulo-ocular reflex (VOR), vestibulo-collic reflex (VCR) and vestibulo-spinal reflex (VSR). These are important to maintain visual focus (VOR), head position (VCR) and body position (VSR). These reflexes are discussed in Section 2.5.2.

## 2.5 Motor outputs

The final component of balance system organisation are motor outputs (Figure 2.1). Motor outputs related to vestibular reflexes control eye movement in the presence of body or spatial motion (ocular reflex), as well as vestibular reflexes that control and maintain upright body position with movement (collic and spinal reflexes).

During standing balance several types of motor outputs are generated by the body and include information from body joints, changes in pressure and percept of touch and sensation (Collins & De Luca, 1993). The biomechanics of the lower limbs exert pressure to ensure upright posture is maintained, but are also influenced by biomechanical constraints such as muscle strength, joint range and stability limits (Collins & De Luca, 1993; Horak, 2006). Postural sway relates to both neural commands and mechanical consequences of somatosensory information (Bacsi & Colebatch, 2005). For postural sway during static conditions, motor outputs are generally based on a closed-loop feedback system, whereby sensory information detects body sway, motor outputs correct for the sway, with the information detected by the sensory systems. This continuous process of a closed-loop feedback model refines postural sway (Peterka, 2018; Peterka, 2002). In cases where balance is at risk of being compromised, open-loop feedback strategies, which are fast corrective responses to maintain postural control may dominate to quickly correct for the potential loss of balance. These processes will be discussed in further detail in Section 2.6.

### 2.5.1 General motor outputs

General motor outputs relate to those that are not explicitly governed by neural commands. Instead, these relate to additional outputs used to maintain upright posture and include mechanical fluctuations of joints to help maintain posture that relate to open-loop feedback strategies (Collins & De Luca, 1995a). For example, ankle proprioceptors for balance control are utilised in quiet stance as they are most closely coded to the oscillation range expected in this condition, approximately 5 degrees (Peterka, 2002). Ankle proprioceptors use a much smaller motion encoding range than the vestibular system (±400 deg for SCC, ±180 deg for otolith organs) and tend to be utilised for conditions where loss of balance is unlikely. Open-loop strategies also occur in instances where balance is maintained over very short time intervals (<1 sec) with small displacements (Collins & De Luca, 1995b).

### 2.5.2 Vestibular mediated outputs

The vestibular system mediates three main motor outputs, the vestibulo-ocular reflex (VOR), vestibulo-collic reflex (VCR) and vestibulo-spinal reflex (VSR). These reflexes enable an individual to maintain a stable visual focus (VOR), maintain a stable head position (VCR) or upright body position (VSR). Vestibular reflex measurement is also used to quantify vestibular system function, which is discussed Section 2.10.

#### 2.5.2.1 Vestibulo-ocular reflex

The VOR prevents retinal slip to maintain a stable visual image on the retina during motion. The primary purpose of the VOR helps to preserve visual acuity during motion by generating a reflexive eye movement in the opposite direction to head movement to stabilise the visual image on the retina.

Physiologically, the VOR is a three-neuron arc mediated by the SCC, with a primary sensory neuron located in Scarpa's ganglion, interneuron at the level of the vestibular nuclei, and oculomotor neurons coursing to extra-ocular muscles (Bronstein et al., 2015). Motion detected by the SCC causes primary vestibular afferents to be innervated in turning causing a compensatory eye movement in equal magnitude and opposite direction to the head movement to maintain gaze stability. The ratio of eye movement to head movement is the VOR gain, which is typically used to measure vestibular outputs (more on this in Section 2.10.1). The visually enhanced VOR (VVOR) relies on the interaction between the visual and vestibular systems. The VOR is enhanced when vision becomes available.

#### 2.5.2.2 Vestibulo-collic reflexes

The VCR are mediated by elements of the peripheral vestibular system and serve a role in stabilizing head position in relation to the body by acting on neck musculature. These reflexes are not essential to maintain upright posture but are nonetheless important as a compensatory mechanism. It is typically considered a righting reflex as it acts on the neck musculature (Herdman & Clendaniel, 2014) to stabilise the head, and can be “turned off” during voluntary head movements (Cullen, 2012).

#### 2.5.2.3 Vestibulo-spinal reflexes

Reflexes mediated by both the proprioceptive system and the peripheral vestibular organs include those that enable one to maintain an upright posture and balance, and collectively are the vestibulo-spinal reflexes (VSR). Vestibulo-spinal pathways play a stabilising role in head and body posture, and selectively adjust postural tone to accommodate unexpected changes in body movement (Cullen, 2012), as well as play a role in balance. The cerebellum regulates the function of these reflexes (McCaslin et al., 2015). Similar to the VOR, a three-neuron arc comprises the most direct pathways to mediate the VSR, but there are more complex pathways that dominate these processes (Goldberg & Cullen, 2011).

The lateral, medial and reticulospinal tracts are the main descending vestibulo-spinal tracts involved in postural control. The lateral vestibular nucleus projects to the lateral vestibulo-spinal tract; the medial and inferior vestibular nuclei project to the medial vestibular spinal tract. The reticular formation in the pons and medulla oblongata projects to the reticulospinal tract (Sengul, 2011).

The VSR's are generally mediated my multiple mechanisms in the body but are most reliant on information from the vestibular system. These work with myotatic (stretch) reflexes used to modulate skeletal muscle tone in the trunk and limbs in response to head and body movement. There is strong evidence to show that the VSR's contribute to standing balance and postural control across standing balance conditions (Bacsi & Colebatch, 2005). As body sway increases the vestibulo-spinal tracts tend to play a more dominant role.

## 2.6 Postural control

Postural control is defined as the ability to maintain equilibrium in an upright position (Cyr et al., 1985; Peterka, 2002). It is a learned skill that relies upon the integration of multiple sensorimotor processes, which include movement and sensory strategies, spatial orientation, and biomechanical constraints (Horak, 2006). Sensory information from the visual, somatosensory and vestibular systems contribute to postural control. The amount of sensory system contributions vary, with their relative weighting dependent on the task and the environmental context. (Horak, 2006). This section will provide an overview of postural control development, how postural stability is maintained, and an internal model of postural control.

### 2.6.1 Postural control development

Postural control and motor development relies on neural mechanisms generated by the central nervous system. Two main models, the reflex hierarchical model and the systems model characterise postural control development, however these models are somewhat age dependent. Woollacott (Woollacott & Shumway-Cook, 1990) describes the reflex hierarchical model, based on the premise that the central nervous system is organised in a vertical hierarchy, with different aspects of postural control mediated by specific areas of the central nervous system (Woollacott & Shumway-Cook, 1990). For example, the spinal cord mediates primitive reflexes, and the brainstem mediates tonic reflexes, such as those arising from the vestibular system. If balance is compromised during motor activity, complex sensory system integration at the level of the cortex is needed. This model proposes the previous motor developmental milestone must be mature before the next milestone can be attained.

A systems approach to postural control assumes that the central nervous system is not the predominant mechanism, but rather, forms part of the various systems within the body involved in postural control (Woollacott & Shumway-Cook, 1990). In this model, complex interactions between the various systems and subsystems enable movement and postural maintenance. While both models are applicable to postural development in children, the reflex hierarchical model seems more fitting for the early stages of postural development. That is, the development and mastery of motor milestones typically occur in a sequential manner, whereby a certain set of skills must be acquired before the next milestone can be achieved. To this end, independent motor milestone development is dependent on maturation of the higher centres within the CNS (Woollacott & Shumway-Cook, 1990). Once fundamental motor milestones have been achieved, a systems approach becomes more relevant in the context of postural control.

Similar models of sensory organisation have been proposed by other authors (Hirabayashi & Iwasaki, 1995) whereby sensory systems are gradually integrated with the CNS, and are age dependent. Earlier developmental processes for postural control are reliant on neuromuscular involvement, where accurate execution of musculoskeletal responses is an important prerequisite for the latter development of sensory organisation. Evaluating postural control using the systems model can help to understand the underlying mechanisms contributing to balance control., and therefore it is reasonable to explore these systems separately where possible (Charpiot et al., 2010). Furthermore, it is hypothesised that that sensory organisation takes longer than motor control acquisition and mastery (Forssberg & Nashner, 1982).

### 2.6.2 Maintaining postural stability

Postural stability is achieved by an individual making postural adjustments to their body position. These can occur under two primary conditions, either prior to (anticipatory postural adjustments) or during (associated postural adjustments) movement to maintain centre of gravity (Wade & Jones, 1997). In anticipatory postural adjustments, we see an increase in compensatory movements when the support surface is moving, or when the substrate changes to be less stable, which decreases the amount of support available (Nouillot et al., 1992). When considering associated postural adjustments, which occur during motion, the centre of gravity changes and postural control is constantly adjusted to adapt to the process of moving to a new position.

Postural control is reliant on two distinct mechanisms involved in motor output which have different central processing requirements: an open-loop feedback system and a closed-loop feedback system. The open-loop system describes a movement that is unregulated, where there is no relationship between a motor output and sensory inputs (in effect, the feedback from sensory system information is ignored) (Peterka, 2002). On the other hand, a closed-loop system consists of a motor output which is refined or regulated by sensory inputs and central processing (Adams, 1971). Both open and closed-loop sensory processes contribute to postural and motor control and depend on several factors including age, intrinsic and extrinsic variables.

Increases in postural sway can be due to various factors, but are generally thought to be affected by any of the following mechanisms: 1) the base of support is sub-optimal which in turn causes an individual to take a compensatory step or movement to retain or regain balance; 2) the environmental context, for standing balance conditions where there is sensory conflict or changes to somatosensory information,  postural sway may increase; 3) an individual's age, it is known that children sway more than adults even during upright static balance conditions, and 4) impairment of any construct related to maintaining balance including sensory inputs, central processing, muscle strength or sensorimotor function.

### 2.6.3 An internal model of postural control

There is evidence to suggest that motor control can still be achieved in the absence of sensory input (Massion, 1994; Miall & Wolpert, 1996). Miall and Wolpert's model of sensory integration is based on the premise that motor control is an anticipatory state; whereby a motor position is estimated, and this position is used to anticipate the next positional state (Miall & Wolpert, 1996). This forward model represents typical behaviour of the motor system related to motor output and includes several parameters related to state (position, acceleration, velocity) to be integrated with sensory inputs and system dynamics to predict the future state. It relies on the premise that information received by the sensory systems are used to inform motor outputs, and these outputs are continually refined, creating continual feedback processing. Error messages between the estimated and actual motor outputs are compared and refined to enable appropriate motor outputs. Over time, this 'internal error model' can be used as a reference point to predict subsequent motor and sensory states. In cases where sensory information is limited or compromised, there exists redundancy within the internal model to ensure that the motor outputs can be achieved, based on previously learned experiences.

Massion described several components of postural control related to reference values to determine the state and position, multisensory inputs to regulate body position and orientation, and flexibility in postural reactions and anticipatory states (Massion, 1994). Within this model, there exists a 'postural body schema' which is the internal representation of body awareness, including vertical referential points and body dynamics (Gurfinkel, 1994). The postural body scheme is based on body kinematics to inform perception of body position in space and can also be utilised when maintaining a stable body position for postural control. This leads to an 'internal' model of postural control, which is based on learned experiences driven by error messages. This is a fundamental component to maintain balance and is predominantly driven by the cerebellum when sensory information is delayed or not available. Both theories enhance the understanding of how balance control can still be achieved with limited sensory inputs.

## 2.7 Sensory organisation and postural control

Section 2.3-2.5 discussed elements required for balance system organisation. Balance control relies on several factors: sensory inputs from visual, somatosensory, and vestibular systems which are integrated via central processing mechanisms to provide motor outputs to maintain balance. The motor adjustment processes involve coordination of musculoskeletal reflexes (Sinno et al., 2021), and feedback systems that contribute to refinement of motor outputs (closed-loop feedback) or reflexive motor outputs to prevent loss of balance (open-loop feedback). The internal model of postural control is used to anticipate and refine various motor states to ensure that balance can be maintained in scenarios where sensory inputs are compromised. This model relates to refined use of sensory system information, where older children and adults have been shown to employ strategies that make more accurate corrections, resulting in less body sway (Riach & Starkes, 1994; Shumway-Cook & Woollacott, 1985).

To date, debates continue regarding which dominant sensory input contributes to postural control for static and dynamic conditions. Lack of consensus regarding postural control strategies also exist between adults and children. It has been postulated that proprioceptive information is dominant in postural control during static, unperturbed conditions, with limited information coming from the vestibular system unless large postural changes are required (Bacsi & Colebatch, 2005; Fitzpatrick & McCloskey, 1994). Other studies have demonstrated that VSR contributions mediated by the vestibular system increase during unstable conditions (Bacsi & Colebatch, 2005). In standing conditions where there is no sensory conflict. Bacsi and Colebatch (Bacsi & Colebatch, 2005) found postural sway was too small to be detected by the vestibular system, but once standing task complexity increased, such as standing on an unstable surface, VSR contributions to maintain posture were noted.

Sensory system contributions to balance control can also vary depending on environmental context. The predominant sensory system during movement can be dependent on the frequency or speed of the movement. Visual and somatosensory systems are more sensitive to low frequency movements, compared to the vestibular system, which is more sensitive to high frequency movements (Howard, 1986). The contribution of different sensory systems can also change as we mature or with pathological processes which may cause one of the senses to work sub-optimally. However, it is still possible to achieve and maintain balance if one of the sensory systems is working sub-optimally, but the process for balance maintenance is more difficult in these circumstances. Therefore, the relative contributions of each sensory system to balance control is implicated by sensory system dysfunction and maturational stage of the given individual. This is particularly pertinent during the developmental stages of motor development.

### 2.7.1 Sensory system contributions to postural control across the lifespan

Younger children have been shown to have greater postural instability than older children. This is thought to be due to changes in the relative weightings of sensory information, and also the integration of these inputs over time (Kirshenbaum et al., 2001). It has also been found that the movement strategies used to maintain balance can change with age (Kirshenbaum et al., 2001). Evidence for the changes in the contribution of each sensory system has been shown by Rine (Rine et al., 1998), using the sensory organisation test in children 3-7.5 years, and adults. They found that children underwent a transitional change in postural control over a period of 3-7 years. By six years of age, somatosensory inputs to postural control were adult like, yet by 7.5 years, vision and vestibular inputs to postural control were not yet effectively integrated. Cuisinier also found that reweighting of visual and somatosensory inputs occur linearly between 7-10 years of age, particularly when somatosensory information is modified (Cuisinier et al., 2011).

If one considers the visual system, generally with increasing age, reliance on the visual system for balance control decreases as somatosensory and vestibular inputs are optimally integrated into the central processing mechanisms. It is well established that children under four years of age are more reliant on visual cues rather than somatosensory or vestibular information (Forssberg & Nashner, 1982; Shumway-Cook & Woollacott, 1985). This works relatively well in simple environments but not for more complex scenarios or with movement where somatosensory or vestibular inputs dominate. In children, inconsistencies across the literature are evident regarding how visual inputs for balance control are utilised and when this becomes similar to adults. Some note that visual inputs to balance control are similar between children 7-8 years and adults (Forssberg & Nashner, 1982), but others note that this can occur as late as adolescence (Hirabayashi & Iwasaki, 1995). Other investigations have not shown visual system predominance in younger children (Foudriat et al., 1993). A transitional shift in reliance on visual information to reliance on somatosensory information for balance control has been noted to occur between 4-6 years (Casselbrant et al., 2007; Shumway-Cook & Woollacott, 1985) but this transitional period does not necessarily follow a linear pattern. The transition of balance control towards reliance on somatosensory inputs occurs in tandem with the timing of important phases of motor development (Forssberg & Nashner, 1982; Shumway-Cook & Woollacott, 1985).

The somatosensory system is thought to be the earliest to integrate to adult form. However there are differences across studies regarding when this occurs; age ranges span from 3-4 years (Hirabayashi & Iwasaki, 1995), between 4-6 years of age (Rine et al., 1998), and 5-8 years of age (Sinno et al., 2021). Somatosensory inputs for postural control are also related to neural, sensorimotor, and motor control mechanisms. Typically during quiet stance, a combination of open-loop and closed-loop feedback strategies are utilised (Collins & De Luca, 1993) but in children, reliance on these systems are likely dependent on age, particularly if sensory contributions for postural control are not yet optimally integrated.

Of the three sensory systems, vestibular contributions to balance control are least well documented. Evidence suggests that vestibular contributions to balance control are minimised during quiet stance, but instead are dominant in complex sensory environments when other sensory information is compromised, or for instances where there is an increased risk of losing balance. This is despite the vestibular system being one of the main afferent sensory projections to the central processing mechanisms for postural stability. This may be related to the fact that vestibular information is multimodal and is integrated with other sensory mechanisms to generate certain motor outputs (such as the VOR and VSR). Various studies in adults have demonstrated that vestibular contributions via VSR measurement to balance control increase with task complexity (Bacsi & Colebatch, 2005), but this has been seldom explored in children. Furthermore, estimation of vestibular contributions to balance control have traditionally relied upon testing which measures overall amount of postural sway under different sensory conditions. The contribution from the vestibular system is thought to be unveiled when testing in complex standing conditions where access to visual and somatosensory inputs are removed. However, there is a lack of evidence of the contribution or its integration over childhood.

Nevertheless, repercussions of sensory impairment, particularly related to vestibular dysfunction have demonstrated that impacts on balance control are more pronounced, suggesting that vestibular system contributions to balance control are important (Black et al., 1988; Ionescu et al., 2020). However, many studies explore sensory contributions to balance control focusing on healthy individuals with normal sensory processes and fewer still have investigated it in childhood.

## PART II: How is balance measured?

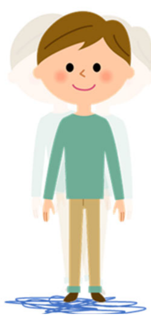
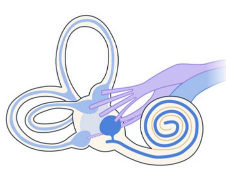
Sensory system contributions are important to provide cues for postural control, with each system 're-weighted' to be more dominant depending on numerous factors. Various neural loops contribute to postural control; closed-loop systems utilise mechanisms to modulate the motor output, whereas open-loop systems provide non-modulated information to peripheral structures, with no way of using feedback to refine the motor output. In children, sensory inputs for balance are also fundamental for motor milestone development and motor proficiency.

Considering balance function broadly, balance measurement can relate to 1) motor tasks related to daily activity, known as functional balance, 2) postural control comparisons across different sensory environments, or 3) focus on discrete sensory systems to quantify function. This PhD project will focus on assessments of functional balance, postural control, and vestibular system assessment, as outlined in Table 2.1.

Numerous studies over the decades have aimed to quantify balance using the various constructs. Measuring functional balance has quantified balance ability and helped to guide interventional approaches for both adults and children. Postural control comparisons using force plate measures have been shown to be overall effective in documenting sensory system contributions to balance control. Early research described afferent information from sensory systems directly modulates outputs to maintain postural stance, yet the complexity of sensory integration has been largely unveiled through more recent literature.

Sensory system assessment can be useful to quantify function and identify any deficits that require further management or intervention. Of the sensory systems used for balance control, the vestibular system is widely explored, and recent literature has shifted this focus to assessment of vestibular function in children.

**Table 2.1.** Three main constructs for balance function explored in the PhD project: relating to functional balance, postural control and sensory system contributions.

| Construct | Used to measure | How is it measured |
|---|---|---|
| **Functional balance**  | Day-to-day balance ability for tasks that involve motor coordination and balance | Set of motor activities subjectively rated by an examiner. Motor activities relate to daily motor tasks such as standing on one leg, walking, jumping, and gross motor skills. |
| **Postural control**  | Motor strategies used to maintain balance across different sensory or environmental conditions. | Quantitative assessment of postural sway using different sensory conditions typically measured using centre of pressure, which is the overall force exerted by the feet to maintain centre of gravity. |
| **Vestibular system contributions**  | Peripheral vestibular function and to an extent, the innervating nerves and vestibular mediated reflexes. | Quantitative measurement of vestibular mediated reflexes. |

## 2.8 Functional balance ability

Functional balance measures quantify balance performance related to daily activities and involve direct observation of functional performance-based tasks. Findings can be used as a baseline measure to better understand functional balance performance, as a reference point for onward referral if skills are not met, or to monitor functional balance performance throughout intervention.

Functional balance measures can be applied across the lifespan. In children, functional balance typically relates to developmental motor milestones across a range of areas (Deitz et al., 2007), and overall balance performance. For adults, functional balance typically relates to task performance for balance during activities of daily living and whether the patient is at risk of falling in these contexts (Langley et al., 2007). Most common measures in adults include the Berg Balance Scale (Berg, 1992) and the Timed Up and Go test (Podsiadlo & Richardson, 1991) for older community dwelling adults.

Clinical Test of Sensory Interaction and Balance (CTSIB) is a measure that can be applied across the lifespan and has been shown to differentiate between people with and without vestibular impairment (Cohen et al., 1993). CTSIB was first described by Shumway-Cook and Horak (Shumway-Cook & Horak, 1986) and included six conditions, three performed on firm ground with eyes open, closed, and visual conflict dome; and three performed on foam with eyes open, closed, and visual conflict dome. This has been largely superseded by the modified version of CTSIB which does not include visual conflict dome conditions, as these conditions provide redundant information (Wrisley & Whitney, 2004). The modified CTSIB is most sensitive in identifying patients with vestibular disorders (Wrisley & Whitney, 2004).

Motor proficiency scales are a widely used assessment measure of motor proficiency in the paediatric population. The Bruininks-Oseretsky Test of Motor Proficiency (BOT-2) is a standardised measure of motor performance across a range of motor activities including fine manual control, manual coordination, body coordination and strength and agility (Bruininks, 2005). The body coordination composite includes the bilateral coordination subtest, which measures motor skills related to physical activity (such as jumping and using hand-eye coordination) as well as a balance subtest which measures motor skills important to maintain posture. Of particular interest to postural control, the balance subtest determines trunk stability, stasis and movement, and visual dependence on motor tasks (Bruininks, 2005).

Functional balance measures are useful to quantify overall balance performance in an individual, yet they do not capture clinically significant changes in postural sway that may be relevant to monitor change in postural control strategies over time.

## 2.9 Postural control measurement

Instrumented measures of postural control have been widely used in the literature to determine postural stability. Historically, assessment has largely focused on adults and utilised for rehabilitative purposes (Furman, 1995; Marioni et al., 2013), but more recently there has been interest in the paediatric space to explore correlates of sensory system contributions dependent on age and assessment condition.

The overall aim of postural control measurement is to explore relative sensory contributions and does this through evaluation of the ways the visual, somatosensory, and vestibular systems work together in different environmental conditions. Measurement of cerebellar contributions to postural control may also be possible depending on the analyses performed. Postural stability is typically measured in a simulated environment and can provide information about overall postural stability using all sensory information, or isolate each sensory system based on sensory input modifications. Force platforms are the gold standard to measure postural stability (Clark et al., 2010) however there remains conjecture regarding the optimal clinical test protocol and standardised clinical application.

Postural sway can be precisely measured using a force platform to document changes in sway over a specified time period. Specifically, the assessment involves the measurement of perturbations exerted by an individual in different sensory conditions during upright stance (single or double leg). Changes in foot pressure are typically dependent on how the sensory environment is manipulated; for conditions where the force plate is tilted or compliant the overall amount of pressure is expected to increase. Postural control patterns in upright stance typically involve body oscillation in the anteroposterior plane (Kohen-Raz et al., 1992).

An individual's inherent body oscillations during upright stance can be measured by the overall amount of foot pressure exerted on the force plate, known as the centre of pressure (CoP). In static conditions this approximates the centre of gravity but for dynamic conditions represents neuromuscular responses (Clark et al., 2018). The CoP path length (amount of pressure exerted over a specified time period), and path velocity (total path length (cm) divided by trial duration (seconds)) in the anteroposterior (AP), or mediolateral (ML) plane are common metrics to measure postural control and are time-domain focused. Although these measures are commonly used, they are limited in detecting the richness of postural sway data as they only present overall amount of postural sway and do not account for context-dependent changes in postural performance (Lacour et al., 2008; Quek et al., 2014). For example, two individuals may show similar overall postural sway scores, but their postural control strategies may be different to maintain their posture: one may show small amplitude, rapidly oscillating movement, whereas another may show larger amplitude, but less rapid movement (Clark et al., 2014).

One way to better understand postural control strategies are via discrete wavelet transform (DWT) analyses, which explore postural sway data as a function of discrete frequency bands and have only recently been considered in the literature as useful measures (Micarelli et al., 2020; Rhine et al., 2017). The wavelet transform involves decomposing postural sway data into discrete frequency bands thought to relate to physiological constructs. High-frequency (fast speed) movement relates to proprioceptive information and use of open-loop strategies (Kirchner et al., 2012), whereas low-frequency (slower speed) movement is thought to be associated with visual and vestibular information (Liang et al., 2014; Paillard & Noe, 2015; Rhine et al., 2017) and related to closed-loop systems. Wavelet analyses enable greater understanding of movement patterns in relation to the physiological constructs of balance control and can help to unveil more subtle postural control strategies of an individual. Using the work of Sim et al (Sim et al., 2018) and Liang et al (Liang et al., 2014), Figure 2.3 shows an adapted version of the relationship between DWT analyses and open-loop or closed-loop signals. The figure has been adapted to include the distinct frequency bands reported by Liang et al (Liang et al., 2014), which will be used in the PhD project.

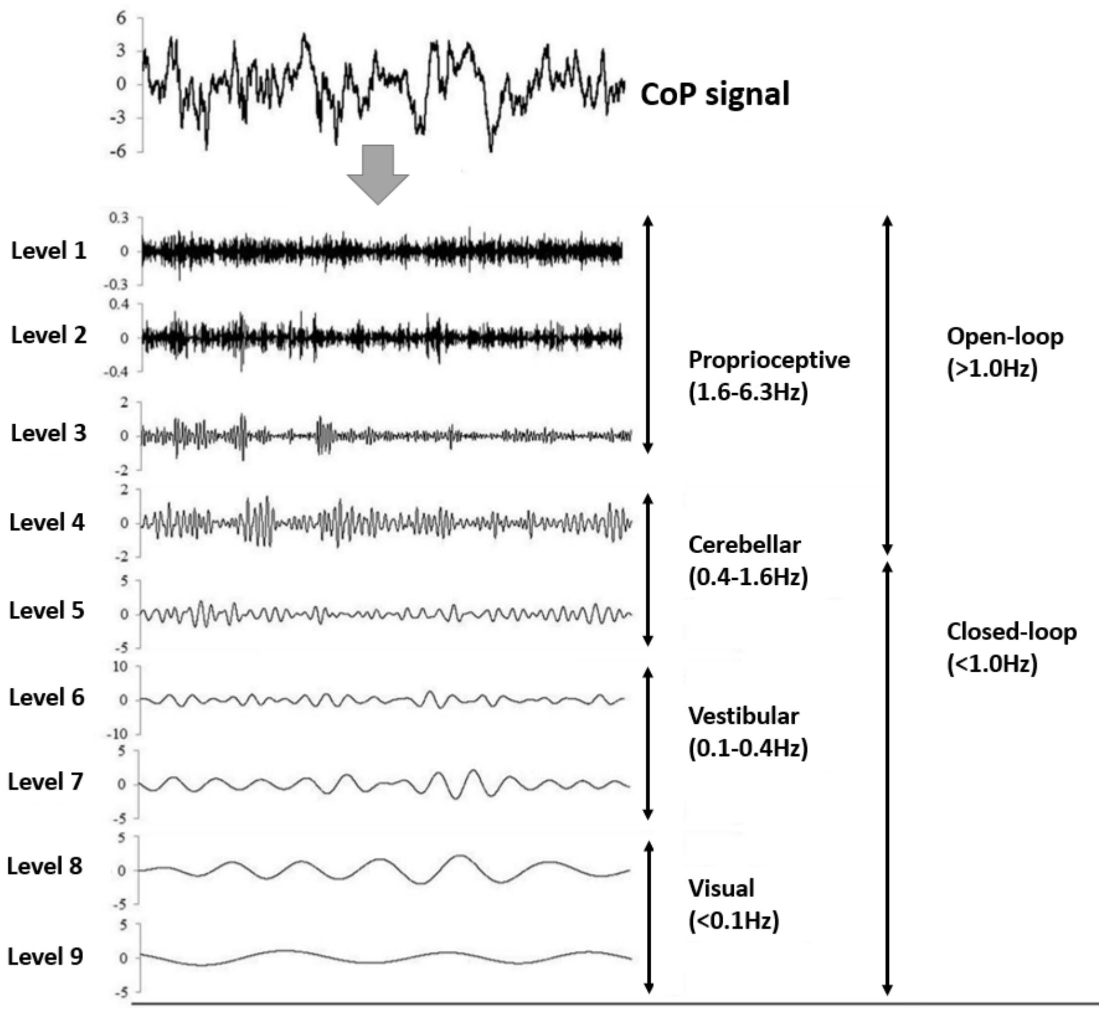



**Figure 2.3.** Relationship between DWT analyses, physiological mechanisms, and open/closed loop systems. Figure adapted from (Sim et al., 2018) and DWT bands from (Liang et al., 2014).

### 2.9.1 Dynamic posturography

Dynamic posturography involves assessment of standing balance on a sway reference board to measure overall sway or diversion from centre of gravity. This board can be manipulated to give conflicting sensory information relative to the other sensory systems being measured and uses a sway reference force plate with conflicting visual stimuli to simulate different conditions. Six conditions are typically derived utilising the sensory organisation test (SOT) and range from standing on a stable surface with a stable visual foreground; to standing with eyes closed on a dynamically tilted or sway referenced surface.

Several authors have utilised sensory organisation testing (SOT) and dynamic posturography to measure postural control maturation in typically developing children (Hirabayashi & Iwasaki, 1995; Rine et al., 1998; Steindl et al., 2006). These studies have shown that sensory integration for postural control in children develops over a time course before reaching adult-like form (Foudriat et al., 1993; Hirabayashi & Iwasaki, 1995; Rine et al., 1998). Hirabayashi & Iwasaki (Hirabayashi & Iwasaki, 1995) studied children from 3-15 years of age and compared SOT with an adult population. Children with mild developmental delay were excluded but not those with otological history (including sensorineural hearing loss, or recurrent middle ear disease). Findings from sensory organisation testing were analysed by examining the ratio of two SOT conditions that best represented the three areas of sensory function (somatosensory, vision, and vestibular). Somatosensory function was not different between the paediatric age groups and adulthood, even for the youngest age group of 3-4 years. On the other hand, the SOT measures for vision showed differences between all groups except for the eldest paediatric when compared to adults. Vestibular function contribution showed the greatest difference across age groups. Differences in ratio scores related to vestibular proficiency were evident across multiple age groups suggesting vestibular system contributions to postural control is perhaps more significant than proposed. Hirabayashi & Iwasaki found developmental differences for the easiest condition across age groups and attributed this difference to basic neuro-muscular mechanisms of sensory and motor processes (Hirabayashi & Iwasaki, 1995). Overall findings show somatosensory integration in young children is similar to adults, but visual and vestibular inputs to postural control are not yet effectively integrated until adolescence.

A transitional period of postural control stability has also been noted in younger children. Rine et al (Rine et al., 1998) focused on dynamic postural stability in different sensory environments, for children between 3 and 7;6 years and compared to an adult population. Rine and colleagues reported significant differences between all groups, with a gradual decrease in postural sway with increasing age, in agreement with other findings in the literature (Foudriat et al., 1993; Hirabayashi & Iwasaki, 1995), but noted that there was a transitional period of postural control strategies across the age group studied. Rine's exclusion criteria were based on parental reports of known histories of sensory loss (vision/hearing) or known neurological or cognitive deficit; Hirabayashi on the other hand did not elaborate on how children were excluded from their study.

There is evidence to suggest that sensory contributions to postural stability in children vary depending on context. A similar age range was included in a study by (Steindl et al., 2006) exploring the relative contributions of the sensory systems to balance and postural stability in typically developing children, using SOT. An interesting outcome from Steindl's study was that postural stability in uncomplex standing conditions (i.e., standing on with eyes open on a flat platform) did not vary greatly from three years of age to adulthood. For more complex sensory environments (i.e., standing with eyes open on a sway-referenced platform) an age effect was observed. These findings highlight that somatosensory system integration has occurred by three years of age for undemanding sensory conditions. On the other hand, complex sensory environments require greater integration of additional sensory systems for standing stability, including consideration of neuromuscular development, not dissimilar to the findings by (Hirabayashi & Iwasaki, 1995).

Despite most studies using questionnaires to exclude known deficits (Rine et al., 1998; Steindl et al., 2006) the studies demonstrate a staged, rather than linear developmental change in postural control over certain time periods (Foudriat et al., 1993; Hirabayashi & Iwasaki, 1995; Rine et al., 1998). Rine noted that the greatest variability of stability scores occurred between 4-6 years, particularly for conditions of conflicting sensory information. Less variability in stability scores has been observed for other studies (Charpiot, 2010 #23} around this age and even younger (Steindl et al., 2006), suggestive that somatosensory integration for postural control has occurred. These observations have been largely cross sectional; given the potential staged changes in postural stability, longitudinal comparisons across individuals may be more suitable.

Dynamic posturography is considered the gold standard of measuring overall postural stability yet clinical applications are significantly influenced by logistical and financial limitations. Thus, clinicians may consider different ways to measure postural stability using simpler measures such as functional tests or a static force plate.

### 2.9.2 Static posturography

Static posturography utilises similar principles as dynamic posturography to measure postural control. However, the force plate is fixed so somatosensory and vestibular inputs are manipulated using simpler measures. Force plate or stabilometry measurements are best to detect subtle changes that subjective measures of postural control, such as balance scales, do not necessarily measure (Clark et al., 2010; De Kegel et al., 2011). Often these assessments include elements of functional tasks related to balance, rather than explicit measures of postural control (De Kegel et al., 2011). The feasibility of these used in a clinical setting are not always possible due to costs involved.

Despite numerous studies in postural control using static posturography, differences in trial duration, conditions assessed, parameters explored, and age groups assessed between studies have led to difficulties in drawing conclusions regarding overall postural control for children. Verbecque's systematic review of postural control (Verbecque et al., 2016) in children demonstrated a range of trial duration, trial number and standing balance conditions. Le Clair and Riach (Le Clair & Riach, 1996) established that test duration is important in the reliability of stability measures, and measures which are too short can significantly impact on reliability of the standing measures.

An alternative and validated measure of standing balance is the use of a Wii Balance board, a commercially available and relatively inexpensive device comprised of four force sensing transducers, with similar characteristics to a force plate setup. This has been validated in numerous studies for both adults (Clark et al., 2010; Holmes et al., 2013) and more recently in children (Lorefice et al., 2015; Rhine et al., 2017).

Many studies have used the modified version of Clinical Test of Sensory Integration and Balance, based on the initial work by Shumway-Cook and Horak (Shumway-Cook & Horak, 1986) as static posturography conditions. The modified CTSIB is a measure of bipedal stance in four conditions: eyes open on a firm surface, eyes closed on a firm surface, eyes open standing on a foam surface, and eyes closed standing on a foam surface. This has been widely accepted as a standard approach for measuring standing balance in adults, yet few studies of standing balance in children have explored all four conditions (Garcia et al., 2011; Micarelli et al., 2020; Riach & Starkes, 1994). For example, in a study by Garcia (Garcia et al., 2011), only two conditions were conducted in eyes open and eyes closed conditions on a stable surface, thus limiting the interpretation of findings in the context of balance stability for more complex standing conditions.

Anthropometric factors such as height and body mass relate to an individual's age. There is conflicting evidence to suggest that these factors can impact on postural control: some found that height or body mass do influence postural control, (Hsu, Kuan, et al., 2009; Schmid et al., 2005), whereas others did not find this association (Barozzi et al., 2014; Peterson et al., 2006). Others did not consider these factors in their studies (Ferber-Viart et al., 2007; Steindl et al., 2006). However, changes in anthropometric factors may require recalibration of the systems used for standing balance, and this continual recalibration can in turn have a greater impact on standing balance whilst children are still undergoing phases of postural development. Changes in body size and mass throughout childhood may well require frequent refinement or recalibration of sensory system integration (Casselbrant et al., 2007).

### 2.9.3 Postural control comparisons between adults and children

Postural control differs between adults and children. It is well known that postural control findings are dependent on the conditions assessed and age ranges explored. The integrative processes for standing balance and approximate ages where children's postural control becomes similar to adults varies greatly between studies and sensory inputs, as discussed in Section 2.7.1. For example, somatosensory inputs to postural control reach adult like form across a wide age range in children. Some suggest this occurs in early childhood from 3-4 years, (Hirabayashi & Iwasaki, 1995) whereas others suggest this occurs later, by 6 years of age (Rine et al., 1998), and 8 years of age (Sinno et al., 2021). Visual and vestibular contributions to balance control are not fully integrated, occurring throughout childhood and well into adolescence (Hirabayashi & Iwasaki, 1995; Steindl et al., 2006). Furthermore, this developmental process may not be linear, and instead involve small turning points across childhood. One turning point tends to be evident at approximately 8 years of age (Figura et al., 1991; Garcia et al., 2011; Riach & Starkes, 1989; Riach & Starkes, 1994).

In children, standing balance differences are evident across age groups. Hsu and colleagues (Hsu, Kuan, et al., 2009) compared age groups between 3-12 years to adults on measures of standing balance across four conditions based on the modified CTSIB (eyes open and closed on firm and foam surfaces). Significant differences were noted in standing balance between younger and older age groups with adults. Postural sway was dependent on the age group and condition: children (from 7 years) showed comparable postural sway to adults in the easiest conditions (when standing on a stable surface); children 8 years and older showed comparable postural sway to adults for more complex standing balance conditions on compliant surfaces with eyes open, and by 12 years of age, no differences to adults were noted across all conditions, consistent with other studies (Ferber-Viart et al., 2007; Steindl et al., 2006). Trial duration may have influenced overall outcomes particularly for younger age groups and their ability to maintain balance over a sixty second period (particularly in eyes closed conditions).

Some studies have demonstrated that at approximately 8 years of age, children undergo a change in postural control development. Specifically, these pertain to the magnitude of sway (including the CoP excursions), responsiveness of sway (related to the root mean square of deviations from the centre of pressure) or related to velocity measures (Verbecque et al., 2016). An additional consideration is whether postural control development follows a linear trajectory and when it approximates adult form. Some authors consider this to occur between 7-10 years of age (Figura et al., 1991; Shumway-Cook & Woollacott, 1985) whereas others argue that this occurs well into adolescence (Barozzi et al., 2014; Ferber-Viart et al., 2007; Garcia et al., 2011; Hirabayashi & Iwasaki, 1995). To better understand postural development, research has focused on models predominately controlled by the CNS, or models which explore the complex integration of sensory systems and other adaptive systems contributing to postural control. What these models have not considered is the discrete development of each sensory process contributing to overall postural control.

### 2.9.4 Strengths and limitations of postural control measurement

Traditional standing balance measures demonstrate clear differences between children and adults for postural control measures which are predominately time-domain focussed. Furthermore, differences in postural control setup, measurements and trial durations do not enable comparison between studies, and while the literature is largely in consensus, there are differences for when sensory system integration approximates adult form. Frequency-domain analysis of postural control using discrete wavelet analyses can provide insight into relative sensory contributions to balance control across standing balance conditions. Yet, this application has not been widely explored in the literature, and less so in children. This novel approach may help to better understand why postural control differs between adults and children, and better differentiate postural sway patterns and strategies across age groups.

Consistent trial duration, parameters, and conditions are crucial to draw comparisons between studies for postural control. Trial duration can vary from 10 seconds (Kolic et al., 2020) up to sixty seconds (Hsu, Kuan, et al., 2009), and trial number from one (Hsu, Kuan, et al., 2009; Riach & Starkes, 1994) up to several (Rival et al., 2005). Trial durations can influence postural control findings; for trials too long there is risk of decreased attentiveness and non-compliance with testing (Steindl et al., 2006); for trials too short there is a risk of not capturing stabilised data.

Centre of pressure measures have found that mean sway velocity was the most reliable parameter of standing balance when using a force plate measure. This is substantiated by other studies exploring the reliability of these tools in a clinical setting (De Kegel et al., 2011; Lin et al., 2008). Whilst posturography is a good measure of overall postural stability, it may not be as useful identifying specific cases of sensory system dysfunction. Sensory integration changes may well be dependent on the conditions measured, and its application to real-life postural stability. Furthermore, the clinical application of this measure is influenced by hardware availability and cost, particularly when using traditional force plate measures.

## 2.10 Peripheral vestibular assessment

Clinical evaluation of the vestibular system provides valuable information about the peripheral vestibular organ function. Specifically, information from the SCC and otolith organs provide useful information to assist with possible site of lesion identification and differential diagnosis of vestibular pathology. Findings from vestibular function assessment can influence management options, particularly for those who experience symptoms of imbalance, dizziness, or vertigo. Figure 2.4 includes an overview of the common clinical vestibular function assessments and what they specifically assess.

| Clinical assessment | Procedure | Measures |
|---|---|---|
| **Anterior SCC:** Video Head Impulse Test | High velocity head impulse downwards when head is positioned in the plane of the ipsilateral anterior SCC | Reduced VOR gain and catch-up saccades would indicate dysfunction of the ipsilateral ASCC |
| **Posterior SCC:** Video Head Impulse Test | High velocity head impulse upwards when head is positioned in the plane of the ipsilateral posterior SCC | Reduced VOR gain and catch-up saccades would indicate dysfunction of the ipsilateral PSCC |
| **Horizontal SCC:** Video Head Impulse Test | High velocity head impulse in the horizontal plane to the ipsilateral side | Reduced VOR gain and catch-up saccades would indicate dysfunction of the HSCC |
| **Utricle:** Ocular Vestibular Evoked Myogenic Potential | Recording of N10-P16 from the under the contralateral eye to air or bone conducted stimuli | Reduced amplitude or absent response under the contralateral eye would indicate dysfunction of the utricle |
| **Saccule:** Cervical Vestibular Evoked Myogenic Potential | Recording of P13-N23 from the ipsilateral sternocleidomastoid (SCM) muscle to air or bone conducted stimuli | Reduced amplitude or absent response from the ipsilateral SCM muscle would indicate dysfunction of the saccule |

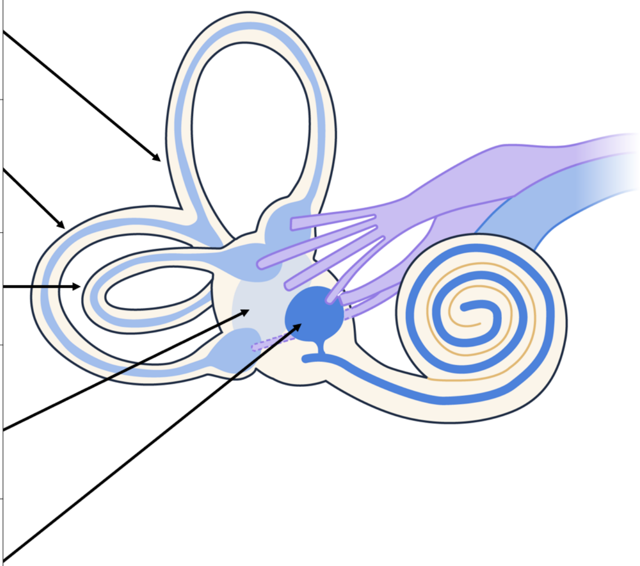


**Figure 2.4.** Overview of common vestibular function assessments. Overall figure adapted from Curthoys (Curthoys, 2012), image adapted from Dingman (Dingman, 2020).

Historically, vestibular function tests have been used to quantify degree of vestibular function in predominately adult populations. However, assessment refinement and emergence of new clinical tools over time have enabled these assessments to be applicable to the paediatric population. This section will outline the common clinical assessments of peripheral vestibular function, which include the video head impulse test to measure SCC function, cervical vestibular evoked myogenic potential (cVEMP) to measure saccule function and ocular vestibular evoked myogenic potential (oVEMP) to measure utricle function. The differences in vestibular findings between adults and children, followed by strengths and limitations of vestibular assessments will be then discussed.

Some vestibular function assessments are not well tolerated by the paediatric population. The caloric assessment, a widely used measurement of HSCC function in adults, has practical limitations for paediatric testing (Cyr et al., 1985). This assessment typically involves a thermal stimulus (air or water) presented to the ear canal, in turn creating endolymph flow in the horizontal SCC, inducing nystagmus generated by the VOR. The assessment is time intensive, requires patient compliance and all irrigations must be completed in order to adequately interpret results. In contrast, rotational (or rotary) chair testing can be used as a screening tool to determine HSCC function. This, and the post rotary nystagmus assessment provide information about VOR generation as the result of rotatory movement in the horizontal plane. Yet rotational chair testing does not quantify the degree or side of dysfunction adequately, as information from both HSCC are acquired simultaneously and is most beneficial in cases where bilateral vestibular dysfunction is suspected.

Many paediatric studies exploring vestibular function have included rotatory assessments as a screening tool. These include establishing function in typically developing cohorts (Charpiot et al., 2010), or identification of vestibular dysfunction in children with SNHL (Crowe & Horak, 1988; Young et al., 1995). More recent studies have considered additional vestibular assessments, including video head impulse test (vHIT) to assess HSCC (Hamilton et al., 2015), and vestibular evoked myogenic potentials (VEMP) to assess saccule function (De Kegel et al., 2012; Leen Maes et al., 2014; L. Maes et al., 2014). While this may reflect evolving technological advancements in vestibular function testing, the importance of diverse vestibular assessments to quantify function cannot be overlooked.

### 2.10.1 Video head impulse test to measure semicircular canal function

The video head impulse test (vHIT) is an extension of the traditional bedside head impulse test and has become a gold standard in quantifying SCC function for high frequency (or daily) movements (L. McGarvie et al., 2015). The primary advantage of this assessment is that is provides localising information for all SCC in three planes of motion: lateral, measuring left and right HSCC; LARP, measuring left anterior/right posterior SCC; and RALP, measuring right anterior/left posterior SCC.

Small magnitude, high velocity head impulses are conducted in the plane of stimulation (left, right, or vertically) whilst the patient visually fixates on a target directly in front of them. The VOR gain is typically derived from the peak velocity of the eye movement (slow phase eye velocity, SPEV) in relation to peak velocity of the head movement (Hamilton et al., 2015; Wenzel et al., 2019), although different methods to determine VOR gain exist (Ross & Helminski, 2016). For example, in a normally functioning vestibular system and test setup, a head impulse to the right will generate an equal magnitude eye movement to the left. When VOR gain is low, the eye deviates from fixation during the head impulse and needs to re-fixate on the target, resulting in a corrective saccade, which is indicative of SCC dysfunction on the suspect side. Historically, this assessment can be performed at the bedside by observing the eye movement, however abnormal VOR gain is difficult to observe if the corrective saccade is covert, or small in magnitude (Halmagyi & Curthoys, 1988). Through recording the eye movements, subtle differences in VOR gain can be determined.

Formative vHIT studies in adults have focused on the importance of correct test technique, as it is known that impulse technique and head impulse velocity greatly influence responses, with optimal test parameters including fast velocities to overcome visual system contributions to balance control (MacDougall et al., 2013; L. McGarvie et al., 2015). Several studies (Bachmann et al., 2018; Ross & Helminski, 2016) have demonstrated that vHIT testing in the paediatric population is a reliable and repeatable assessment tool and the head impulse quality, not quantity is important in this setting (Wenzel et al., 2019).

### 2.10.2 Vestibular Evoked Myogenic Potentials to measure otolith function

Otolith function is commonly measured using vestibular evoked myogenic potentials (VEMP) (Colebatch et al., 1994). The premise of VEMP relies on two fundamental principles: 1) otolith responsiveness to low frequency, high intensity acoustic/vibratory stimuli, and 2) short-latency output measurement via tonic muscle activity at various sites on the neck and face. There are two typical VEMP assessments: cervical VEMP (cVEMP) measures saccule function, and ocular VEMP (oVEMP) measures predominately utricle function.

#### 2.10.2.1 cVEMP

Cervical VEMP (cVEMP) is a useful assessment to provide localising information for saccule function. It has been widely used as a clinical measure in the adult population (Colebatch et al., 1994; Welgampola & Colebatch, 2001a), and also used to quantify saccule function in children (Fuemmeler et al., 2020; Hsu, Kuan, et al., 2009; Kelsch et al., 2006; Picciotti et al., 2007; Rodriguez et al., 2019; Zhou et al., 2014). cVEMP generation is part of a disynaptic pathway, involving the saccule, afferent vestibular projections, and vestibular nuclei. Loud acoustic stimuli presented to the ear evokes a short-latency inhibitory output measured from a tonically contracting sternocleidomastoid muscle (SCM) (Halmagyi & Curthoys, 2021). The cVEMP response is recorded ipsilaterally so responses recorded from the SCM on one side corresponds to the saccule on the same side. Responses are recorded from electrodes placed on the SCM belly resulting in an evoked potential comprising of a peak (p13) and trough (n23) and an interpeak amplitude (p13-n23) (Rosengren et al., 2010; Rosengren et al., 2019). The procedure is quick, non-invasive and the method of SCM contraction can be modified to suit the patient.

Differences in test protocol and stimulus parameters, including the stimulus type and intensity recording method and VEMP analysis (regarding whether responses are obtained at a set or individualised presentation level) can all affect cVEMP interpretation. The degree of SCM contraction can also directly influence responses (Rodriguez et al., 2019), and thus, where possible strategies to ensure equal muscle contraction should be employed via visual observation of tonic contraction, or use of electromyographic (EMG) rectification, which are response curves which are corrected to the background myogenic activity (Colebatch et al., 1994).

Loud low frequency stimuli are shown to preferentially activate the irregular afferents of the utricular and saccular maculae (Abdullah et al., 2017; Curthoys et al., 2012) and are typically presented via air conduction or bone conduction. The literature has demonstrated the use of a standard intensity, low frequency stimulus; this induces a vibration evoked response, thought to share similar neural mechanisms as the VCR and VOR reflexes evoked by perturbations (Rosengren & Colebatch, 2018). Stimulus intensity can impact the response amplitude but have little effect on latency differences in adults. In children, small ear canal volumes cause an increase in stimulus intensity, and therefore a larger amplitude, and needs to be considered in the context of optimal intensities without risking safety (Thomas et al., 2017). A small conductive hearing loss can attenuate the stimulus reaching the otolith organs therefore influencing responses. In these cases, bone conducted stimuli may be considered.

### 2.10.2.2 oVEMP

Ocular VEMP (oVEMP) is based on a similar paradigm to cVEMP, consisting of a di-synaptic pathway, involving predominately the utricle (with a small contribution from the saccule), afferent vestibular projections, and vestibular nuclei. Loud acoustic stimuli presented to the ear or upper forehead (as a vibration) evoke short-latency outputs measured from the inferior oblique muscle. Responses are recorded from electrodes placed on the skin surface located near the belly of the inferior oblique muscle, which becomes more prominent under the skin surface when the eyes are in the upward position. In contrast to cVEMP, oVEMP responses are a crossed myogenic potential, so responses recorded from under the ipsilateral eye correspond to the contralateral utricle (Rosengren et al., 2019).

The oVEMP evoked potential response comprises two excursions, n1 (or n10), and p1 (or p16), and an interpeak amplitude (n10-p16). A baseline measure can also be used, with amplitude between Baseline-n10 (base-n10) quantified in a clinical setting. Both latency and amplitude measures are used to quantify utricular function. The oVEMP procedure is quick and non-invasive, with most efficient responses achieved with bone conducted stimuli applied to Fz, due to simultaneous stimulation of both otoliths (Todd et al., 2007).

## 2.10.3 Adult and child comparisons

Recent studies have aimed to quantify differences in peripheral vestibular function between adults and children across a range of clinical vestibular assessments. Several studies have explored vHIT in children and adults and demonstrated no differences in VOR gain across age groups (Bachmann et al., 2018; Ross & Helminski, 2016). In Ross's study, peak head velocities in the paediatric cohort were significantly slower in all planes when compared to adults. Ross and Helminski hypothesized that peak head velocity differences related to reduced cervical spine stiffness in childhood. Yet no differences between paediatric age groups were noted, suggesting that cervical spine stiffness does not vary that much in children and perhaps does not play as large a role as Ross and Helminski considered.

Some early studies of VHIT in children showed several limitations related to head impulse procedure or technique. These include slow head impulse velocities (Bachmann et al., 2018; Hamilton et al., 2015; Ross & Helminski, 2016), rebounding head impulse technique (Hülse et al., 2015) or suboptimal setup related to apparatus setup (poor goggle fit) (Ross & Helminski, 2016).

VOR gain values for typically developing children are inconsistent across the literature. While some note similar VOR gain between children and adults (Hamilton et al., 2015; Janky & Givens, 2015; Ross & Helminski, 2016), others have indicated that VOR gain is dependent on age or the plane of movement that vHIT is performed (Bachmann et al., 2018; Wiener-Vacher & Wiener, 2017). However, the vHIT directly utilises the VOR, which has been demonstrated to change with increasing age (Charpiot et al., 2010; Micarelli et al., 2020). Normative values for VOR gain for vHIT has been established in adults, however few studies have determined normative data in children. Of those that have, normative data has been collected on a smaller scale (Hamilton et al., 2015; Janky

& Givens, 2015). Normative data for vHIT utilising fast head impulses in children has not been quantified comprehensively.

VEMP testing can be applied across the lifespan from infancy through to late adulthood (Hsu, Wang, et al., 2009; Iwasaki et al., 2008; Rosengren et al., 2019; Welgampola & Colebatch, 2001a; Zhou et al., 2014). Kelsch and colleagues (Kelsch et al., 2006), were one of the first groups to explore cVEMP testing in a paediatric population from 3-11 years of age. Overall findings summarised normative data for p13/n23 latencies and amplitudes, with no significant differences in p13 latencies, and p13-n23 amplitudes between age groups. n23 was significantly earlier in the younger age groups, for one side only (left); an unusual finding given the consistent acquisition method between sides, but perhaps related to test order, (i.e., if one side was preferentially tested before the other) which was not included in the methodology. Although group sizes were small and VEMP responses were not controlled for, this study summarises saccule function in paediatric populations well. When comparing cVEMP responses to adults Picciotti et al (Picciotti et al., 2007) found no significant differences in response characteristics in typically developing children (from 3-15 years). They proposed that saccule, vestibular nuclei, and afferent fibre maturation are complete by 3 years of age.

General consensus in the literature is that cVEMP latency differences have been observed between children and adults (Hsu, Wang, et al., 2009; Rodriguez et al., 2019; Valente, 2007), although some studies refute this claim (Picciotti et al., 2007). Shorter cVEMP latencies have typically been noted in children and are thought to be related to anatomical differences in head circumference, neck length (Fuemmeler et al., 2020; Rodriguez et al., 2019; Wang et al., 2008) and possible developmental differences in the pathway function including increases in myelination and conduction velocities for adults (Hsu, Wang, et al., 2009; Nikiforidis et al., 1993). Studies in infants have also found prolonged latencies and attribute this to maturational effects (Young, 2015). Amplitude differences, however, remain somewhat disputed and are related to the concept of EMG rectification. It is known that SCM contraction is linearly related to the cVEMP response magnitude (Chang et al., 2007; Lee Lim et al., 1995; McCaslin et al., 2013). Unrectified amplitudes have demonstrated differences between adults and children, yet normalised cVEMP amplitudes are also correlated with age, showing differences in amplitude responses between younger children, older children and adults (McCaslin et al., 2013).

In contrast to cVEMP measures, oVEMP response latencies and amplitudes have been shown to be similar between adults and children (Hsu, Wang, et al., 2009; Kuhn et al., 2018). In children, early oVEMP latencies (n10) are similar to adults (Hsu, Wang, et al., 2009; Kuhn et al., 2018), whereas for later latencies (p16) there remains conflicting arguments with differences thought to be related to mode of stimulation (Chou et al., 2012; Kuhn et al., 2018). Most of the studies exploring VEMPs in children have focused on one measure only (cVEMP or oVEMP), or only compared child responses (Kelsch et al., 2006; Kuhn et al., 2018; McCaslin et al., 2013; Young, 2015). Of the studies that have compared both VEMP responses and compared to adults, most have focused on reliability measures using a range of stimulus parameters or setups (Fuemmeler et al., 2020; Greenwalt et al., 2021; Rodriguez et al., 2019).

## 2.11 Strengths and limitations of measuring balance

The literature has demonstrated a range of clinical techniques used to quantify balance. These span from functional motor tasks related to daily activities, to computerised methods of postural control, to discrete measurement of the peripheral vestibular system. While functional balance tasks can provide the clinician with an overview of functional balance performance related to age and motor-based abilities, it does not quantify the degree of functional balance performance in relation of balance system organisation, nor capture clinically significant changes for certain tasks. Some functional balance measures also have floor or ceiling effects (Franjoine et al., 2003), and are most useful for detecting moderate or significant functional balance deficits Functional balance assessments are typically age specific or need to be modified so are not directly comparable between adults and children. Test administration and subject compliance can also influence functional balance outcomes.

Postural control differences between adults and children have been well established using static and dynamic posturography (Barozzi et al., 2014; Hirabayashi & Iwasaki, 1995; Hsu, Kuan, et al., 2009; Riach & Starkes, 1994). Both measures use force plates to determine overall centre of pressure exerted on the platform; dynamic posturography uses sway referenced environments. Children generally show greater postural sway across sensory conditions, and this increases with more complex sensory environments. Yet there are conflicting outcomes related to sensory system reliance and the age that this approximates adult form; differences in studies may stem from differences in test setup and postural sway analyses. Most analyses are time domain focused outcomes and quantify sensory system reliance based on comparisons between test conditions. An alternative, yet relatively unexplored approach would be to explore postural control in the context of discrete wavelet transform analyses, where data is broken down into the discrete frequency bands hypothesised to correlate with physiological constructs of sensory information.

While posturography is a useful clinical measure, generous funding and resources are needed to implement instrumented postural control measures in a regular clinical setting. However, there are cost effective alternatives for static posturography; the Wii Balance Board has been proven to be comparable to traditional force plate measures and is available at a significantly reduced cost (Clark et al., 2018). Furthermore, functional balance and posturography have typically been explored as discrete components and measured as such, with inferences of sensory inputs assumed rather than explicitly explored.

Peripheral vestibular function can be reliably measured in the adult and paediatric population, with a range of clinical assessments used to quantify function. Differences in findings exist between adults and children in the literature, highlighting the need for paediatric focused normative data, utilizing a consistent approach to test setup, and test administration. For some assessments, testing may be influenced by additional factors such as middle ear pathology (for VEMP testing when using air-conducted stimuli), sub-optimal fit of the test apparatus (e.g. goggle fit for vHIT), or patient compliance with test setup or procedure.

Furthermore, most studies have focused on discrete assessments of balance and not considered these elements cohesively. For example, postural control measures or measures of otolith function have been compared between children and adults, but these measures of balance have not been considered together. Recent literature is moving towards a more integrated overview of these constructs in the context of balance control (Abdullah et al., 2017; Janky & Givens, 2015), but focus has mainly been on clinical subgroups where balance may be impaired (Cushing et al., 2008; Janky & Givens, 2015; Leen Maes et al., 2014). For typically developing children, establishing the relationship between constructs is an area requiring further exploration. Utilising a range of clinical assessments can provide the clinician with a broader overview of understanding balance control in the individual.

## PART III: Sub-optimal balance: Are there consequences?

As described in Section 2.3-2.5, balance control relies on multiple sensory inputs, central processing mechanisms, sensorimotor mechanisms, and motor outputs. Balance control, in theory, is still possible in the absence of some sensory information, but the extent of balance performance is dependent on which sensory systems are compromised and the postural control task. Sensory systems can be compromised due to a decrease in function, or due to external variables which render the sensory system suboptimal, therefore requiring re-weighting of other sensory information to maintain balance. For example, the visual system may work optimally when navigating in a brightly lit environment, but in darkness, reliance on visual information decreases substantially due to loss of visual acuity in this environment.

Balance control can be affected by a decrease in sensory function relating to visual, somatosensory, or vestibular inputs. Changes to visual acuity, or changes in peripheral vision will affect an individual's ability to utilise vision for balance control. Changes to proprioceptive inputs and outputs, such as motor strength differences, sense of pressure/touch sensation in the lower limbs and feet, peripheral neuropathy or changes to biomechanics will affect the perception of postural control, as well as feedback mechanisms for balance maintenance. A change to vestibular inputs from one or both vestibular apparatuses can significantly impact on balance control and cause changes to self-perception of motion. These factors can be influenced by erroneous vestibular signals projecting to the central mechanisms, in turn affecting the information processed.

Central processing effects can have a negative impact on maintaining balance. Suboptimal connectivity, disruption to central processing (in cases of cerebellar disease, of ineffective cerebellar processing) can impact on refinement of closed-loop mechanisms to maintain balance control in different contexts.

These elements can also have consequences for vestibular-mediated reflexes (VOR, VCR, VSR), or general motor outputs related to sensorimotor or feedback mechanisms. Changes to motor outputs and motor function can also compromise balance control, with changes to muscle strength or peripheral neuropathy affecting somatosensory inputs but also outputs required for closed feedback mechanisms to maintain posture.

## 2.12 Functional consequences of sub-optimal balance

Sub-optimal balance can relate to the individual, motor task or environmental condition. Impairment of sensory system information (visual, vestibular, or somatosensory), errors with central integration or internal postural control models, or motor output impairments can cause loss of balance and symptoms of dizziness, vertigo, or sensory conflict. These impairments may be temporary or permanent.

As discussed in Section 2.6.3, the internal model of postural control enables errors in balance system organisation to be overcome by the recalibration of sensory states. This is based on the redundancy in the model to use information about existing states to predict motor tasks, and refine the model based on the actual motor task executed. Where possible, re-calibration occurs over a period of time and may require some assistance, but the redundancy in the postural control system makes it is possible that balance can be maintained when only two of three sensory systems are working optimally. Despite this, balance may still be compromised for certain contexts. In circumstances of vestibular impairment, increased postural sway may relate to impaired sensory information from the vestibular system, or poorer feedback mechanisms relating to the vestibular mediated reflexes, which can subsequently impact on balance and postural control.
Environmental condition can significantly impact balance performance. For people with sub-optimal balance control, even simple environmental contexts such as standing still

on a firm surface with eyes open may be challenging. Challenges with sub-optimal balance are often amplified in conditions where there is conflicting sensory information or in unfamiliar environmental contexts. For example, if an individual has vestibular impairment, they may be able to walk along the beach in daylight, but once night falls, the loss of adequate visual inputs may make walking along the beach impossible, due to conflicting sensory inputs and the existing vestibular impairment.

Several repercussions of sub-optimal balance performance have been reported in the literature and include difficulties with navigation, physical changes to gait (Halmagyi et al., 1994), increased risk of falls (Cuevas-Trisan, 2019), and visual acuity difficulties (Braswell & Rine, 2006). Increased cognitive load is also a consequence of suboptimal balance (Bigelow & Agrawal, 2015) as well as loss of confidence (Brown et al., 2001) and mental health repercussions including anxiety and depression (Jacob & Furman, 2001; Jacobson & Newman, 1990). These symptoms can significantly impact on daily physical activities and participation (Brown et al., 2001). In children, sub-optimal balance may cause motor milestone delays (De Kegel et al., 2012; Leen Maes et al., 2014), impact on daily balance or manifest as activity limitations (Cushing et al., 2013; Cushing & Papsin, 2018). There is also evidence to suggest sub-optimal balance can have a negative impact on educational outcomes (Bigelow & Agrawal, 2015; Franco & Panhoca, 2008).

## 2.13 Balance in children with sensory impairment

Changes to somatosensory, visual, or vestibular systems can have a consequential impact on balance performance. Sensory system impairment can be congenital, related to a genetic mutation (syndromic or non- syndromic) or structural abnormality, or acquired at any point throughout the lifespan. Balance in individuals with visual impairment can be dependent on the nature of the vision impairment, particularly if acquired or congenital. Congenitally blind individuals perform similarly on standing balance tasks with standard and modified inputs when compared to individuals with vision, but those with acquired vision loss are significantly less stable (Schwesig et al., 2011). Somatosensory impairment can also impact on balance, particularly in relation to foot or lower limb somatosensation (Manor et al., 2010; Zarkou et al., 2020). The significance of sensory impairment can be influenced by numerous factors, including whether the impairment is congenital or acquired (Schwesig et al., 2011), with evidence to suggest that vestibular impairment has substantial impacts on balance performance (Black et al., 1988; Halmagyi & Curthoys, 2021; Rine et al., 2004).

Some clinical subgroups are at increased risk of vestibular impairment by nature of their aetiology. One such group are children with sensorineural hearing loss, a permanent hearing impairment related to loss of sensory hair cells (or stereocilia) within the Organ of Corti, or due to changes to supporting structures of the cochlea or vestibulo-cochlear nerve. Considering the anatomical location of the auditory and vestibular structures it is not surprising vestibular deficits may be associated with hearing impairment. Vestibular impairment is closely correlated with conditions affecting auditory structures as there is a close anatomical correlation (Cushing et al., 2013; De Kegel et al., 2012; Janky & Givens, 2015; L. Maes et al., 2014). The risk of vestibular impairment can be related to aetiology but can vary in clinical presentation. For example, for children with Usher's Syndrome (Friedman et al., 2011), or Enlarged Vestibular Aqueduct (Madden et al., 2003; Sheykholeslami et al., 2004), varied clinical presentations of vestibular dysfunction are common. Surgical consequences for cochlear implantation can impact on vestibular function in a small proportion of individuals (Cushing et al., 2008; Tribukait et al., 2004). Conditions affecting the auditory and vestibular structures can have functional and consequential impacts if left undiagnosed.

Motor skill assessment in children with sensorineural hearing loss has been well documented in the literature (Crowe & Horak, 1988; Rine et al., 2000). However, much focus has been on identifying deficits in one sensory system, with limited consideration of the relative contribution of the other sensory systems to overall balance. Crowe & Horak (Crowe & Horak, 1988) explored motor proficiency in children with sensorineural hearing loss, with groups divided according to the presence or absence of peripheral vestibular function measured using a rotational chair to provide an overall estimate of bilateral, non-localising HSCC function. Overall findings showed that those with vestibular impairment had motor proficiency difficulties, but children with hearing loss but normal vestibular function showed no differences in motor performance. A study by Rine and colleagues (Rine et al., 2000) exploring motor proficiency over a twelve-month period provides insight that children with sensorineural hearing loss can show persistent delays in motor proficiency. Later studies have since demonstrated that motor performance can be impaired in children with sensorineural hearing loss and adequate peripheral vestibular function (Leen Maes et al., 2014). What remains unclear are the broader mechanisms contributing to this documented delay and whether this relates only to sensory system impairment or related to sub-optimal sensory system integration.

Combining clinical assessments of vestibular function and functional balance measures may be used as a better predictor of overall balance performance (De Kegel et al., 2012; Inoue et al., 2013). In their study of hearing-impaired children aged between 3-12 years, De Kegel and colleagues utilised two vestibular assessments to measure overall HSCC function (rotational chair) and saccule function (cVEMP) in combination with tests of motor performance. Children who had vestibular impairment had poorer motor performance. Similar conclusions have been reported in children with profound hearing impairment across a variety of aetiologies (Inoue et al., 2013). These studies highlight the importance of considering multiple assessments, including vestibular tests to quantify function, particularly for those who at risk of delay or divergence from typical development.

## 2.14 Balance in children with sensory and central processing differences

Some individuals experience both sensory and central processing issues which can impact on balance performance. One group of individuals who commonly present with motor impairment are those with autism. This neurodevelopmental condition is characterised by deficits in communication, social-emotional reciprocity, and restrictive, repetitive behaviours or interests, with heterogeneity of presenting symptoms (Association, 2013). The underlying mechanisms for motor impairments in autism are complex: while no specific structural abnormalities exist with this neurodevelopmental condition (Weimer et al., 2001), deficits in central integration may contribute to the impairments observed. For children with autism, evidence of motor impairment has been described through standardised measures of gross motor function using the BOT, and postural control differences (Minshew et al., 2004). For younger children, this has also been demonstrated through differences in motor milestone development, where infants spend more time in simpler postures (such as prone play), rather than complex postures (such as sitting or crawling) (Nickel et al., 2010). Historically, cerebellar inputs were thought to affect postural control abilities in children with autsm (Kohen-Raz et al., 1992), however evidence suggests that other factors, including functional connectivity of brain structures, may have a larger role to play (Just et al., 2004; Minshew et al., 2004).

Sensory integration challenges may be experienced by children with autism, particularly when somatosensory information is modified. This in turn requires greater reliance on visual and vestibular information to provide adequate information for postural stability. Minshew and colleagues (Minshew et al., 2004) demonstrated this finding across a broad age range of individuals with autism, providing insight that these differences are not necessarily confined to childhood development. Other studies have demonstrated similar findings that postural control differences exist for conditions where sensory information is modified (Molloy et al., 2003). On the other hand, Mache, and colleagues (Mache & Todd, 2016) observed greater postural sway for children with autism in both baseline and foam compliant conditions. The proportion of sway difference between the two conditions was similar between the groups; that is, children with autism showed proportional sway increases similar to the typically developing group. Therefore, it is reasonable to suggest that larger baseline postural sway may impact on motor skill performance. While Mache's findings are less likely to be generalised due to study methodology, they shed light on an interesting finding that in fact, standing balance can differ between groups even in the simplest condition where all sensory systems are utilised.

Although peripheral vestibular function in Minshew's study (Minshew et al., 2004) was not explicitly assessed, poorer postural stability observed with modified sensory inputs suggests that sensory system integration may be different for individuals with autism, or there exists an underlying vestibular impairment that has not been identified.

Vestibular function for children with autism has not been an area of clinical interest for decades, until recently (Oster & Zhou, 2022). Of the studies exploring vestibular function, most have focused on individuals with a range of neurodevelopmental disorders (such as attention deficit hyperactivity disorder, autism spectrum disorder, specific learning disorder, or intellectual developmental disability), and of the studies, most have focused on one discrete measure of vestibular function mainly rotational chair (Furman et al., 2015; Goldberg et al., 2000; Lotfi et al., 2017). Furthermore, conflicting evidence of vestibular impairment is evident (Van Hecke et al., 2018). Evidence of normal VOR gain in children with autism contributes to the understanding that the regions in the cerebellum which mediate the VOR are normal, yet this is not a direct measure of peripheral vestibular function (Goldberg et al., 2000). Increased oVEMP amplitudes have been reported in children with autism who experience acoustic hypersensitivity, thought to be due to superior semicircular canal dehiscence; a vestibular pathology arising from the presence of a third mobile window in the labyrinth (Thabet, 2014). This pathology also presents with generalised symptoms of imbalance and further research is required to better understand this finding and the possible associations of this condition with overall postural control in children with autism. A recent retrospective study (Oster & Zhou, 2022) found a small proportion of children with autism had elements of vestibular impairment via vHIT and cVEMP measures; although it is unclear if other aetiologies such as hearing loss contributed to those findings.

Characteristics of vestibular function in children with autism have been unexplored and those studies that have looked at vestibular function, have assessed only discrete portions of the vestibular system often in isolation. Literature has, however, focused more on motor skill development, and standing balance in the context of postural control. While many studies have suggested there is impairment in the sensory integration of proprioceptive, visual, and vestibular systems, many have overlooked the assessment of discrete constructs, including the vestibular system, as well as how the sensory systems work together.

## 2.15 Summary

Balance control is reliant on several multimodal processes including information from sensory inputs, central processing, motor outputs, sensorimotor mechanisms, and other considerations. Several ways to measure balance control have been discussed, with evidence to suggest balance control is different between adults and children. Most measures of functional balance, postural control, and vestibular function have been explored discretely and not from an integrated perspective. Cross sectional comparisons may not adequately capture developmental processes for balance control.

Presently, there does not exist a range of normative, clinical outcomes that can be applied across multiple balance constructs for children between 5-12 years. Considering functional balance, postural control and vestibular function together will form a basis for a novel clinical protocol and be some of the first exploratory research to be conducted and validated in this cohort of children. Proposed clinical assessments will contribute to greater understanding of peripheral vestibular organ function and postural control strategies in children.

Furthermore, for individuals with sensorimotor, central processing or vestibular deficits, balance control can be affected. Functional consequences of sub-optimal balance relate to impacts on daily activities, mental health, literacy skills, safety, and motor skill development. A paediatric focus to measure functional balance, postural control and vestibular performance has only recently been considered for children who demonstrate balance concerns, and of these studies, most have focused on vestibular impairment. Addressing the current evidence gaps is essential to better understand the importance of a cohesive approach to balance assessment and how these outcomes can inform intervention.

# Chapter 3: Rationale, Aims and Hypotheses

## 3.1 Rationale

The research aimed to explore vestibular function, functional balance and postural control in children 5-12 years of age.

Differences between child and adult vestibular function have been described but not extensively explored relating to vestibular system contributions for postural control. Otolith comparisons between adults and children have been established, yet most literature has only focused on one discrete measure of otolith function. Furthermore, clarifying differences in balance function between adults and children across otolith and postural sway measures may provide better insight for understanding nuanced differences in postural sway strategies, given the literature does not demonstrate consensus for postural sway strategies in children.

While recent research has focused on documenting vestibular function in children, most studies have only captured the discrete elements of vestibular and motor proficiency but not explored the assessments together. Establishing normative data in typically developing children via a comprehensive range of balance measures may help to identify children who demonstrate differences in balance function and be used to inform management. Documenting balance measures over time may also help to understand the relationship between constructs. There remains conjecture regarding the relationship between motor proficiency and vestibular function specifically.

Motor milestone delays can be evident across a range of conditions, but the underlying mechanisms for the motor delay is not always clear. Children with sensorineural hearing loss can show motor milestone delays and varying degrees of vestibular dysfunction, but the relationship between these constructs has not been considered comprehensively. Quantifying overall balance function using vestibular and motor proficiency outcomes may help to identify the causes of motor milestone delays and provide clearer management pathways.

Children with autism may also show motor milestone delays and difficulties with overall balance function, but vestibular contributions have not been widely reported in the literature. Establishing vestibular function in this clinical subgroup and understanding the relationship between constructs used for balance function are two areas for further research.

## 3.2 Aims and hypotheses

Aim 1:

For typically developing children between 5-12 years of age: a) compare measures of otolith function, and b) compare postural sway measures and postural sway strategies to a young-middle aged adult cohort.

Hypotheses:

1) Otolith function will differ between adults and children, with children showing smaller responses and shorter latencies across assessments.

2) Postural sway will be larger in children across all measures of standing balance and will demonstrate greater reliance on visual and somatosensory information.

3) In children, shorter VEMP latencies and smaller VEMP amplitudes will be associated with more postural sway.

Aim 2:

To describe the vestibular and motor proficiency development in typically developing children 5-12 years of age through a) peripheral vestibular assessment, functional balance and postural sway measures, and b) monitoring vestibular postural control development at three time points over a twelve-month period.

Hypotheses:

1) Peripheral vestibular function will be positively correlated with increasing age; postural sway will be negatively correlated with increasing age.

2) Typically developing children will show no substantive changes in peripheral vestibular function over a twelve-month period but will show an improvement in postural sway performance.

Aim 3:

For children between 5-12 years of age with bilateral sensorineural hearing loss: a) compare functional balance, postural sway, and vestibular function to typically developing children with normal hearing, and b) determine the relationship between these measures.

Hypotheses:

1a) Postural sway measures will be larger for children with sensorineural hearing loss across conditions where sensory information is modified,

1b) Children with sensorineural hearing loss will show reduced peripheral vestibular function when compared to children with normal hearing,

2) The degree of peripheral vestibular function will influence motor skill performance and postural stability.

Aim 4:

For children between 5-12 years of age with autism: a) compare functional balance, postural sway, and vestibular function to typically developing children, and b) determine the relationship between these measures.

Hypotheses:

1a) Postural sway measures would be larger for children with autism across conditions where sensory information is modified,

1b) Children with autism will show similar peripheral vestibular function to typically developing children,

2) Motor skills will be negatively correlated with postural sway measures.

# Chapter 4: METHODOLOGY

## 4.1 Design and setting

An overview of each study including the research aims, participants and study design is presented in Table 4.1. All child data was collected as part of the PhD project. For Study 1, cross sectional data from typically developing children collected at time point 1 was complemented by cross sectional adult data obtained previously (Vitkovic et al., 2016). Study 2 included cross sectional and longitudinal comparisons of typically developing children. Age matched cross-sectional data from Study 2 (time point 1) was compared to children with SNHL in Study 3 and children with autism in Study 4.

**Table 4.1.** Study design for each PhD aim

| **Study** | **Research Aims** | **Participants** | **Study design** |
|---|---|---|---|
| Comparison of postural control and otolith function between children and adults | For typically developing children between 5-12 years of age: a) compare measures of otolith function, and b) compare postural sway measures and postural sway strategies to an adult cohort. | Comparison of typically developing children to adult established normative data | Cross sectional |
| Developmental trajectory of vestibular function and motor proficiency in typically developing children | To describe the vestibular and motor proficiency development in typically developing children 5-12 years of age through a) peripheral vestibular assessment, functional balance and postural control measures, and b) monitoring vestibular postural control development at three time points over a twelve-month period. | Typically developing children with normal sound detection thresholds | Cross sectional<br><br>Longitudinal (three data points over 12-month period) |
| Vestibular function and postural control in children with sensorineural hearing loss (SNHL) | For children between 5-12 years of age with bilateral sensorineural hearing loss: a) compare functional balance, postural sway, and vestibular function to typically developing children with normal hearing between 5-12 years of age, and b) determine the relationship between these measures. | Comparison of children with normal sound detection and children with bilateral sensorineural hearing loss | Cross sectional |
| Vestibular function and postural control in children with autism | For children between 5-12 years of age with autism: a) compare functional balance, postural sway, and vestibular function to typically developing children between 5-12 years of age, and b) determine the relationship between these measures. | Comparison of typically developing children with normal sound detection and children with autism | Cross sectional |

## 4.2 Participants

A total of 56 school aged children between 4 years, 11 months and 12 years, 11 months years were recruited between January 2018 - January 2020. Recruitment sites included the University of Melbourne Audiology Clinic, Melbourne Cochlear Implant Clinic at the Royal Victorian Eye and Ear Hospital, and The Royal Children's Hospital. The researcher contacted clinical managers or hospital department managers prior to recruitment and attended each recruitment site to provide information regarding study detail, the recruitment process and time commitment involved for recruitment sites and participants. A key contact at each recruitment site was established, with advertising and study material provided to them in person and via email. For some participant groups, recruitment also occurred through word of mouth via special interest groups for private speech pathologists and paediatricians across metropolitan Melbourne. Information regarding the recruitment process and study detail was also provided to those individuals, however, they did not form the primary source of recruitment. There was no access to a central database which captured all participant groups, therefore those recruited represented a convenience sample and were potentially a more motivated cohort than the general population.

Child participants were assigned to one of the three groups: typically developing children; children with sensorineural hearing loss; and children with autism. See sections 4.2.1.1,4.2.2.1 and 4.2.3.1 for inclusion and exclusion criteria. All guardians and participants spoke English as their first language, and none had known cognitive impairment at the time of assessment. Children were excluded from participating if they had a longstanding history of chronic otitis media with effusion, defined as recurrent episodes (≥2) of middle ear effusion over a six-month period requiring medical intervention. Middle ear effusion can impact balance performance (Pazdro-Zastawny et al., 2018), and also affect vestibular assessment. If middle ear effusion was present at the time of assessment, participants were excluded from that assessment point.

To address Aim 1 of the thesis, a comparative cohort of eighty-five adults aged between 19 and 56 formed the final group of participants, which was collected from a separate study between 2014 - 2016. Adults were recruited through the University of Melbourne

Department of Audiology and Speech Pathology and data collection was conducted over this time.

### 4.2.1 Typically developing group

Children forming the typically developing group were sourced from the University of Melbourne Audiology Clinic clinical research database or via word of mouth within the Department of Audiology and Speech Pathology. Families of children who had attended University of Melbourne Audiology Clinic and who had consented to contact for research opportunities were posted a study invitation letter. Potential participants and their families were also approached following their routine clinical appointments if they fit the selection criteria. Follow-up telephone contact 1-2 weeks following letter mailout was an opportunity to confirm letter receipt, describe the study further and screen for inclusion. If verbal consent was obtained, assessment was arranged at a mutually agreeable time at the University of Melbourne Audiology Clinic. If families were still unsure at the time of telephone contact regarding participation but had not declined, then another follow up call was made approximately 2 weeks following initial telephone contact to determine participation interest.

#### 4.2.1.1 Inclusion criteria

Any child aged between 5 and 12 years was eligible for inclusion if they met the following criteria:

1. Normal sound detection thresholds (<20 dB HL) across all octave frequencies
2. The child's age at the time of data collection was between 5 years, 0 months and 12 years, 11 months.
3. No history of chronic otitis media with effusion
4. No reported history of vestibular symptoms
5. No known history of additional neurodevelopmental diagnoses
6. Developmental motor milestones were typically acquired

Criteria 4-6 were established via guardian interview during the initial telephone call and confirmed via questionnaire (refer to Section 4.4.1). Children were excluded from participating if their guardians answered yes to any balance health concerns, additional neurodevelopmental diagnoses, or developmental milestone delay (deemed greater than six months beyond the expected milestone range)

### 4.2.2 Sensorineural hearing loss group

Children who formed this group were sourced from the Royal Victorian Eye and Ear Hospital Otology and Cochlear Implant Clinics. Otolaryngologists and paediatricians based at the Royal Children's Hospital were also involved in participant recruitment. Families of children who had provided consent to contact for research opportunities were posted a study invitation letter. Potential participants and their families were also approached following their routine clinical appointments if they fit the selection criteria. Following the letter of invitation, a telephone call 1-2 weeks later was used to confirm letter receipt, gauge interest in study participation and screen for inclusion in the study.

#### 4.2.2.1 Inclusion criteria

Any child aged between 5 and 12 years were eligible for inclusion in the sensorineural hearing loss group if they met the following criteria:

1. Bilateral, sensorineural hearing loss, of any degree, established via behavioural testing.
2. A minimum of 12 months device use required for cochlear implant and/or hearing aid users.
3. No history of chronic otitis media with effusion
4. No known additional neurodevelopmental diagnoses

Criteria 3 and 4 were established via guardian interview during the initial telephone call and confirmed via questionnaire (refer to Section 4.4.1). Developmental motor milestone delay was not an exclusion criterion for this group given the high prevalence reported in the literature (Crowe & Horak, 1988; Leen Maes et al., 2014; Rine et al., 2000). Eleven children were assigned to the sensorineural hearing loss group.

### 4.2.3 Autism group

The final paediatric group included in this study were children with a clinical diagnosis of autism spectrum disorder. Children from this subgroup were recruited from various sites including University of Melbourne Audiology Clinic, private paediatricians and speech pathologists across metropolitan Melbourne whose clinical caseload included children with autism. Information regarding the recruitment process and study detail was provided to those individuals.

#### 4.2.3.1 Inclusion criteria

Any child aged between 5 and 12 years were eligible for inclusion in the autism group if they met the following criteria:

1. Normal sound detection thresholds (<20 dB HL) across all octave frequencies
2. No history of chronic otitis media with effusion
3. The child's age at the time of data collection was between 5 years, 0 months and 12 years, 11 months.
4. Clinical diagnosis of autism spectrum disorder established via multidisciplinary clinical assessment from a paediatrician, speech pathologist and psychologist, according to DSM-V diagnostic criteria (Association, 2013).

Potential participants were excluded from participating in the study if they had a documented sensorineural hearing loss or longstanding history of middle ear disease. Developmental motor milestone delay was not considered an exclusion criterion for this group given incidence of motor delay for autistic children (Hilton et al., 2012; Provost et al., 2007). Eleven children were recruited for this group.

### 4.2.4 Adult groups

Retrospective data from the two adult groups were used in Study 1 (Comparison of otolith function and postural control in children and adults). Participants were recruited through the University of Melbourne Audiology Clinic and an institution-wide advertisement.

#### 4.2.4.1 Inclusion criteria

For both adult groups, inclusion criteria were:

1. Normal sound detection thresholds (<20 dB HL) across all octave frequencies
2. No reported history of balance difficulties.

Eighty-three adults were included for data comparison and were separated based on the assessments they underwent: either postural control assessment or VEMP assessment.

## 4.3 Institutional approval

Ethical approval for this study was obtained from the Human Research Ethics Committee (HREC) at the Royal Victorian Eye and Ear Hospital, Melbourne, Australia (approval number 17-1348H), and registered through the University of Melbourne HREC (approval number 1750810.1). The research was conducted in accordance with the tenets of the Declaration of Helsinki, and written consent was obtained from all legal guardians of participants following explanation of the rationale, purpose and participant requirements of the study. Child participants provided verbal agreement prior to their participation. Appendix A includes ethics approval documentation. All changes to documentation, procedures or communication processes were ratified by the RVEEH ethics committee and approved by the University of Melbourne HREC. This included an amendment to use de-identified, retrospective adult data as part of the project.

## 4.4 Materials and Methods

The following section outlines the experimental methods utilised in the four studies. Study 1 methodology (Chapter 5) includes comparisons of three clinical assessments (refer to Sections 4.4.4 and 4.4.6) and compares the typically developing child group to adults. Study 2 (Chapter 6) includes an in-depth analysis of each individual assessment using a repeated measures paradigm for the typically developing group (refer to Sections 4.4.3, 4.4.4, 4.4.6). Study 3 (Chapter 7) and Study 4 (Chapter 8) compares child subgroups across all clinical assessments (refer to Sections 4.4.3- 4.4.6).

### 4.4.1 Questionnaire

The questionnaire (Appendix B) was utilised as a screening tool to determine inclusion into the study, and then subsequently used to collect demographic data.

The screening questions to determine participant eligibility into the study included information about the child's overall development (Section 2.1), whether the child met motor milestones at expected ages (Section 2.3) and established if the child had a history of chronic ear infections or grommets (Section 3.1). If eligible, and once written consent was obtained, demographic data was subsequently sought from the other elements of the questionnaire. This was completed by the parent prior to the commencement of the assessment.

The study-designed questions covered domains of physical health including current health status, history of major illnesses or ongoing health problems, and information about general motor milestone development. Information about hearing health was also obtained including history of middle ear infections or surgical history of grommets. For children with SNHL, information was obtained about degree of hearing loss, aetiology of hearing loss and any history of congenital hearing loss in the participant's family. Balance health was determined by a range of symptoms including the description of vertigo, dizziness, clumsiness, or frequent falls. If guardians answered yes to any of these questions, they were encouraged to provide more detail regarding what context symptoms occurred, symptom frequency and impacts.

### 4.4.2 Audiometry and Immittance

Audiometry and immittance testing procedures were conducted in a sound treated booth at each assessment point.

An Interacoustics Affinity PC based audiometer (Interacoustics, Middelfart, Denmark) was used to establish behavioural hearing thresholds and GSI Tympstar (Grason -Stadler Instruments) used for immittance testing. Behavioural thresholds were obtained via air conduction for octave frequencies from 250Hz – 8kHz. Bone conduction was conducted when thresholds were 20dBHL or greater to determine the type of hearing loss.

Immittance testing was used to determine middle ear status and confirm any contraindications to the assessment battery. Tympanometry findings assessed middle ear compliance and ipsilateral acoustic reflex screening (at 1kHz) used to determine the stapedial reflex neural pathway.

#### 4.4.2.1 Audiometry and Immittance outcome measures

The four-frequency hearing level average (4FAHL) based off frequencies 0.5,1,2,4kHz was used to categorise hearing levels, from normal hearing to profound hearing loss. The 4FAHL of both ears were used for inclusion into the participant subgroups.

Tympanometry results were categorised into A, B or C, classified according to Jerger (Jerger, 1970). Children with middle ear effusion (defined as a type B tympanogram, with low equivalent volume with no middle ear compliance) or eustachian tube dysfunction (type C tympanogram) and absent acoustic reflexes at the time of assessment were excluded from the assessment point.

### 4.4.3 Video Head Impulse Test (vHIT)

The video head impulse test (vHIT) quantifies high frequency semicircular canal function through measurement of eye velocity in relation to head velocity. During the assessment, coplanar pairs are stimulated depending on the direction of the head impulse. The horizontal SCC form one coplanar pair, the left anterior and right posterior SCC form the LARP coplanar pair, and the right anterior and left posterior SCC form the RALP coplanar pair. For each condition, the slow phase eye velocity of the vestibular ocular reflex (VOR) was compared to the velocity of the head rotation. An overall VOR gain value can determine SCC function for high frequency rotations.

#### 4.4.3.1 vHIT Setup and Procedure

Head impulses were recorded using the GN Otometrics ICS impulse system (GN Otometrics, Taastrup, Denmark). The lightweight goggles comprised a video camera to record the right eye, and three miniature gyroscopes used to detect head velocity in the relevant planes of motion (horizontal, and in the LARP and RALP planes). An image of the right eye was reflected from a lens to the camera and was recorded using a sampling rate of 250Hz.

Children wore lightweight goggles adjusted to fit the head without slipping from the correct positioning. Minor adjustments to the head strap or the eye cushion were sufficient to ensure correct positioning throughout the assessment. Eye position was calibrated using two laser dots (fixed relative to head position) separated 15 degrees from each other, with the child instructed to follow the laser dot with their eyes whilst keeping their head still.

The researcher performed vHIT in three planes (lateral, LARP, RALP) by moving the child’s head in the plane of interest using high velocity, small amplitude impulses that were unpredictable in direction. During the vHIT assessment, children were instructed to fixate on a small static target 1 metre directly in front of them, at eye level, and maintain this visual fixation for the duration of the assessment.

For the lateral condition assessing the horizontal SCC, the magnitude of the head impulses ranged 15-20 degrees from centre to the left and right. Peak velocity of the head impulses ranged from 150-250 degrees per second using real-time feedback from the software.

Conducting the vertical impulses required a change in head and body position for the child. For the LARP condition, the head and body were positioned 35-45 degrees to the right of the fixation point, and for the RALP condition, the head and body were positioned 35-45 degrees to the left of the fixation point. Similarly, to the horizontal condition, impulse magnitude ranged 15-20 degrees from centre in the vertical plane (up and down). Peak velocity of the head impulses ranged from 100-250 degrees per second quantified using real-time feedback from the software. In all conditions, a minimum of ten impulses were obtained for each SCC assessed and gain measures used for analyses were the average of all impulses.

#### 4.4.3.2 vHIT outcome measures

Data were analysed using OTOsuite Vestibular Software (Version 2.0, build 605). The ratio of slow phase eye velocity of the VOR to head velocity for each impulse, was determined by computing an overall gain value extracted from the areas under the curve of eye velocity (with saccades removed), divided by the area under the curve of head velocity. Individual examination of each head impulse and condition was performed by the researcher, who excluded artifacts due to goggle slippage or blinking, as well as impulses which were not within the specified speeds or had abnormal morphology (Mantokoudis et al., 2015). Overt and covert saccades were also detected by the software and were included in post assessment analyses.

Once this was completed, an average VOR gain value was calculated from all impulses collected for each SCC and used for comparisons.

### 4.4.4 Vestibular Evoked Myogenic Potentials (VEMP)

Vestibular evoked myogenic potentials (VEMP) were used to quantify otolith function. VEMP are short-latency evoked potential responses elicited by low frequency stimuli and controlled by myogenic activity. High intensity, low frequency stimuli activate the otolith afferents which in turn initiate various vestibular reflexes. cVEMP responses infer saccule and/or inferior vestibular nerve function via measurement of an inhibitory response to the stimulus, recorded through tonic contraction of the SCM. oVEMP responses infer utricle and/or superior vestibular nerve function, via measurement of an excitatory response to the stimulus, recorded through tonic activation of the extraocular muscles.

#### 4.4.4.1 cVEMP Setup and Procedure

cVEMPs were obtained with a two-channel setup using the Natus Bio-logic Navigator Pro Auditory evoked potential (AEP) system with Bio-Logic AEP Version 7.0.0 software (Natus, Pleasanton, CA, USA).

Acoustic stimuli were delivered via air conduction using electromagnetically shielded 50-ohm ERA-3 insert phones (Etymotic Research, Elk Grove Village, IL, USA). A 500Hz tone burst stimulus of condensing polarity was presented at a range of stimulus intensities: from 88dB SPL – 113 dB SPL in children; 88dB SPL – 123 dB SPL in adults) to ascertain VEMP threshold. These presentation levels are consistent with existing studies exploring cVEMP (Kelsch et al., 2006; L. Maes et al., 2014; Rodriguez et al., 2019; Zhou et al., 2014). Stimuli were presented at a rate of 5.1Hz and sixty-four presentations were averaged per trial. A linear ramp (with equal rise, fall and plateau of 1 msec) was applied to the stimulus. Electromyogenic activity was amplified 50,000 times and a band-pass filter applied between 10Hz and 2000Hz. An additional notch filter (set at 50Hz, pre-determined by the auditory evoked potential software to prevent 50 Hz mains interference) was also applied. The epoch was set to 53.3ms with a 20.1ms pre-stimulus interval.

VEMP responses were recorded using a four-electrode montage setup: ground/common at Nz (nasion, low forehead), reference (non-inverting) electrode at the sternoclavicular junction (top of sternum) and two inverting electrodes placed on the belly of each sternocleidomastoid muscle on the left and right. Disposable Ambu Neuroline 720 surface electrodes (Ambu, Copenhagen, Denmark) were used. An exfoliant scrub was used to reduce impedance between skin and the electrode, and testing began once all impedances were below 5 kΩ. Both ipsilateral and contralateral traces were recorded, but only the ipsilateral traces were analysed. A schematic diagram of electrode placement for cVEMP testing is presented in Figure 4.1.

The primary method for eliciting cVEMP responses was the elevation method where participants lifted their head from a semi- recumbent position, causing bilateral tonic contraction of the sternocleidomastoid (SCM) muscles, the active recording sites. Due to device limitations, EMG rectification was not available on the software during assessment but EMG activity and SCM contraction was visually monitored by the examiner, and post stimulus rectification was applied to waveforms. VEMP rectification was performed using the full wave rectification method, whereby absolute values of all points along the VEMP trace were compared to the pre-stimulus rectified wave buffer. Each raw trace was rectified first and then averaged as per clinical guidelines (Rosengren et al., 2010).

A minimum of two averaged responses were obtained for each condition: at maximum presentation levels (113 dB SPL), and in 5dB decrements below the maximum presentation level, until the response was absent. The cVEMP threshold was selected at the lowest intensity where a clearly defined evoked potential was present (p13 and n23 within the expected latency range). Given responses involve myogenic activity, the presence of fatigue was controlled by presenting the stimulus alternately to each ear and allowing rest breaks between each trial.

To ensure the evoked potential responses were valid, two control traces were conducted at the end of cVEMP assessment. The control traces comprised of 1. recording with myogenic activity but no acoustic stimulus, and 2. recording with acoustic stimulus but no myogenic activity. Evoked potential responses that looked like either control trace were removed prior to analysis.

### 4.4.4.2 cVEMP outcome measures

Responses were averaged and labelled using established criteria for cVEMP: an initial positive deflection (p1 or p13) followed by a negative deflection (n1 or n23). p13 and n23 latencies were marked, and the inter-amplitude between p13 and n23 was obtained. These metrics were marked and calculated for responses at the maximum presentation level and threshold.

### 4.4.4.3 oVEMP Setup and Procedure

oVEMPs were also obtained with a two-channel setup using the Natus Bio-logic Navigator Pro Auditory evoked potential (AEP) system with Bio-Logic AEP Version

7.0.0 software (Natus, Pleasanton, CA, USA). Stimuli were presented via bone conduction using a Brüel & Kjær Mini-shaker Type (B&K MS) 4810, a handheld electromechanical vibrator fitted with a short M4 bolt (2cm) terminated in a bakelite cap (1.6cm in diameter). The B&K MS was integrated into the Navigator Pro via a DSE Stereo Integrated Amplifier A2760.

A 500Hz tone burst stimulus of condensing polarity was presented at a maximum presentation level 128 dB peak force level (pFL) for children and 142 dB pFL for adults, and at lower levels to determine oVEMP threshold. Stimuli were presented at a rate of 4.1Hz, and thirty sweeps were averaged for each trial. A linear ramp (with rise/fall time of 0.25 msec and plateau 1 msec per cycle) was applied to the stimulus. Electromyogenic activity was amplified 30000 times and a band pass filter applied between 10 and 500Hz. An additional notch filter (set at 50Hz, as predetermined by the AEP software) was applied. The epoch was set to 53.3ms with a 20.1 pre-stimulus interval. The stimulation voltage was decreased in 5dB steps for threshold seeking. This presentation level is congruent with existing studies exploring oVEMP in children (Young, 2015).

Responses were recorded using a four-electrode montage setup: ground/common at the sternoclavicular joint (top of sternum), a non-inverting reference electrode on the chin and two inverting electrodes aligned with each pupil and placed on the extraocular muscles under each eye (inferior rectus and inferior oblique muscles). An exfoliant scrub was used to reduce impedance between skin and the surface electrode, and testing began once all impedances were below 5 kΩ. Both ipsilateral and contralateral traces were recorded simultaneously and analysed due to the otolith stimulation causing activity in the contralateral extraocular muscles.

The researcher held the B&K MS at Fz and supported its weight during stimulus presentation. This was to ensure that the stimulus was delivered at a consistent coupling force and that a repeatable tap was delivered with little pressure on the skull (Chou et al., 2012). Participants lay supine and maintained an upward gaze 15 degrees from vertical (towards their eyebrows) for the duration of the stimulus (Govender et al., 2009). This method raised the muscle belly of the extraocular muscles (the inferior oblique muscle) closer to the electrode, which has been demonstrated to yield higher amplitude responses than other sites (Chou et al., 2012; Hsu, Wang, et al., 2009; Todd et al., 2007).

Traces were obtained at maximum presentation levels and in 5dB decrements below the maximum presentation level, until the response was absent. The lowest intensity where a robust evoked potential was considered the oVEMP threshold. To ensure repeatability, a second trace at the maximum presentation level and threshold level was conducted. Two control traces were also conducted at the end of each assessment comprising 1: No stimulus with myogenic activity, and 2: Stimulus with no myogenic activity.

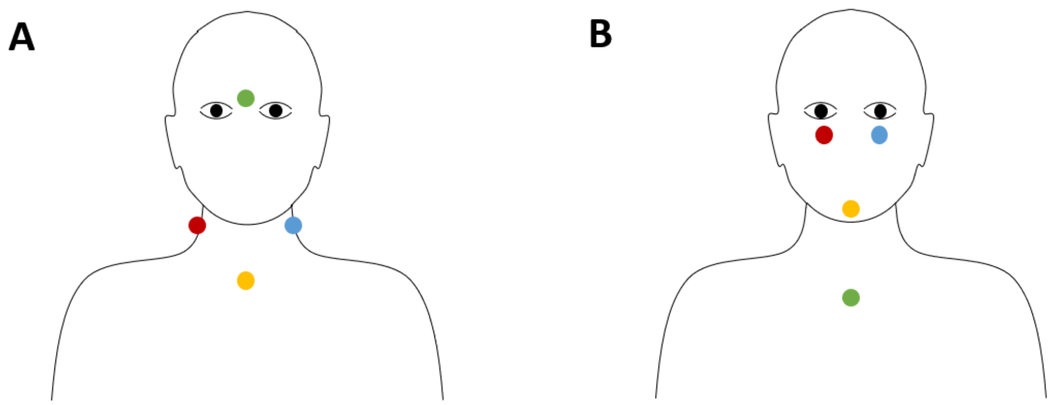



**Figure 4.1.** Electrode placement for cVEMP (A) and oVEMP assessment (B). Ground is green, non-inverting is yellow, and the inverting electrodes are red and blue.

### 4.4.4.4 oVEMP outcome measures

Responses were recorded using established labelling criteria for oVEMP: a baseline measure, initial negative deflection (n10 or n1) followed by a positive deflection (p16 or p1). Baseline, n10 and p16 latencies were marked for each trace, and the amplitude between Baseline-n10 and n10-p16 was obtained. These metrics were marked and calculated for the responses at maximum presentation level and threshold. For both VEMP procedures, preliminary trace analysis occurred during the assessment. Responses were averaged for comparisons. Latency and amplitude measures were confirmed post assessment.

### 4.4.5 Motor proficiency

Two tests of motor proficiency were used to quantify gross motor skills and functional balance ability. Both assessments were used to establish body coordination skills, and to compare balance tasks to other clinical tests of peripheral vestibular function and overall static posturography measures.

#### 4.4.5.1 BOT-2 Setup and Procedure

The Bruininks-Oseretsky Test of Motor Proficiency, Second Edition™ (BOT-2) (Bruininks, 2005) was used to evaluate motor performance in the areas of fine manual control, manual coordination and body coordination. This assessment is widely considered as one of the most comprehensive standardised assessments of motor proficiency for children (Deitz et al., 2007)

This assessment was administered to participants and provided a comprehensive measure of gross motor skills and balance tasks appropriate for the age group in this study. The standardised test battery was used, including the equipment and instructional easel. Two subtests of the BOT-2 were administered to participants: bilateral coordination and balance. These collectively formed a body coordination composite score which was used for analysis.

Participants completed a set of tasks to assess gross motor skills and body coordination. Tasks included jumping in place, standing heel-to-toe, and standing on one leg. Administration of the subtests were sequenced to perform bilateral coordination tasks first, followed by balance tasks, as per BOT-2 recommendations (Bruininks, 2005). Each task was taught to the child prior to them completing it, either via physical demonstration, verbal instruction, or use of the BOT-2 task easel, which included instructional pictures for each task. Given the standardised nature of the assessment, administration was strictly in accordance with guidelines based on BOT-2 recommendations (Bruininks, 2005). The average duration of the assessments was 10-15 minutes for both subtests, including breaks given as required.

### 4.4.5.2 Pediatric Balance Scale Setup and Procedure

The Pediatric Balance Scale is a well-established assessment tool of motor function for school aged children (Franjoine et al., 2003). This measure enables assessment of motor function in relation to functional balance ability (or activities of daily living) without the use of specialized equipment.

Participants completed a set of fourteen motor tasks and were rated according to their performance. Tasks included sitting to standing, standing on one leg, and turning 360 degrees in place. The tasks relate to maintaining balance (through static body stability tasks) and achieving balance through dynamic body stability tasks (Verbecque et al., 2015). Each task was subjectively rated by the examiner from 0-4: 0, being unable to complete the task and 4 being able to complete within the specified time frame competently. The assessment was performed on firm surface underfoot and with shoes on. Assessment time spanned 10-15 minutes depending on participant compliance.

### 4.4.5.3 Motor proficiency outcome measures

BOT-2 measures were analysed using sex specific norms to account for any difference in performance observed on specific items of the BOT-2 subtests (Bruininks, 2005). Previous studies have reported that females outperform males on motor coordination tasks involving dexterity and control of distal musculature (Nicholson & Kimura, 1996). Standard scores and percentile ranks were used for each subtest and the body coordination composite score.

PBS overall scores were compared to normative age ranges established by Franjoine and colleagues (Franjoine et al., 2010). This data has been well established to be reliable measures of functional balance particularly for children with mild-moderate motor delays (Franjoine et al., 2010).

### 4.4.6 Static Posturography

Static posturography was used to measure postural sway in adults and children. During the assessment, the participant stands upright (in bipedal stance) for a short period of time. This is conducted with modified environmental inputs (standing with eyes open and closed, for example), to explore the relative contributions of the sensory systems in each standing condition. The centre of pressure (CoP), the overall foot pressure exerted on the platform is measured in each condition, which can provide an indication of overall amount of postural sway (path length), speed of the postural sway (path velocity), as well as discrete wavelet transformation (DWT) measures, where the path velocity is broken down in the discrete frequency bands of oscillation.

#### 4.4.6.1 Static Posturography Setup and Procedure

Computerized posturography assessment was conducted using the Nintendo Wii platform (WBB) to determine postural sway. This platform has been established to have comparable sensitivity to traditional force plate measures (Clark et al., 2010; Lorefice et al., 2015). The WBB was calibrated according to Clark et al (Clark et al., 2010) and Vitkovic (Vitkovic et al., 2016) and interfaced with a laptop via Bluetooth. Data were recorded on a laptop with custom software created in LabVIEW (Version 8.5, National Instruments, Austin Tx, USA) and then extracted for further analysis. Calibration, setup measures and data processing were conducted according to established measures (Clark et al., 2010; Holmes et al., 2013).

Postural sway was measured objectively across four sensory conditions comprising: standing on a firm surface with eyes open (EO), and eyes closed (EC); followed by standing on a foam surface with eyes open (FEO) and eyes closed (FEC). Conditions were adapted from the Clinical Test of Sensory Interaction and Balance (CTSIB) (Shumway-Cook & Horak, 1986), however arm position differed slightly: instead of arms crossed in front of the torso, arms were held beside the torso. A trial duration of 30 seconds was chosen based on previously reported studies exploring standing balance in children (Figura et al., 1991). This is also a sufficient duration to accurately record sway (Le Clair

& Riach, 1996). The foam cushion used for FEC and FEC conditions was a 5cm high-density thermoplastic polyurethane and fit completely over the WBB.

A practice trial was conducted at the beginning to ensure the participant understood the task. Trials were conducted in order of increasing difficulty. The assessment was conducted without shoes and participants kept their feet 10cm width apart. Gridlines were used to assist with appropriate foot placement. For each trial, participants were instructed to stand as still as possible with hands by their sides. The assessment was completed in an ambient room of similar dimensions to a sound treated room. During the assessment, the examiner was seated next to the child, in front of the laptop computer but able to view the participant's facial cues and body position.

All participants underwent a minimum of two trials (maximum of three) in each condition. The trial was discontinued if the participant opened their eyes (in eyes closed conditions), stepped off the board, or lost balance before the end of the trial. For these participants, an extra trial was provided. After the assessment, the examiner measured the participant's height and weight.

Trial duration was 60 seconds for adult participants aged between 21 and 56. Setup and procedures were otherwise the same.

#### 4.4.6.2 Static Posturography outcome measures

Data was collected and processed according to Holmes (Holmes et al., 2013) and Clark (Clark et al., 2010). The median score for each condition was used in the statistical analyses to ensure the CoP trace was representative of the condition, as some variation can occur between first and second trials (Clark et al., 2010). For adults, the first half of the sixty second trial (30 seconds total) was selected for data analysis to be aligned with trial durations used in the child cohort.

Nine measures were used to compare postural sway for all conditions (EO, EC, FEO, FEC), comprising path length velocity (cm/s), and four distinct bandwidths measured on the anteroposterior plane. The bandwidths included ultralow (<0.10 Hz) very low (0.10-

0.39 Hz), low (0.39-1.56 Hz) and moderate (1.56-6.25 Hz) frequencies. These bandwidths are hypothesised to correlate with postural movements associated with the visual system (ultralow) (Chagdes et al., 2009; Friedrich et al., 2008), the vestibular system (very low) (Oppenheim et al., 1999), cerebellar system (low) and spinal reflexive loops including muscular activity (moderate) (Liang et al., 2014). These metrics have been established to be reliable measures of standing balance (Liang et al., 2014; Micarelli et al., 2020).

## 4.5 Missing data

The original study design for the thesis included longitudinal data comparisons for all study participants. The declaration of a global pandemic in 2020 precluded participant recruitment and retention, subsequently impacting sample group sizes for comparison and longitudinal data collection between 2020-2021. Across all groups several data points were unable to be collected.

For participants enrolled at the beginning of the project, given the longitudinal nature of Study 2, some participants did not continue beyond the initial assessment. This was the case for six typically developing children, and one child with SNHL.

Fourteen children from the typically developing group were unable to be assessed for their final appointment due to the COVID-19 restrictions placed on research data collection, resulting in loss of the 12-month data collection point for these children. Data collection was also disrupted for two children in the SNHL group and seven children in the autism group, impacting on their six-month and twelve-month data collection points. Initial analyses considered longitudinal comparisons for each child subgroup, however given the inability to collect longitudinal data in a timely manner (due to COVID-19 restrictions), cross sectional comparisons were made for Study 3 and Study 4.

# Chapter 5: POSTURAL CONTROL AND OTOLITH FUNCTION IN TYPICALLY DEVELOPING CHILDREN

This chapter presents the findings of a comparative study exploring differences in postural control and otolith function between typically developing children aged 5-12 years and adults. This manuscript was submitted to Gait and Posture in April 2023. The submitted manuscript presented includes journal specific headings.

## 5.1 Abstract

**Background:** Postural control is dependent on the complex integration of somatosensory, visual, and vestibular information. For children the integration of sensory system information is influenced by numerous factors, yet vestibular system contributions to postural control, particularly otolith function, have not been widely considered.

**Research Question:** Do children use similar postural control strategies to adults and is otolith function similar?

**Methods**: Thirty-five typically developing children (5 - 12 years of age) were compared to normative adult datasets. Participants had normal hearing sensitivity and no history of balance concerns. Postural sway was measured using static posturography and included centre of pressure (CoP), and discrete wavelet transform (DWT) analyses where postural sway data is broken down into discrete frequency bands. Otolith function was determined using cervical and ocular vestibular evoked myogenic potentials (cVEMP, oVEMP). General linear modeling and ANOVA explored differences between children and adults, and multiple regression was used to determine the relationship between measures.

**Results:** Children <8 years (mean age, 6.89±0.75 years) had greater postural sway when compared to older children (mean age, 10.42±1.37 years) and adults (mean age 26.84±7.03 years). This was for postural sway across all standing balance conditions, and across most DWT frequency bands, suggesting less effective sensory system integration. Children showed significantly shorter cVEMP (p13, n23) and oVEMP (p16) latencies and smaller amplitude responses compared to adults. Otolith function in children was correlated with postural control, where some latencies correlated with greater sway, predominately for standing balance conditions where vision was available.

**Significance:** Findings confirm that postural control patterns and otolith function differ between adults and children, and the association between vestibular inputs and postural control in children. Otolith function and postural control integration continues throughout childhood. Clinical assessment of peripheral vestibular function and postural control provides a cohesive understanding of balance control in children.

## 5.2 Introduction

The ability to maintain balance requires simultaneous integration from the visual, somatosensory and vestibular systems. In children, the progressive development of this skill is confounded by numerous factors including physical, neurological, sensorimotor development, as well as motor learning (Riach & Starkes, 1994). Postural control progressively improves with age (Foudriat et al., 1993; Hirabayashi & Iwasaki, 1995; Shumway-Cook & Woollacott, 1985), yet anthropometric correlates such as height and body mass do not account for change in postural control after approximately 4-6 years of age (Barozzi et al., 2014; Micarelli et al., 2020; Mickle et al., 2011; Riach & Starkes, 1994). The differences that remain between adults and children suggest that other, more complex integration is involved.

Sensorimotor mechanisms contribute different weightings to postural control (Riach & Starkes, 1994). Closed-loop strategies typically monitored by sensory feedback enable controlled, subtle changes to maintain balance. These corrective changes in posture relate to sensory transduction, processing and muscle activation to maintain balance, even in upright, quiet stance (Peterka, 2002). Conversely, open-loop strategies which are fast corrective responses can be a less predictable way to account for changes in postural control.

By 8 years of age, children undergo a fundamental change in postural control development (Figura et al., 1991; Garcia et al., 2011; Riach & Starkes, 1989; Riach & Starkes, 1994). This potentially relates to sensorimotor development, which can undergo a period of change between 5-8 years (Kirshenbaum et al., 2001), or changes in the organizational processes required for sensory system integration (Hirabayashi & Iwasaki, 1995). Children use visual and somatosensory information for postural control in a similar way to adults by 7 years, yet vestibular system contributions to postural control is not integrated until adolescence (Hirabayashi & Iwasaki, 1995; Shumway-Cook & Woollacott, 1985).

Static posturography provides an estimate of postural sway while the individual attempts to stand still. Center of pressure (CoP) measures between sensory conditions are commonly used to understand an individual's sensory contributions to postural control. However, discrete wavelet transform (DWT) analyses may enable greater understanding of these constructs (Chagdes et al., 2009; Quek et al., 2014). During postural sway measurement in various standing balance conditions, DWT analyses simultaneously break down postural sway data into discrete frequency bands based on the speed of sway (see Figure 5.1). Balancing typically consists of a variety of different contributing mechanisms overlaid to maintain upright posture, for example 1) relatively low speed and force magnitude natural sway as the body explores its limit of stability, and 2) high speed and force magnitude muscle contractions to prevent exceeding the tipping point. Certain frequency bands contain movements occurring at these speeds and are believed to represent contributions from the different physiological mechanisms, even across the different sensory test conditions: vision (<0.1Hz), vestibular (0.1-0.5Hz) and somatosensory (0.5-1.0Hz) (Chagdes et al., 2009; Oppenheim et al., 1999). DWT measures therefore provide the potential for a more nuanced understanding of the relative physiological contributions compared to traditional measures.

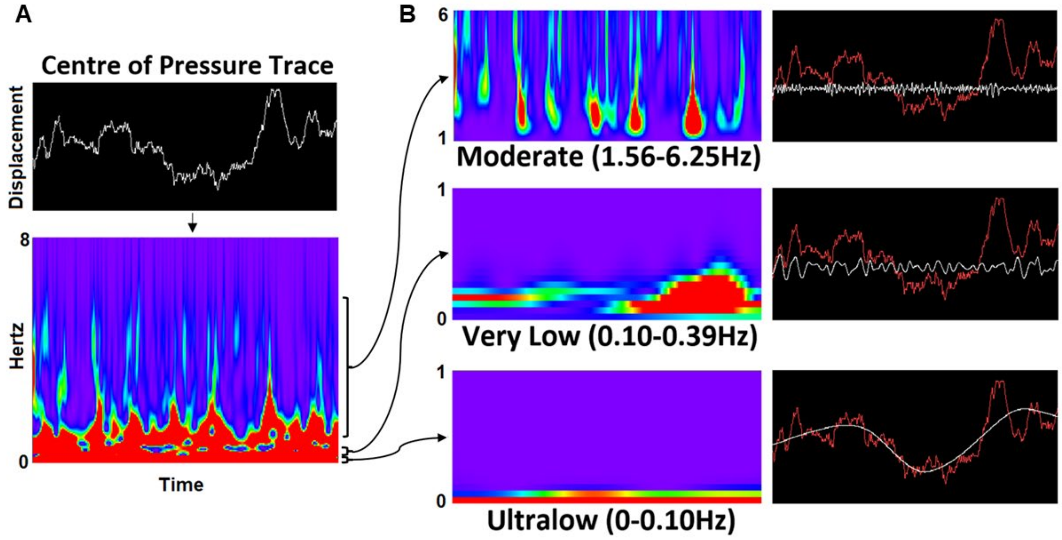



**Figure 5.1.** Diagram showing how the wavelet analysis extracts data. Top left image (A) shows the centre of pressure (COP) trace in terms of displacement (y-axis) over time (x-axis). This signal is converted into frequency content of the signal over time, with red indicating a high level of signal energy and purple being a low level of energy. These data are separated into distinct frequency bands and the displacement data for each band are analysed separately as can be seen in the right image of the figure (B). In the furthest graphs to the right of the figure the original trace (red line) is shown in each graph, and the trace for that specific band (red) is also shown. The bottom graph is ultralow (i.e., very slow moving) frequency, and as such maps the underlying trend of the signal. The graphs above this represent increasingly rapid moving bands; hence the traces represent faster moving components of the signal.

A potential contributor to age-related differences in postural control is the vestibular system. Vestibular reflexes contribute to standing balance by stabilising the head and body and are most active when reliance on the vestibular system increases (Herdman & Clendaniel, 2014; Welgampola & Colebatch, 2001b). The semicircular canals and otolith organs both contribute to postural control via feedback control systems (Nashner et al., 1989). Semicircular canal (SCC) function is typically quantified via measurement of the vestibulo-ocular reflex (VOR), and can be measured using caloric, rotational chair, or video head impulse testing (vHIT) (Hamilton et al., 2015; Janky & Rodriguez, 2018; Wiener-Vacher & Wiener, 2017). In children, VOR values as measured by vHIT testing remains variable (Bachmann et al., 2018; Hamilton et al., 2015; Janky & Givens, 2015; Ross & Helminski, 2016; Wiener-Vacher & Wiener, 2017). Otolith function is typically measured using vestibular evoked myogenic potentials (VEMP): short latency evoked potential responses elicited by a low frequency stimulus and modulated by myogenic activity (Colebatch et al., 1994). Otolith function between adults and children has demonstrated differences for cervical VEMP (cVEMP), but not ocular VEMP (oVEMP). Children have shorter cVEMP latencies (Hsu, Wang, et al., 2009; Rodriguez et al., 2019; Valente, 2007) and while neural maturational differences may contribute to this, other factors, including anatomical differences in head and neck are also likely to influence responses (Chang et al., 2007; Rodriguez et al., 2019; Wang et al., 2008). On the other hand, oVEMP response latencies and amplitudes are similar (Hsu, Wang, et al., 2009; Kelsch et al., 2006; Kuhn et al., 2018). While these studies provide an insight into vestibular function in children, implications of these findings in the context of postural control have not been widely explored for bipedal stance.

The aim of this study was to 1) determine postural control and otolith function in children and adults, and 2) determine the relationship between postural control and otolith function in children. We hypothesized that 1) otolith function would differ between groups, and that children would rely more on visual and somatosensory information to maintain balance; and 2) in children, shorter VEMP latencies and smaller amplitudes would be associated with more postural sway.

## 5.3 Materials and Methods

**Participants**

Thirty-five children aged between 5 and 12 years of age were recruited to the study. All children underwent static posturography, VEMP assessment, as well as audiometry and immittance testing to determine sound detection and middle ear status. Children were compared to two adult groups comprising retrospective data from 50 adults who underwent static posturography (Group A), and 33 adults who underwent VEMP testing (Group B). No adults underwent both assessments. Sample size was based on a priori power analysis (G* Power, (Faul et al., 2007)) using statistical power of 0.8, significance level of 0.05 and medium effect size of 0.5.

All participants had normal hearing sensitivity (four-frequency pure tone average ≤20dB) and no reported history of balance difficulties. In addition, child participants had no known neurodevelopmental or motor delays, or recent history of middle ear disease as determined by parental questionnaire. The study was ethically approved (17-1348H) and all procedures were conducted according to the tenets of the Declaration of Helsinki. Written consent was obtained from all participants or guardians.

**Standing balance**

Computerized static posturography assessment was conducted using the Nintendo Wii Balance Board (WBB), a portable force plate with reliability and validity comparable to traditional force plate measures (Clark et al., 2010; Lorefice et al., 2015). The WBB was calibrated according to Clark et al (Clark et al., 2010) and interfaced with a laptop via Bluetooth. Data were recorded at the native frequency (≈40Hz) on a laptop with custom software created in LabVIEW (Version 8.5, National Instruments, Austin Tx, USA).
Objective measurement of postural sway was conducted in four sensory conditions: standing with eyes open on a firm surface (EO), standing with eyes closed on a firm surface (EC), standing with eyes open on a foam surface (FEO) and standing with eyes closed on a foam surface (FEC).

Participants stood barefoot with feet 10cm apart on the WBB or foam; gridlines ensured foot placement accuracy. Participants stood as still as possible with arms by their sides and completed three 30-second trials for each condition. If the participant did not meet test condition assumptions the trial was re-attempted. Height and body mass were measured prior to assessment.

Centre of pressure (CoP) measures included path velocity, the overall amount of postural sway as a function of time (cm/s), and DWT path velocity, a method which separates the CoP data into discrete frequency bands. Three frequency bands were measured: ultralow (0-0.10Hz), very low (0.10-0.39Hz), and moderate (1.56-6.25Hz); and chosen as they best represented the different sensory systems of interest for this study (Clark et al., 2010; Quek et al., 2014; Salavati et al., 2009). Wavelet data were extracted using the protocol described by Clark et al (Clark et al., 2014) which incorporated a Symlet-8 wavelet transform with the detail levels separated and joined where necessary to derive the specific frequency bands. Data were analysed for the anteroposterior plane, as most sway occurs in this plane during bipedal stance. Specifically, this resulted in one variable not derived from DWT analysis (path velocity), and three DWT path velocity variables (ultralow DWT path velocity, very low DWT path velocity, moderate DWT path velocity). Median measures were used in statistical analyses.

**Vestibular Evoked Myogenic Potentials**

Vestibular Evoked Myogenic Potentials (VEMP) were obtained using the Natus Bio-logic Navigator Pro auditory evoked potential system (Natus, Pleasanton, CA, USA). cVEMP stimuli were delivered via air conduction using ERA-3 insert phones (50-ohm) at a rate of 5.1Hz and intensity of 113 dB SPL in children and 123 dB SPL in adults, based on clinical guidelines.

Electrode montage for cVEMP included a common electrode placed at Nz, non-inverting electrode placed at the sternoclavicular junction and two inverting electrodes placed on each sternocleidomastoid muscle (SCM) belly. cVEMP responses were elicited using bilateral SCM contraction (Papathanasiou et al., 2014). Participants lay semi-recumbent (approximately 20 degrees from supine) and from this position, raised their head when stimuli were presented. EMG monitoring was not possible due to device limitations, but SCM contraction symmetry and degree of head elevation was visually monitored by the examiner. Post stimulus rectification (PSR) was applied to the cVEMP waveforms. cVEMP latencies p13, n23, and peak-to-peak amplitude (p13- n23) were measured.

oVEMP stimuli were delivered via bone conduction using a hand-held electromechanical vibrator (Brüel & Kjær Mini-shaker Type 4810) placed at Fz. Stimulus rate was 4.1Hz and intensity ranged between 128 dB pFL in children and 142 dB pFL in adults, based on clinical guidelines. Electrode montage for oVEMP included a common electrode at the sternoclavicular junction, non-inverting electrode on the chin, and two inverting electrodes on the lower orbit of each eye, in line with the pupil centre. During oVEMP assessment, participants lay supine and maintained an upward gaze position of 15 degrees for the stimulus duration. oVEMP latencies n10, p16, as well as base-to-peak amplitude of the n10 response (base-n10), and peak-to-peak amplitude (n10-p16) were measured.

For both VEMP assessments waveform responses were accepted and averaged when two clear responses were observed.

**Statistical analysis**

Data were analysed using MINITAB-19 statistical package. VEMP latencies were normally distributed based on statistical analyses, but VEMP amplitudes and CoP data were not. One-way ANOVAs were used for VEMP analyses (including latencies and log-transformed amplitudes) across age groups with post hoc Tukey analyses. General linear modelling was used for log-transformed CoP analyses. Dependent variables included path velocity and each DWT frequency band; independent variables included age categories and standing balance conditions (EO, EC, FEO, FEC). In children, multiple linear regression explored the relationship between otolith function and static posturography. Height and body mass were considered as covariates for CoP and regression analyses. The significance level was set at a p value of 0.05. Effect sizes were calculated using Hedges's *g* (Lakens, 2013).

## 5.4 Results

**Group demographics**

Children were allocated to two groups: comprising 15 children <8 years old (mean age, 6.89±0.75 years; range, 5.00-7.83 years; 8 females [53.3%]), and 20 children ≥8 years old (mean age 10.42± 1.37 years; range 8.00-12.5 years; 13 females [65%]). Fifty adults (mean age 26.84±7.03 years; range 21-56 years; 40 females [80%]) underwent static posturography, and a different cohort of 33 adults (mean age 23.00± 1.8 years, range 19-28 years; 23 females [69.7%]) underwent VEMP assessment.

**Standing balance**

For all groups, greater postural sway was observed when various sensory inputs were eliminated (Figure 5.2). Body mass was associated with path velocity for conditions where foam was used (FEO, FEC); but not for conditions without foam (EO, EC) [EO: $F(2,81)=67.42$, $p<0.001$; EC: $F(2,81)=60.48$, $p<0.001$; FEO: $F(2,81)=62.94$, $p<0.001$; FEC: $F(2,81)=43.33$, $p<0.001$]. Post hoc analyses showed significant findings when comparing all age groups across all conditions (Table 5.1). Younger children (<8) demonstrated significantly more postural sway than their older counterparts and greater response variability (Figure 5.2).

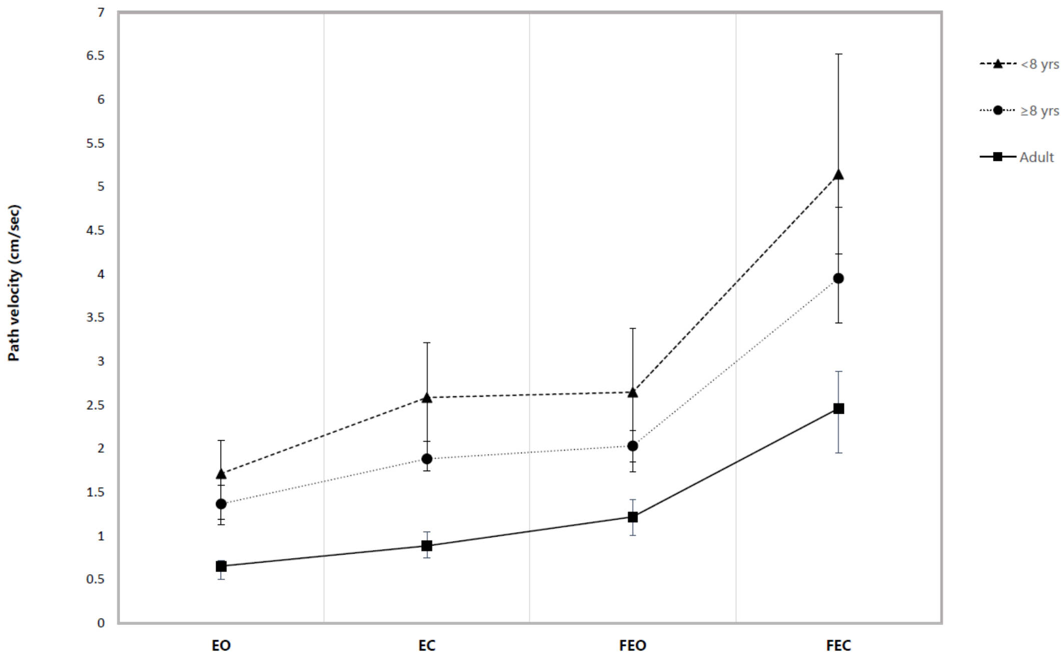



**Figure 5.2.** Data points represent the median path velocity and IQR across four standing balance conditions: eyes open standing on a firm surface (EO); eyes closed standing on a firm surface (EC), eyes open standing on a foam surface (FEO), and eyes closed standing on a foam surface (FEC). Significant differences were noted between age groups across all conditions. Younger children showed more variability in standing balance measures than older children and adults.

**Table 5.1.** Group comparisons for static posturography measures, including path velocity across the four standing conditions, and DWT path velocity across frequency bands (eyes open condition).

| | | **Individual group** | | | **Post hoc comparisons** | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | **<8 yrs** | **≥8 yrs** | **Adult** | **<8 yrs vs ≥8 yrs** | | **<8 yrs vs Adult** | | **≥8 yrs vs Adult** | |
| | | **Mdn (IQR)** | **Mdn (IQR)** | **Mdn (IQR)** | **ES** | **Adj P** | **ES** | **Adj P** | **ES** | **Adj P** |
| ***Path velocity (cm/sec)*** | ***EO*** | 1.71 (0.91) | 1.37 (0.45) | 0.65 (0.21) | 0.98 | **.001** | 4.28 | **<.001** | 3.46 | **<.001** |
| | ***EC*** | 2.59 (1.31) | 1.88 (0.34) | 0.89 (0.30) | 0.84 | **.006** | 3.65 | **<.001** | 2.79 | **<.001** |
| | ***FEO*** | 2.65 (1.65) | 2.03 (0.36) | 1.22 (0.42) | 1.06 | **<.001** | 3.37 | **<.001** | 2.84 | **<.001** |
| | ***FEC*** | 5.14 (2.29) | 3.95 (1.33) | 2.46 (0.94) | 0.96 | **<.001** | 2.39 | **<.001** | 1.57 | **<.001** |
| ***DWT path velocity (cm/sec)*** | ***Ultralow (vision)*** | 0.10 (0.08) | 0.07 (0.03) | 0.05 (0.03) | 0.56 | .102 | 1.41 | **<.001** | 1.01 | **<.001** |
| | ***Very low (vestibular)*** | 0.30 (0.17) | 0.24 (0.12) | 0.16 (0.09) | 1.07 | **.022** | 1.94 | **<.001** | 1.08 | **<.001** |
| | ***Moderate (somatosensory)*** | 0.82 (0.36) | 0.62 (0.27) | 0.28 (0.08) | 0.75 | **.014** | 4.08 | **<.001** | 3.06 | **<.001** |

Significant values in bold (p<.05). Abbreviations: DWT = discrete wavelet transform; cm/sec = centimetres per second; EO = eyes open, EC = eyes closed, FEO = foam eyes open, FEC = foam eyes closed; Mdn = median, IQR = interquartile range; ES = effect size (calculated using Hedges *g*); Adj P = adjusted p value (Tukey post hoc analysis).

When standing with eyes open on a firm surface DWT path velocities decreased with age (Figure 5.3). Overall significant differences were observed with eyes open for moderate [$F(2, 80)=59.58$, $p<0.001$]; very low [$F(2, 80)=12.40$, $p<0.001$] and ultralow [$F(2, 80)=11.92$, $p<0.001$] frequency bands. Post hoc analyses revealed significant differences between each age group for very low (vestibular), and moderate (somatosensory) frequency bands; younger children demonstrated significant increases in path velocities for these frequency bands compared to older children and adults. For the ultralow (visual) frequency band, the adult group showed significantly less postural sway compared to both child groups (Table 5.1).

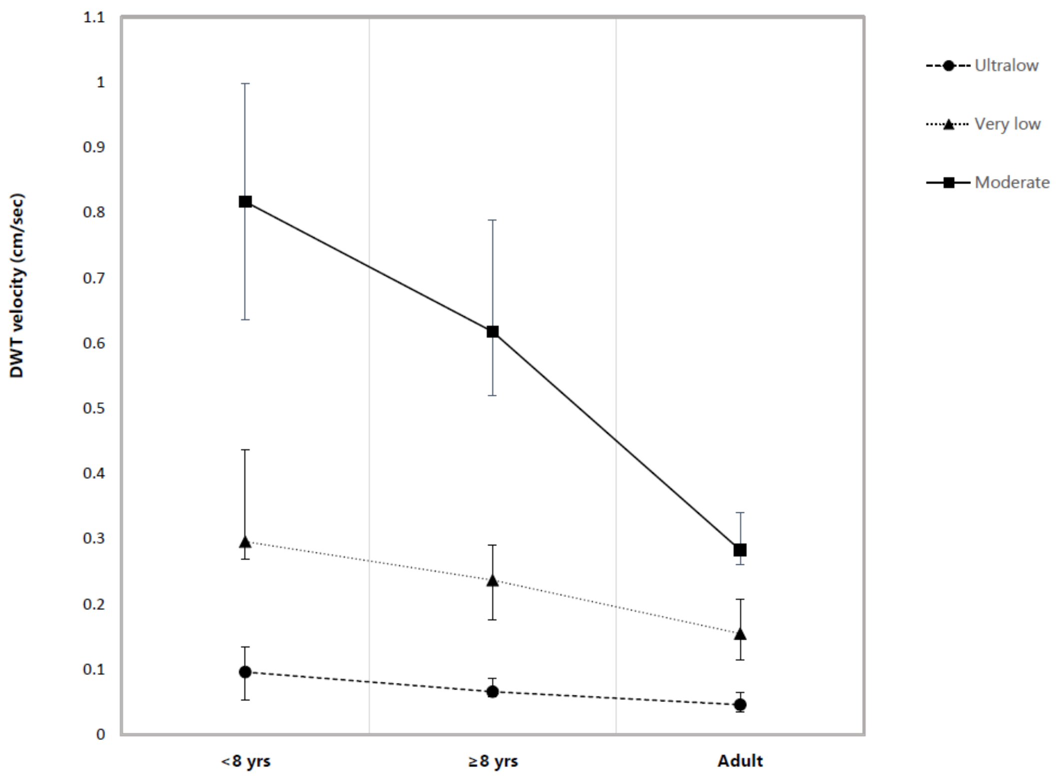



**Figure 5.3.** Data points represent median path velocity for each DWT frequency band, across age groups. Significant differences were observed across all frequency bands between children and adults. Both groups of children had similar DWT path velocities in the ultralow frequency DWT band. Very low and moderate DWT frequency bands were significantly different across all age groups, with younger children showing larger DWT path velocities for these bands.

**VEMP comparisons**

No statistical differences between left and right responses were noted so responses were averaged. One child refused VEMP testing, but for all others, present cVEMP response rates were 100% in children, and 91% in adults. cVEMP latencies and amplitudes differed between adults and children [p13: $F(2,61) = 24.16$, $p = <0.001$; n23: $F(2,61) = 33.75$, $p = <0.001$; p13-n23: $F(2, 61) = 11.12$, $p = <0.001$], as demonstrated in Table 5.2. Post-hoc analyses showed shorter p13 and n23 latencies in both child groups compared to adults; and child groups did not differ significantly. Children <8 years and children ≥8 years showed significantly smaller cVEMP amplitudes than adults. No cVEMP amplitude differences were observed between the younger and older children.

oVEMP response rates were 94% in children, and 97% in adults. oVEMP comparisons showed significantly shorter p16 latencies in children when compared to adults, but no differences between n10 measures [p16: $F(2,60) = 28$, $p = <0.001$; n10: $F(2,60) = 0.82$, $p = 0.443$] (Table 5.2). Post hoc comparisons revealed this was evident for both younger and older children, but p16 latencies did not significantly differ between the child groups.

Significant group differences were noted for oVEMP n10-p16 amplitudes [$F(2,61) = 12.64$, $p = <0.001$], but not base-n10 amplitudes [$F(2,61) = 0.74$, $p = 0.482$]. Both groups of children (younger and older age groups) showed significantly smaller n10-p16 amplitudes than adults; no differences were observed between older children and younger children (Table 5.2).

**Table 5.2.** Group comparisons for cVEMP (rectified) and oVEMP latencies and amplitudes across age groups. Descriptive statistics were dependent on data distribution.

| | | | Individual group | | | | | Post hoc comparisons | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| ***VEMP latencies (ms)*** | | **N** | **<8 yrs** | **N** | **≥8 yrs** | **N** | **Adult** | **<8yrs vs ≥8yrs** | | **<8yrs vs adult** | | **≥8yrs vs adult** | | **Overall P** |
| | | | **Mean (95% CI)** | | **Mean (95% CI)** | | **Mean (95% CI)** | **ES** | **Adj P** | **ES** | **Adj P** | **ES** | **Adj P** | |
| ***cVEMP*** | ***p13*** | 14 | 13.03 (12.36, 13.71) | 20 | 13.44 (12.88, 14.00) | 30 | 15.43 (14.98, 15.90) | 0.34 | .629 | 1.78 | **<.001** | 1.62 | **<.001** | **<.001** |
| | ***n23*** | | 19.02 (18.19, 19.85) | | 19.37 (18.68, 20.07) | | 22.42 (21.85, 22.99) | 0.27 | .792 | 2.05 | **<.001** | 1.89 | **<.001** | **<.001** |
| ***oVEMP*** | ***n10*** | 12 | 10.40 (9.91, 10.88) | 20 | 10.02 (9.64, 10.40) | 31 | 10.24 (9.94, 10.54) | 0.43 | .442 | 0.20 | .850 | 0.25 | .631 | .443 |
| | ***p16*** | | 12.88 (12.28, 13.50) | | 13.02 (12.55, 13.49) | | 14.96 (14.58, 15.34) | 0.12 | .936 | 2.06 | **<.001** | 1.82 | **<.001** | **<.001** |
| ***VEMP amplitudes (µV)*** | | **N** | **<8 yrs** | **N** | **≥8 yrs** | **N** | **Adult** | **<8yrs vs ≥8yrs** | | **<8yrs vs adult** | | **≥8yrs vs adult** | | **Overall P** |
| | | | **Mdn (IQR)** | | **Mdn (IQR)** | | **Mdn (IQR)** | **ES** | **Adj P** | **ES** | **Adj P** | **ES** | **Adj P** | |
| ***cVEMP*** | ***p13-n23*** | 14 | 11.25 (5.41) | 20 | 13.23 (7.10) | 30 | 19.69 (14.67) | 0.28 | .684 | 0.98 | **<.001** | 0.97 | **<.001** | **<.001** |
| ***oVEMP*** | ***base-n10*** | 12 | 6.83 (5.63) | 20 | 7.49 (6.25) | 31 | 9.70 (5.62) | 0.11 | .938 | 0.38 | .523 | 0.26 | .667 | .482 |
| | ***n10-p16*** | | 7.84 (9.76) | | 12.63 (9.23) | | 20.19 (9.74) | 0.58 | .175 | 1.49 | **<.001** | 1.08 | **.005** | **<.001** |

Significant values in bold (p<.05). Abbreviations: VEMP = vestibular evoked myogenic potentials, cVEMP = cervical vestibular evoked myogenic potentials; oVEMP = ocular vestibular evoked myogenic potentials; ms = milliseconds; µV = microvolts; 95% CI = confidence interval; Mdn = median; IQR = interquartile range; ES = effect size (calculated using Hedges *g*; Adj P = adjusted p value with Tukey post hoc analysis).

**Relationship between standing balance and otolith function in children**

Elements of otolith function predicted postural sway during eyes open conditions. When standing on a firm surface, p13 latencies significantly predicted postural sway β=.041, *t* (32)=2.97, $p<.01$; and explained a significant proportion of variance in postural sway scores, $R^2$ =.44, $F(1, 32)=8.85$, $p<.01$. This was also evident when on a foam surface; β=.041, $t$ (32) = 2.68, $p$ =.012; with a significant proportion of variance in postural sway scores, $R^2$ =.38, $F$ (1, 32)=7.15, $p$=.012. No other significant relationships were noted between cVEMP amplitudes, oVEMP latencies or amplitudes across standing balance conditions. Height and body mass did not predict postural sway measures across any standing balance condition.

# 5.5 Discussion

Findings from this study demonstrate that both otolith function and postural control differ between children and adults, and that children use different sensory mechanisms to adults to maintain postural control. Furthermore, p13 latencies predicted postural sway scores in standing balance conditions with eyes open.

Children in this study show reduced postural control when compared to adults, and this difference increased when sensory information was manipulated. This finding agrees with existing literature (Barozzi et al., 2014; de Sá et al., 2018; Ferber-Viart et al., 2007; Riach & Starkes, 1994; Sakaguchi et al., 1994). Younger children showed greater variability in postural sway than older children and adults. This variability may indicate developmental differences within each of the age groups studied; larger variability is suggestive of a less developed postural control system.

The sensory processes used to maintain balance were the focus of DWT analyses. Ultralow DWT frequency contributions to postural control relate to visual information (Chagdes et al., 2009; Micarelli et al., 2020; Rhine et al., 2017), whereas very low and moderate frequency bands are thought to represent vestibular and somatosensory contributions respectively (Chagdes et al., 2009; Quek et al., 2014). In children, increased postural sway for very low and moderate frequency bands suggests less effective postural control integration when compared to adults, even in conditions of quiet stance with eyes open. Furthermore, postural control differences may also be related to sensorimotor mechanisms particularly regarding the transition from open-loop to closed-loop predominance (Riach & Starkes, 1994; Steindl et al., 2006). Both child groups showed similar reliance on visual system information, but differences in other sensory mechanisms. This suggests DWT may be a useful way to categorize sensory system contributions without the need for undergoing all postural control measures.

Functional differences in vestibular system contributions to balance control were evident in the present study: elements of otolith function predicted postural sway in eyes-open conditions on firm and foam surfaces. However, this relationship does not fit with the proposed hypotheses; longer, rather than shorter p13 latencies corresponded to greater postural sway. Furthermore, this relationship was only noted for postural sway conditions with access to visual information; therefore, in these conditions, less reliance on vestibular information was expected. Additionally, there were a few outliers in the dataset which may have contributed to these results. Therefore, the significance of these findings is uncertain in explaining the relationship given other results in this study. Further research may be required to confirm this finding.

Children showed shorter cVEMP latencies than adults, in agreement with other studies (Hsu, Wang, et al., 2009; Rodriguez et al., 2019; Young et al., 2009). cVEMP amplitude differences were also noted which have not been widely reported in the literature and may be dependent on the mode of cVEMP collection. Latency differences in children have been attributed to various developmental factors, including anatomical differences in the head and neck, increased myelination and changes in neural conduction velocities (Holmes, 1986; Hsu, Wang, et al., 2009; Rodriguez et al., 2019; Young et al., 2009). These factors and possible developmental effects may contribute to the differences in VEMP responses seen in this study.

oVEMP latency (p16) and amplitude differences were observed between children and adults, in contrast to existing literature (Chou et al., 2012). The differences in peak to peak (n10-p16) amplitude between children <8 and adults may be related to anatomical variations. Differences in recording parameters, including stimulation frequency, rate, and mode of transduction may explain latency differences. There is some evidence that bone conducted stimuli yield shorter latency responses (Abdullah et al., 2017; Iwasaki et al., 2008), however this has not been widely explored in the paediatric population.

**Limitations**

There is some evidence to suggest that SCC function plays a role in postural control for certain conditions (Janky et al., 2022) but this was not considered in the present study. While children underwent vHIT assessment in a broader study, there were no comparative adult groups available in our research database. Comprehensive assessment of the peripheral vestibular system may provide a more cohesive perspective on the relative contributions to postural control.

cVEMP assessment was performed without real-time EMG monitoring, and neck length was not measured; both factors can impact on the interpretation of cVEMP amplitude and are a limitation to the current study. Post-stimulus rectification was applied to the cVEMP waveforms prior to analysis.

Furthermore, an adolescent age group would have provided a comparison point between adult and child groups. Adult data were obtained from a research database, and each adult group completed either VEMP or static posturography, not both. Therefore, the relationship between VEMP and standing balance measures were not considered for adults.

## 5.6 Conclusion

This study demonstrates differences in otolith function and postural control patterns between children and adults and highlights the importance of age-specific normative data. Study outcomes may also inform clinical assessment protocols and serve as comparative measures for children who demonstrate delays in motor development. Future research should focus on further exploration of the relationship between vestibular inputs and postural control mechanisms.

# Chapter 6: PERIPHERAL VESTIBULAR FUNCTION, FUNCTIONAL BALANCE AND POSTURAL CONTROL IN TYPICALLY DEVELOPING CHILDREN

This chapter outlines normative data and longitudinal comparisons of peripheral vestibular function, functional balance and postural control measures in typically developing children. This is explored through measurement of:

1. Clinical vestibular assessments documenting peripheral vestibular organ function, including assessment of the semicircular canals and otolith organs
2. Functional balance measures documenting sensory system integration, including standardised measures of body coordination and balance, in addition to an assessment of standing (static) balance with modified environmental inputs.

## 6.1 Sample characteristics

Thirty-five children between 4 years, 11 months and 12 years, 11 months of age were recruited from the University of Melbourne Audiology Clinic between January 2018 and March 2020.

All children recruited met the following inclusion criteria:

1. normal sound detection, characterized by normal hearing sensitivity as defined by the four-frequency pure tone average of 500Hz, 1kHz, 2kHz and 4kHz ≤20 dB HL
2. no recent history of chronic middle ear disease (< six months),
3. no reported balance concerns, and
4. no known neurodevelopmental or motor delays.

Criteria 1 and 2 were determined at each assessment point, and 3 and 4 were determined by parental questionnaire at the initial assessment.

Three assessment points were considered: an initial assessment (Time point 1), and two further assessments conducted at six months (Time point 2) and twelve months (Time point 3) following the initial assessment.

## 6.2 Assessment

At each point a range of clinical assessments and functional balance measures were performed as outlined in Chapter 4.1. Pure tone audiometry and immittance testing documented hearing thresholds and middle ear status. Vestibular assessments relating to all peripheral vestibular structures (HSCC, ASCC, PSCC, saccule, utricle) were obtained bilaterally and included in analyses. Functional balance measures documented sensory system integration, including standardised measures of body coordination and balance, in addition to static balance with modified environmental inputs. Height and weight characteristics were collected at each assessment point. Total test time at each data point was approximately 75 minutes.

All thirty-five children underwent the initial assessment, twenty-nine children completed a second assessment, and fifteen children completed three assessments. Time point comparisons focused on the twenty-nine children who had baseline and six-month data, as well as the smaller subset of fifteen children who completed all three data points. Attrition rate across time points was most likely due to COVID-19 restrictions placed on research data collection, particularly for the latter time points. Table 6.1 provides a summary of anthropometric and audiological findings at each assessment point.

**Table 6.1.** Participant characteristics of typically developing children aged 5-12 years.

| | | | | Anthropometrics | | Four frequency average hearing level (4FA HL) | |
|---|---|---|---|---|---|---|---|
| | N | Male: Female ratio | Mean Age (range) | Height (cm) (SD) | Body mass (kg) (SD) | Left (SD) | Right (SD) |
| ***Time point 1: Baseline*** | 35 | 21:14 | 8.91 (5.0-12.5) | 136.23 (12.92) | 32.86 (8.44) | 7.18 (4.95) | 6.81 (4.61) |
| ***Time point 2: Six months*** | 29 | 18:11 | 9.40 (5.5- 12.8) | 138.83 (12.27) | 35.55 (8.90) | 8.23 (4.42) | 7.31 (4.60) |
| ***Time point 3: Twelve months*** | 15 | 8:7 | 10.71 (6.0-13.08) | 147.20 (13.58) | 43.61 (9.66) | 8.42 (6.33) | 9.83 (5.86) |

## 6.3 Missing data

Across all assessment points, missing data related to participants not tolerating electrodes for VEMP testing (8 children), or not wanting to proceed further with vHIT testing (10 children). Technical malfunction precluded responses being recorded for oVEMP on two occasions and vHIT on two occasions. All children completed functional balance and static posturography measures. For some children an additional trial during static posturography was required due to excessive movement (6 children) or opening their eyes during eyes closed conditions (8 children). In this case, responses from three best (or correct) conditions were used in the statistical analyses.

## 6.4 Statistical analyses

Outcome measures included latencies and amplitudes for (VEMP), VOR gain (for vHIT), BOT-2 percentile ranks, BOT-2 balance scale score, BOT-2 body coordination scale score, PBS overall score, and CoP data (path velocity, DWT analyses for ultralow, very low, low and moderate frequency bands). The Anderson Darling test of normality was used to determine statistical distribution of the outcome measures, and dot plots used to visually inspect the data.

VEMP latencies, VOR gain and BOT-2 measures (percentile ranks, balance scale score, body coordination scores) were normally distributed. cVEMP and oVEMP inter-amplitudes, and all CoP measures were not normally distributed so were log transformed for statistical analyses. PBS data were log transformed. Potential confounders were identified *a priori* from existing literature and included age for all outcome measures, height and weight for cVEMP and postural sway measures.

Descriptive statistics for all raw data were summarised for each time point and included mean, standard deviations (SD), medians and interquartile ranges (IQR) based on data distribution.

General linear modelling was used for initial and six-month assessment comparisons. Effects of age were explored with time point 1 data using mixed effects modelling and multiple regression. Height and weight covariates were included in the modelling. For participants who completed all three assessments (n = 15), mixed effects modelling was used. For vHIT, comparison of time point, with effects of ear and age included as potential confounders. For cVEMP, comparison of time point, with effects of height, weight and age included as potential confounders. For oVEMP, comparisons of time point, and age as a potential confounder was considered.

For multiple comparisons, post hoc Tukey analyses were conducted to explore individual differences. The significance level was set at a p value of 0.05.

# PART I: Balance measures: Normative data

## 6.5 Semicircular canal function as measured by vHIT

Initial statistical comparisons separated left and right responses due to VOR gain differences reported for GN Otometrics goggles in the literature (L. McGarvie et al., 2015). Independent t-tests revealed significant differences between left and right HSCC (left HSCC mean [SD] = 0.94 [0.06], right HSCC mean [SD] = 0.98 [0.05], p=0.020) but not for other canals assessed (left ASCC mean [SD] = 0.93 [0.01], right ASCC mean [SD]

= 0.89 [0.15], p=0.357; left PSCC mean [SD] = 0.92 [0.13], right PSCC mean [SD] = 0.91 [0.12], p=0.774).

Pooled data based on the canal assessed was then compared to provide the normative data range for clinical application (Figure 6.1). Overall VOR gain for each SCC plane is presented in Table 6.2 and summarises the normative data for this assessment in typically developing children between 5-12 years. Post hoc Tukey comparisons showed significantly higher VOR gain for the vHIT lateral condition (HSCC) when compared to vertical canals (ASCC: adj p=0.025; PSCC: adj p=0.047).

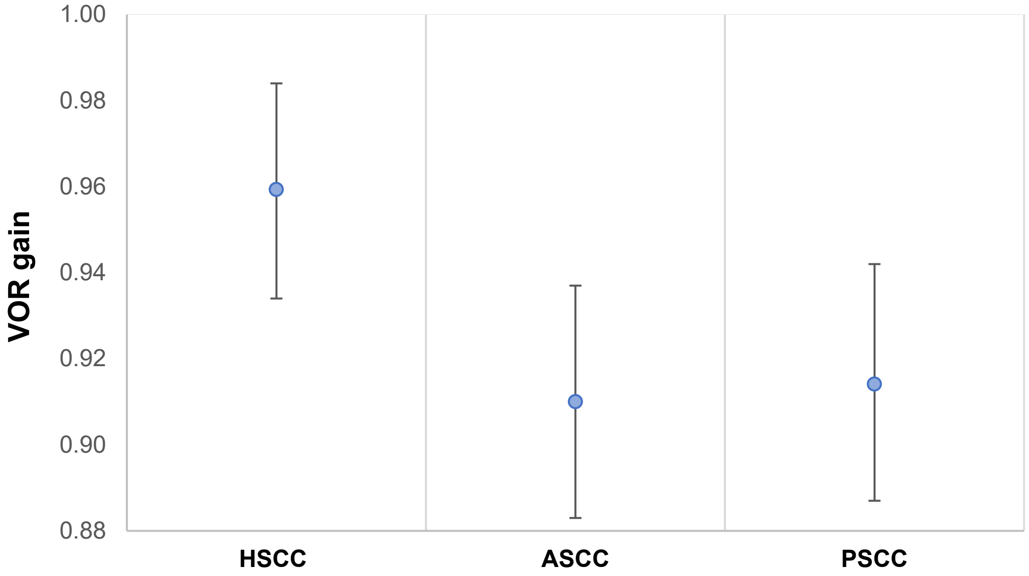



**Figure 6.1.** Means and 95% confidence intervals for pooled vHIT data.

**Table 6.2.** Normative vHIT data for typically developing children between 5-12 years.

| *vHIT plane* | N | Mean (SD) | Range | Normative range^ |
|---|---|---|---|---|
| ***HSCC*** | 70 | 0.96 (0.06) | 0.82-1.12 | (0.84 – 1.08) |
| ***ASCC*** | 60 | 0.91 (0.13) | 0.61-1.22 | (0.64 -1.18) |
| ***PSCC*** | 58 | 0.91 (0.12) | 0.67-1.19 | (0.68 – 1.15) |

Abbreviations: vHIT = video head impulse test; HSCC = horizontal semicircular canal; ASCC = anterior semicircular canal; PSCC = posterior semicircular canal.
^Normative range based on two standard deviations from the mean.

# 6.6 Saccule function as measured by cVEMP

No significant differences between left and right cVEMP responses were noted so data was pooled for comparison. Comparisons for p13, n23 latencies and p13-n23 amplitudes (rectified and unrectified responses) were conducted at 113 dB SPL and at the softest stimulus intensity that elicited a repeatable cVEMP response, denoted as the cVEMP threshold. Figure 6.2 provides an example of an 11-year old's unrectified cVEMP obtained at 113 dB SPL and at their threshold (103 dB SPL). The median cVEMP threshold was 108 dB SPL (range: 98-113 dB SPL). Table 6.3 outlines descriptive characteristics for saccule function.

**Table 6.3.** cVEMP normative data at maximum and threshold presentation levels.

| ***cVEMP latencies (ms)*** | | **N** | **Mean (SD)^** | **Mdn (IQR)^** | **Range** |
|---|---|---|---|---|---|
| *Presentation at 113 dB SPL* | *p13* | 66 | 13.33 (1.26) | 13.48 (12.52 – 14.08) | 9.71-15.75 |
| | *n23* | | 19.28 (1.46) | 19.43 (18.14-20.41) | 15.54-22.72 |
| *Presentation at threshold (88-113 dB SPL)* | *p13* | | 13.47 (1.45) | 13.29 (12.67 – 14.52) | 9.71-16.55 |
| | *n23* | | 19.16 (1.49) | 19.15 (18.90 – 20.33) | 15.95-22.51 |
| ***cVEMP amplitudes*** | | 66 | **Mean (SD)** | **Mdn (IQR)** | **Range** |
| *Presentation at 113 dB SPL* | *p13-n23 (µV)* | | 99.81 (62.96) | 83.65 (54.34- 135.62) | 14.14-273.95 |
| | *p13-n23 (rectified)* | | 13.03 (5.13) | 12.37 (8.93 - 16.56) | 3.90-27.51 |
| *Presentation at threshold (88-113 dB SPL)* | *p13-n23 (µV)* | | 64.46 (32.42) | 57.21 (40.58 -79.37) | 14.14-158.49 |
| | *p13-n23 (rectified)* | | 11.66 (5.34) | 10.54 (6.85 - 14.86) | 4.73-28.73 |

Abbreviations: cVEMP = cervical vestibular evoked myogenic potentials; ms = milliseconds; µV = microvolts; dB SPL = decibels sound pressure level
^ Both mean and medians are provided for each outcome measure, however based on statistical analyses, cVEMP latencies were normally distributed, cVEMP amplitudes were not normally distributed.

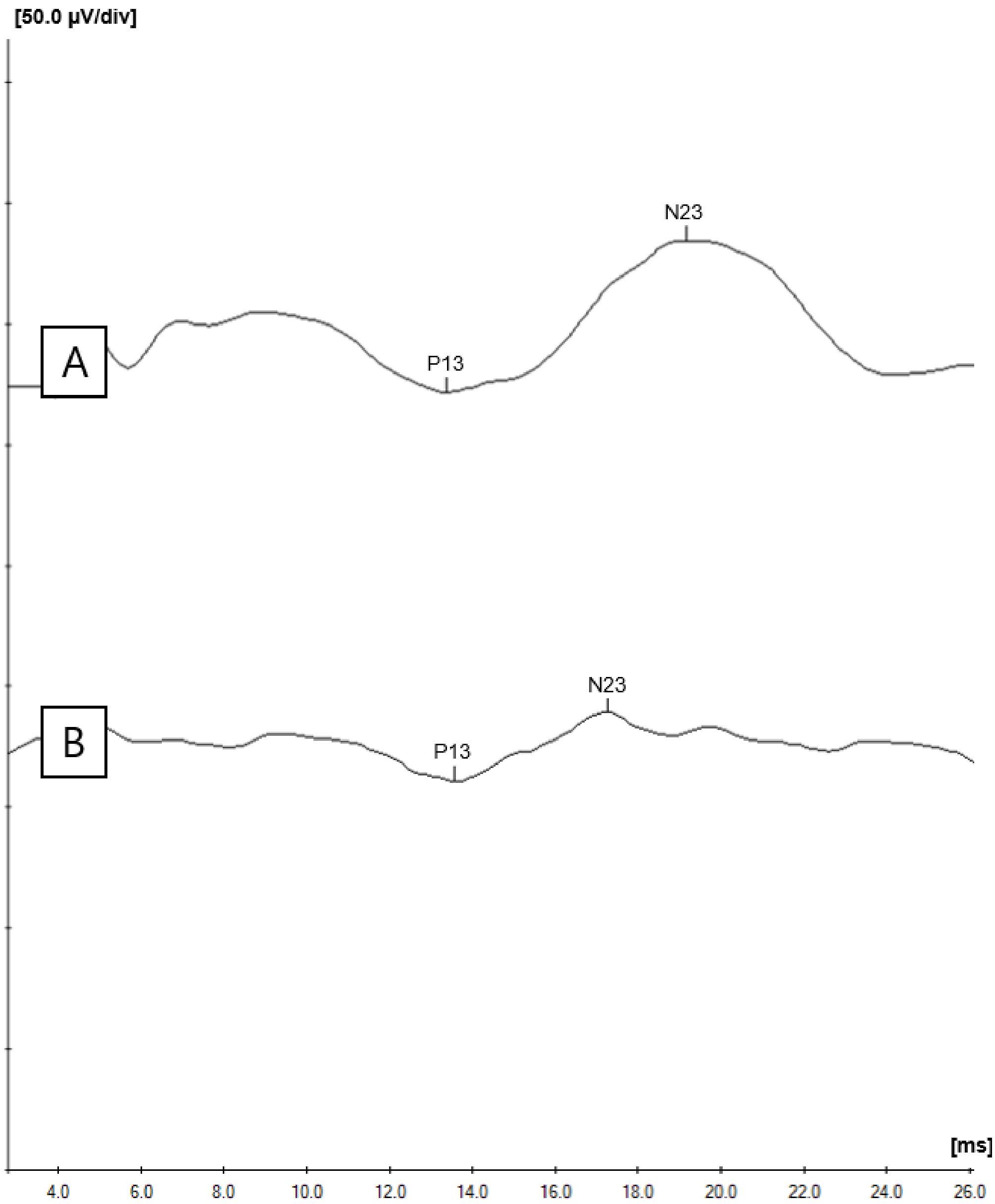



**Figure 6.2.** Example of unrectified cVEMP obtained at 113 dB SPL (A) at 103 dB SPL (B), the child's cVEMP threshold level.

# 6.7 Utricle function as measured by oVEMP

Left and right responses for oVEMP did not differ and so were pooled for comparison across all metrics, which included n10, p16 latencies, as well as interamplitude comparisons between a baseline-n10, and n10-p16. Responses were compared at a set presentation level (128 dB pFL), and at threshold, the softest stimulus intensity that elicited a repeatable oVEMP response. Figure 6.3 provides an example of an 11-year old's unrectified oVEMP obtained at 128 dB pFL and at their threshold (123 dB pFL).

The median oVEMP threshold was 123 dB pFL (range: 113-128 dB pFL). Table 6.4 outlines oVEMP descriptive characteristics.

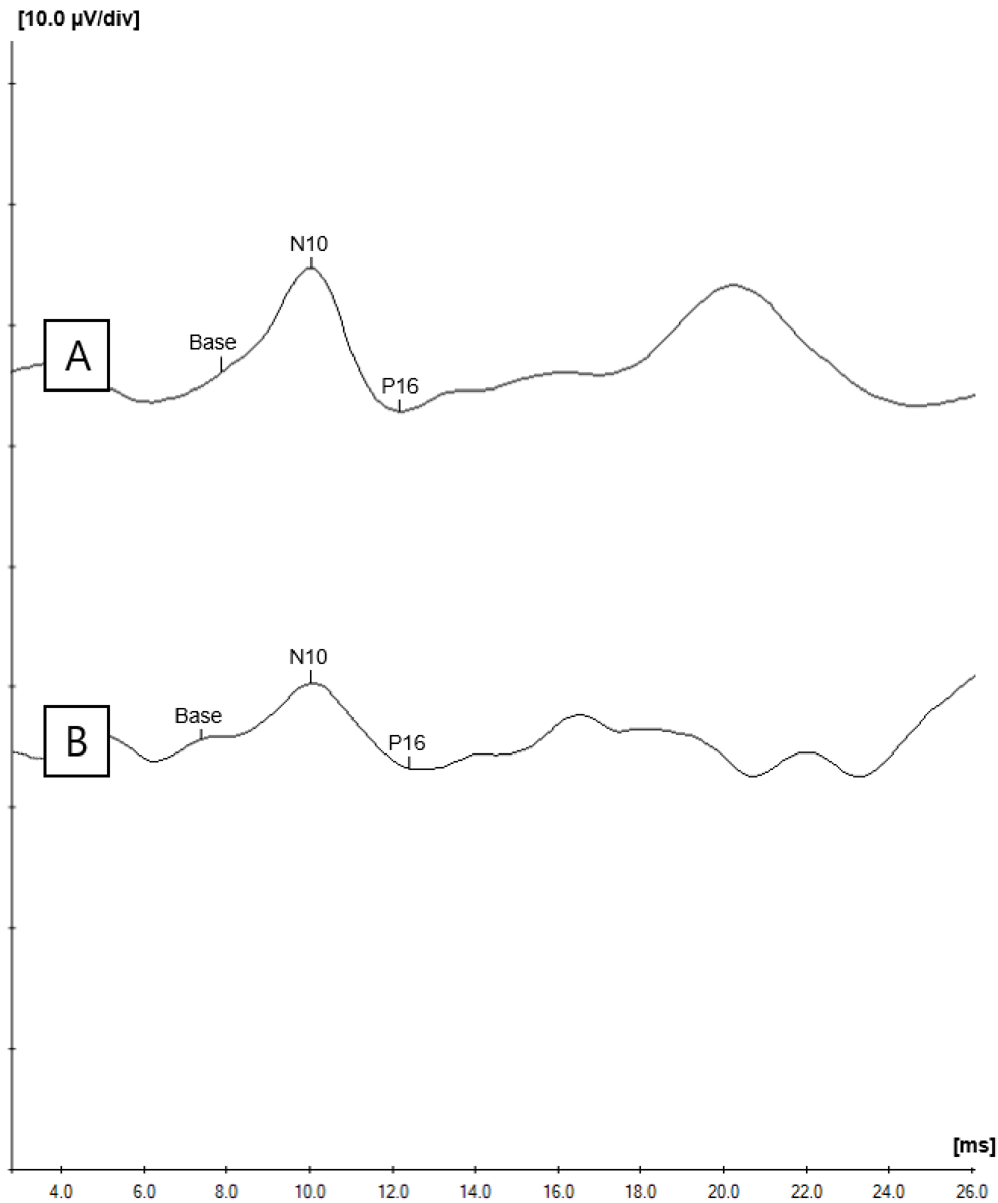



**Figure 6.3.** Example of oVEMP obtained at 128 dB pFL (A) and at 123 dB pFL (B), the child's oVEMP threshold level.

**Table 6.4.** oVEMP normative data at maximum and threshold presentation levels.

| ***oVEMP latencies (ms)*** | | **N** | **Mean (SD)^** | **Mdn (IQR)^** | **Range** |
|---|---|---|---|---|---|
| *Presentation at 128 dB pFL* | *n10* | 64 | 10.16 (0.88) | 10.09 (9.88-10.72) | 7.38-12.07 |
| | *p16* | | 12.97 (1.11) | 12.90 (12.07-13.74) | 10.82-15.50 |
| *Presentation at threshold (113-128 dB pFL)* | *n10* | | 10.20 (0.76) | 10.25 (9.88-10.59) | 8.01-12.07 |
| | *p16* | | 12.87 (1.07) | 12.80 (12.07-13.61) | 10.61-15.50 |
| ***oVEMP amplitudes (µV)*** | | 64 | **Mean (SD)** | **Mdn (IQR)** | **Range** |
| *Presentation at 128 dB pFL* | *base-n10* | | 8.89 (5.75) | 7.13 (5.07-11.87) | 2.12-31.71 |
| | *n10-p16* | | 12.83 (8.07) | 10.62 (7.57-16.52) | 2.71-41.19 |
| *Presentation at threshold (113-128 dB pFL)* | *base-n10* | | 7.88 (3.98) | 7.07 (4.80-9.21) | 1.72-20.96 |
| | *n10-p16* | | 10.48 (6.23) | 9.05 (5.97-31.74) | 2.49-31.47 |

Abbreviations: oVEMP = ocular vestibular evoked myogenic potentials; ms = milliseconds; µV = microvolts; dB pFL = decibels peak force level
^ Both mean and medians are provided for each outcome measure, however based on statistical analyses, oVEMP latencies were normally distributed, oVEMP amplitudes were not normally distributed.

## 6.8 Postural sway as measured by static posturography

All children underwent static posturography assessment across four standing balance conditions: standing with 1) eyes open on a firm surface, 2) eyes closed on a firm surface, 3) eyes open on a foam surface, and 4) eyes closed on a foam surface. Figure 6.4 depicts postural sway median and interquartile ranges across the four standing balance conditions, and Figure 6.5 provides an example of postural sway in a 9-year-old across all standing balance conditions. Mixed effects modelling was used to compare log transformed postural sway data across conditions with anteroposterior path velocity as response, condition as factor, and height, weight and age considered as covariates.

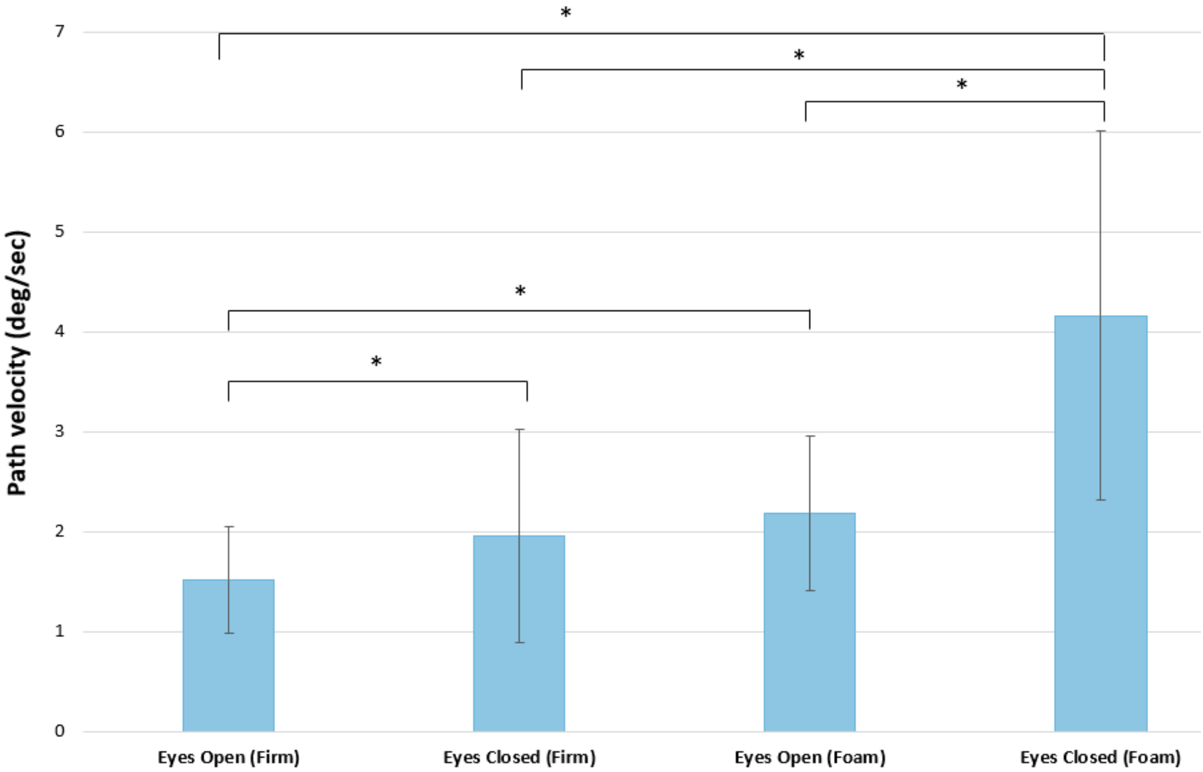



**Figure 6.4.** Median path velocities across each standing balance condition.

Significant differences were observed between eyes open (firm) and all other conditions (eyes closed firm: adj $p<0.001$; eyes open foam: adj $p<0.001$; eyes closed foam: adj $p<0.001$), as well as foam eyes closed with all other conditions (eyes open firm: adj $p<0.001$; eyes closed firm: adj $p<0.001$; eyes open foam: adj $p<0.001$). Eyes closed on firm and eyes open on foam conditions were not significantly different from one another (adj $p=0.268$). Notably, eyes closed conditions (standing on firm and foam surfaces) had larger variability in responses than eyes open conditions. Height and weight did not influence postural sway in any conditions (height adj $p=0.118$; weight adj $p=0.154$). Age of assessment had a significant effect on postural sway overall ($\beta= -0.047$, $t(31) = -2.835$, $p=0.008$). When adjusted for age, significant differences across standing balance conditions were still observed. Refer to Part IV for a breakdown of age effects on posturography measures.

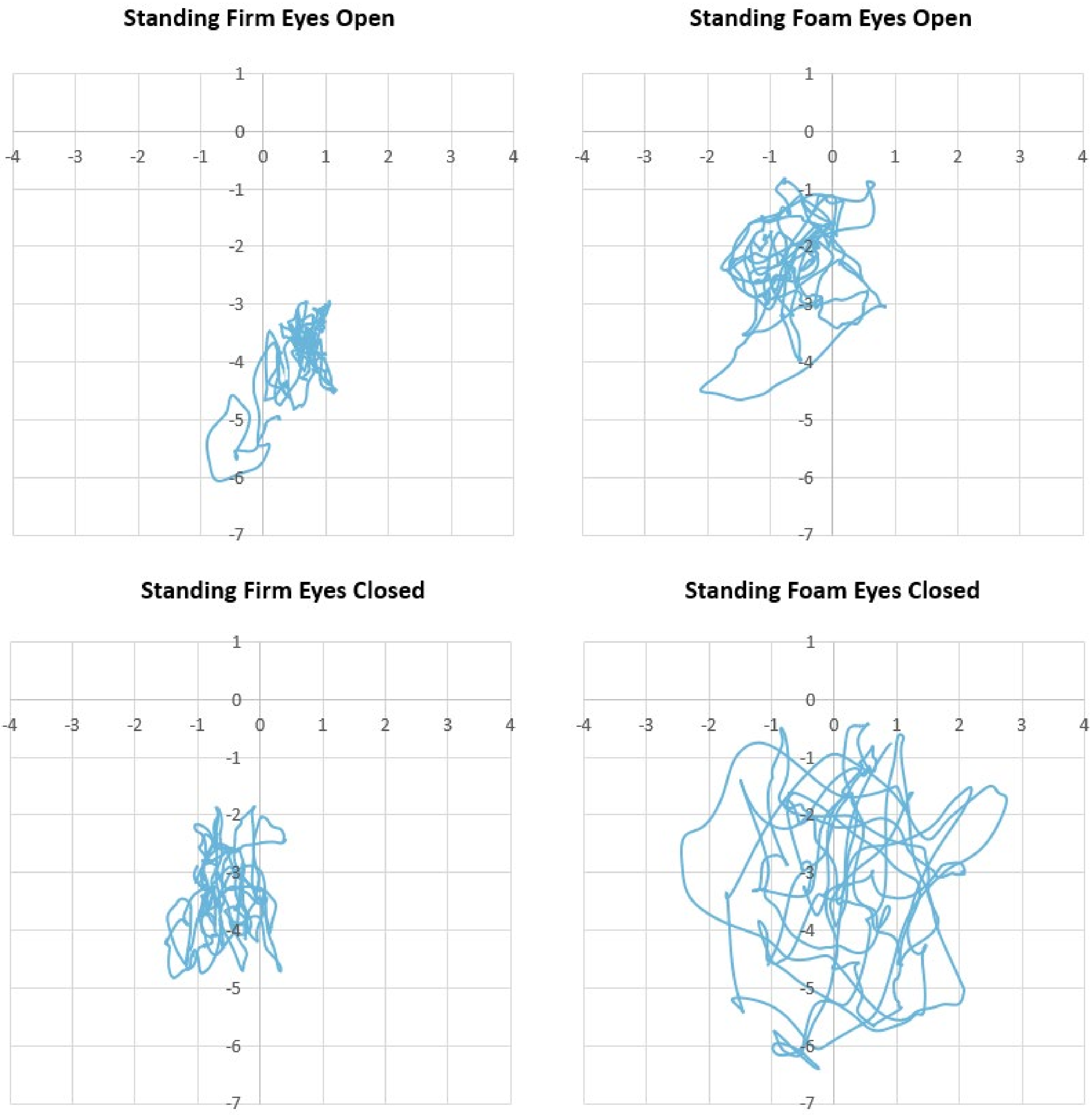



**Figure 6.5.** Example of CoP path trajectory and length across four standing conditions in a 9-year-old. There is gradual increase in path trajectory and length as task complexity increases, from eyes open and closed on firm surfaces, to standing with eyes open and closed on foam surfaces.

## 6.9 Sensory system integration as measured by DWT analyses

Postural sway data was broken down into discrete frequency bands for comparison across standing balance conditions. Age, height and weight were considered as covariates in these analyses. When accounting for these factors, significant differences in DWT across standing balance conditions was still observed as demonstrated in Table 6.5. Age influenced DWT frequency bands relating to visual, vestibular and cerebellar information, with younger children demonstrating larger increases in DWT across these frequency bands across all conditions. Height influenced DWT frequency band relating to vestibular information. No significant age effects were noted for the moderate DWT band corresponding to somatosensory information.

Post hoc analyses showed significant differences in DWT velocities across standing balance conditions (Table 6.6). For conditions where eyes were closed on a firm surface (condition 2) and then eyes open on foam (condition 3), the DWT moderate, low and ultralow bands were similar, but the very low frequency band was different. DWT bands for all other standing balance conditions were significantly different from one another. Large effect sizes ranging from 0.5-3.6 were noted when comparing DWT frequency band composition across standing balance conditions. To show the effects of the different sensory contributions to balance control more clearly, Figure 6.6 demonstrates DWT path velocities expressed as medians for each standing balance condition.

**Table 6.5.** Sensory system integration across standing balance conditions using DWT frequency bands. Standing with eyes open on firm and eyes closed on foam affected all DWT frequency bands; standing with eyes closed affected DWT moderate and very low frequency bands; standing with eyes open on foam affected the DWT moderate frequency band only.

| | **Eyes Open (Firm)** | | | **Eyes Closed (Firm)** | | | **Eyes Open (Foam)** | | | **Eyes Closed (Foam)** | | | **Age** | | | **Height** | | | **Weight** | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | **β** | **95% CI** | **p** | **β** | **95% CI** | **p** | **β** | **95% CI** | **p** | **β** | **95% CI** | **p** | **β** | **95% CI** | **p** | **β** | **95% CI** | **p** | **β** | **95% CI** | **p** |
| ***DWT moderate (somatosensory)*** | -0.20 | (-0.22, -0.18) | **<.0001** | -0.03 | (-0.05, -0.01) | **.018** | -0.04 | (-0.06, -0.01) | **.004** | 0.27 | (0.24, 0.29) | **<.0001** | -0.02 | (-0.06, 0.02) | .368 | -0.00 | (-0.01, 0.01) | .733 | -0.00 | (-0.01, 0.01) | .719 |
| ***DWT low (cerebellar)*** | -0.21 | (-0.24, -0.19) | **<.0001** | -0.02 | (-0.05, 0.00) | .073 | -0.02 | (-0.04, 0.01) | .127 | 0.25 | (0.22, 0.28) | **<.0001** | -0.04 | (-0.07, -0.01) | **.013** | 0.00 | (-0.01, 0.01) | .536 | -0.00 | (-0.01, 0.01) | .901 |
| ***DWT very low (vestibular)*** | -0.22 | (-0.25, -0.19) | **<.0001** | -0.07 | (-0.09, -0.04) | **<.0001** | 0.00 | (-0.02, 0.03) | .749 | 0.29 | (0.26, 0.31) | **<.0001** | -0.09 | (-0.13, -0.05) | **<.0001** | 0.01 | (0.01, 0.02) | **.001** | -0.00 | (-0.01, 0.01) | .549 |
| ***DWT ultra low (vision)*** | -0.11 | (-0.15, -0.07) | **<.0001** | 0.00 | (-0.03, 0.04) | .873 | -0.01 | (-0.05, 0.02) | .432 | 0.12 | (0.09, 0.16) | **<.0001** | -0.06 | (-0.10, -0.01) | **.015** | 0.01 | (-0.00, 0.01) | .140 | 0.00 | (-0.01, 0.01) | .990 |

Significant values in bold (p<.05). Abbreviations: DWT = discrete wavelet transform; 95% CI = 95% confidence interval; Adj P = adjusted p value (Tukey post hoc analysis).

Regression coefficients reflect the mean difference in DWT frequency band path velocity across the four standing balance conditions (adjusted for age, height and weight).

**Table 6.6.** Results of DWT path velocities and post hoc analyses of DWT differences across standing balance conditions. Each standing balance condition was compared.

| **Condition** | **EO** | **EC** | **FEO** | **FEC** | **EO:EC** | | **EO:FEO** | | **EO:FEC** | | **EC:FEO** | | **EO:FEC** | | **FEO:FEC** | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | **Mdn (IQR)** | **Mdn (IQR)** | **Mdn (IQR)** | **Mdn (IQR)** | **ES** | **Adj P** | **ES** | **Adj P** | **ES** | **Adj P** | **ES** | **Adj P** | **ES** | **Adj P** | **ES** | **Adj P** |
| ***DWT moderate (somatosensory)*** | 0.72 (0.38) | 0.97 (0.56) | 0.97 (0.31) | 2.05 (1.19) | 1.24 | **<.0001** | 1.26 | **<.0001** | 3.29 | **<.0001** | 0.05 | .986 | 1.92 | <.0001 | 2.06 | **<.0001** |
| ***DWT low (cerebellar)*** | 0.65 (0.28) | 0.98 (0.40) | 1.07 (0.58) | 2.03 (0.97) | 1.64 | **<.0001** | 1.47 | **<.0001** | 3.61 | **<.0001** | 0.03 | .998 | 2.13 | <.0001 | 1.89 | **<.0001** |
| ***DWT very low (vestibular)*** | 0.27 (0.13) | 0.35 (0.19) | 0.44 (0.29) | 0.80 (0.57) | 1.17 | **<.0001** | 1.48 | **<.0001** | 3.24 | **<.0001** | 0.48 | **.013** | 2.34 | <.0001 | 1.69 | **<.0001** |
| ***DWT ultralow (vision)*** | 0.08 (0.05) | 0.09 (0.09) | 0.10 (0.05) | 0.13 (0.06) | 0.65 | **.002** | 0.59 | **.010** | 1.49 | **<.0001** | 0.10 | .938 | 0.72 | .001 | 0.89 | **<.0001** |

Significant values in bold (p<.05). Abbreviations: EO = eyes open (firm); EC = eyes closed (firm); FEO = foam eyes open; FEC = foam eyes closed; DWT = discrete wavelet transform; Mdn = median; IQR = interquartile range; ES = effect size (calculated using Hedges g); Adj P = adjusted p value (Tukey post hoc analysis).

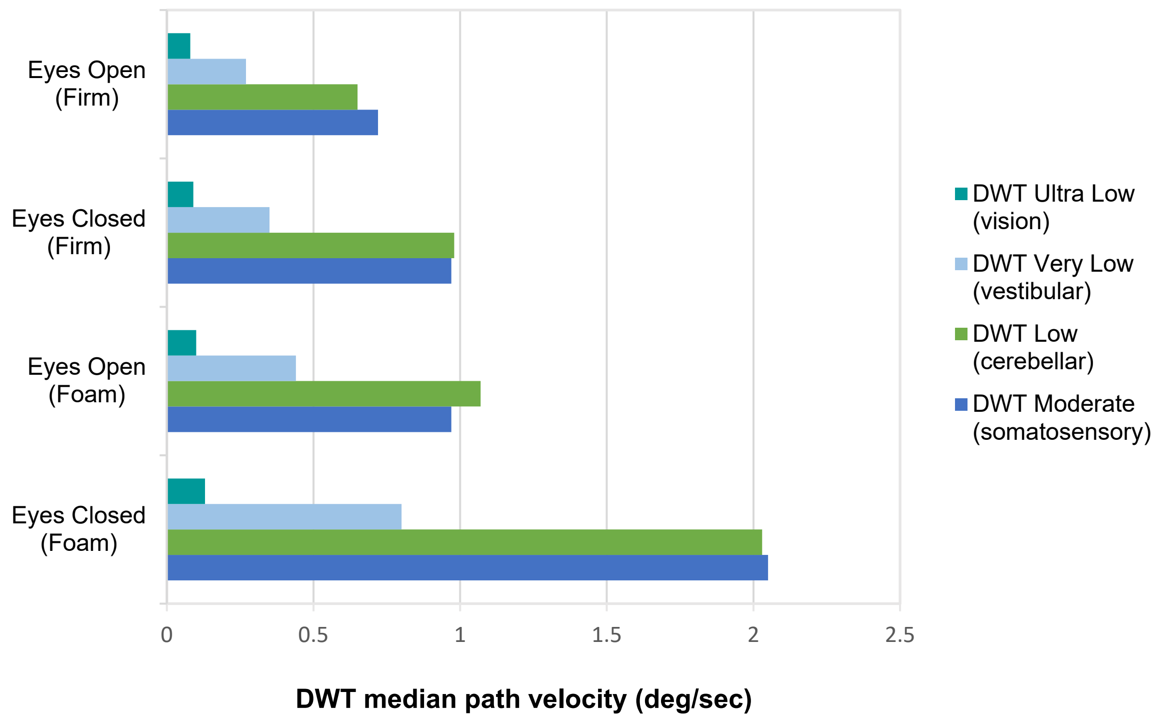



**Figure 6.6.** Median DWT path velocities across standing balance conditions.

# PART II: Longitudinal comparisons

## 6.10 Peripheral vestibular function: six-month comparisons

Twenty-nine children completed initial and six-month data points. Three more children completed vertical canal vHIT at the six-month time point, but four did not have all vertical canals assessed.

### 6.10.1 Semicircular canal function: six-month comparisons

vHIT comparisons at the six-month point did not vary significantly from baseline data for HSCC (p=0.098), ASCC (p=0.567), or PSCC (p=0.632) (Table 6.7).

When considering differences between left and right ears, only the HSCC condition showed a significant ear difference (HSCC p< 0.001), with vertical canals showing no effects of ear tested with VOR gain (ASCC: p=0.864; PSCC: p=0.217).

**Table 6.7.** Six-month comparisons for VOR gain in each vHIT condition

| *vHIT* | N | Time point | VOR gain Mean (SD) | Range | Adj P |
|---|---|---|---|---|---|
| ***HSCC*** | 58 | 1 | 0.96 (0.06) | 0.82-1.11 | .369 |
| | 58 | 2 | 0.98 (0.08) | 0.81-1.10 | |
| ***ASCC*** | 48 | 1 | 0.91 (0.13) | 0.61-1.20 | .255 |
| | 51 | 2 | 0.90 (0.11) | 0.67-1.18 | |
| ***PSCC*** | 46 | 1 | 0.92 (0.13) | 0.67-1.14 | .057 |
| | 51 | 2 | 0.90 (0.12) | 0.70-1.08 | |

Abbreviations: vHIT = video head impulse test; HSCC = horizontal semicircular canal; ASCC = anterior semicircular canal; PSCC = posterior semicircular canal; VOR = vestibulo-ocular reflex.

Differences may relate to the number of children who underwent vHIT at the six-month time point but not at the initial assessment. This is most notable for vertical canals, where more responses were collected at the second time point compared to the first time point.

## 6.10.2 Saccule function: six-month comparisons

cVEMP latencies did not significantly change over a six-month period, yet cVEMP amplitudes showed a significant decrease in amplitudes over time. This was evident for rectified VEMP amplitudes across time points. Height and weight were not associated with VEMP outcomes across time points.

**Table 6.8.** Six-month comparisons for cVEMP data.

| *cVEMP latencies (ms)* | | N | Time point | Mean (SD) | Range | Adj P |
|---|---|---|---|---|---|---|
| ***Presentation at 113 dB SPL*** | *p13* | 54 | 1 | 13.39 (1.22) | 9.71-15.75 | .287 |
| | | 55 | 2 | 13.59 (1.16) | 10.54-14.39 | |
| | *n23* | 54 | 1 | 19.25 (1.45) | 15.54-20.41 | .533 |
| | | 55 | 2 | 19.18 (1.74) | 13.46-20.21 | |
| ***Presentation at threshold (88 – 113dBSPL)*** | *p13* | 54 | 1 | 13.49 (1.44) | 9.71-16.55 | .551 |
| | | 55 | 2 | 13.65 (1.34) | 10.54-16.96 | |
| | *n23* | 54 | 1 | 19.18 (1.50) | 15.95-22.51 | .874 |
| | | 55 | 2 | 19.19 (1.73) | 13.46-22.79 | |
| ***cVEMP amplitudes*** | | | **Time point** | **Mdn (IQR)** | **Range** | **Adj P** |
| ***Presentation at 113 dB SPL*** | *p13-n23 (μV)* | 54 | 1 | 86.98 (56.49-140.19) | 14.14-273.95 | **.010** |
| | | 55 | 2 | 80.75 (34.75-135.22) | 12.68-241.43 | |
| | *p13-n23 (rectified)* | 54 | 1 | 12.22 (8.94-15.83) | 5.39-27.51 | **.012** |
| | | 55 | 2 | 10.23 (6.86-15.98) | 2.84-28.65 | |
| ***Presentation at threshold (88 – 113dBSPL)*** | *p13-n23 (μV)* | 54 | 1 | 57.92 (46.70-81.25) | 14.14-158.49 | **.037** |
| | | 55 | 2 | 55.22 (26.75-73.18) | 12.68-204.74 | |
| | *p13-n23 (rectified)* | 54 | 1 | 10.77 (7.94-15.02) | 4.73-28.73 | **.001** |
| | | 54 | 2 | 7.95 (6.25-11.12) | 2.84-21.03 | |

Significant values in bold ($p<.05$). Abbreviations: cVEMP = cervical vestibular evoked myogenic potentials; ms = milliseconds; μV = microvolts; dB SPL = decibels sound pressure level

## 6.10.3 Utricle function: six-month comparisons

Overall utricle function did not change significantly over a six-month, period. n10-p16 amplitude at threshold just achieved significance, with baseline oVEMP amplitudes larger than oVEMP amplitudes at six months.

**Table 6.9.** Six month comparisons for oVEMP data

| *oVEMP latencies (ms)* | | N | Time point | Mean (SD) | Range | Adj P |
|---|---|---|---|---|---|---|
| ***Presentation at 128 dB pFL*** | *n10* | 54 | 1 | 10.83 (0.93) | 7.38-12.07 | .259 |
| | | 52 | 2 | 10.42 (1.21) | 7.38-13.65 | |
| | *p16* | 54 | 1 | 13.07 (1.16) | 10.82-15.50 | .385 |
| | | 52 | 2 | 13.31 (1.57) | 10.51-16.34 | |
| ***Presentation at threshold (113-128 dB pFL)*** | *n10* | 54 | 1 | 10.22 (0.78) | 8.01-12.07 | .321 |
| | | 52 | 2 | 10.40 (1.06) | 8.01-13.65 | |
| | *p16* | 54 | 1 | 12.94 (1.11) | 10.61-15.50 | .617 |
| | | 52 | 2 | 13.06 (1.47) | 9.88-16.23 | |
| ***oVEMP amplitudes (µV)*** | | | **Time point** | **Mdn (IQR)** | **Range** | **Adj P** |
| ***Presentation at 128 dB pFL*** | *base-n10* | 54 | 1 | 7.13 (2.73-31.71) | 2.73-31.71 | .343 |
| | | 52 | 2 | 6.19 (2.15-22.31) | 2.15-22.31 | |
| | *n10-p16* | 54 | 1 | 10.91 (2.71-41.19) | 2.71-41.19 | .091 |
| | | 52 | 2 | 9.00 (1.53-30.05) | 1.53 - 30.05 | |
| ***Presentation at threshold (113-128 dB pFL)*** | *base-n10* | 54 | 1 | 7.31 (1.82-20.96) | 1.72-20.96 | .096 |
| | | 52 | 2 | 5.99 (2.15-19.79) | 2.15- 19.79 | |
| | *n10-p16* | 54 | 1 | 10.08 (2.71-31.74) | 2.71-31.74 | **.050** |
| | | 52 | 2 | 7.95 (1.53-21.41) | 1.53-21.41 | |

Significant values in bold (p<.05). Abbreviations: oVEMP = ocular vestibular evoked myogenic potentials; ms = milliseconds; µV = microvolts; dB pFL = decibels peak force level

## 6.10.4 Postural sway: six-month comparisons

Mixed effects modelling was used to compare log transformed postural sway data across conditions with path velocity as the response (EO, EC, FEO, FEC), assessment point as factor, and height, weight and age considered as covariates.

No significant differences were noted for postural sway across a six-month period. Table 6.10 outlines median path velocity and IQR for each standing balance condition six months apart.

**Table 6.10.** Six-month comparisons for path velocities across each standing balance condition.

| *Standing balance condition* | N | Time point | Path velocity Mdn (IQR) | Range | Adj P |
|---|---|---|---|---|---|
| *Eyes Open (Firm)* | 29 | 1 | 1.51 (1.21-1.74) | 0.96-2.65 | .832 |
| | 29 | 2 | 1.52 (1.32-1.90) | 0.95-3.99 | |
| *Eyes Closed (Firm)* | 29 | 1 | 1.96 (1.69-2.86) | 1.32-4.26 | .988 |
| | 29 | 2 | 2.24 (1.31-1.90) | 0.87-4.41 | |
| *Eyes Open (Foam)* | 29 | 1 | 2.18 (1.82-2.65) | 1.46-5.37 | .479 |
| | 29 | 2 | 2.30 (1.95-2.97) | 1.37-6.23 | |
| *Eyes Closed (Foam)* | 29 | 1 | 4.16 (3.28-5.26) | 2.44-7.07 | .783 |
| | 29 | 2 | 4.16 (3.65-5.09) | 2.65-8.24 | |

## 6.11 Peripheral vestibular function: twelve-month comparisons

### 6.11.1 Semicircular canal function: twelve-month comparisons

vHIT comparisons at the twelve-month point for the fifteen children did not vary significantly from baseline or six-month data. No significant change in VOR gain was noted for HSCC and ASCC conditions, but PSCC conditions varied across twelve-month time points, with VOR gain significantly lower at the twelve-month point when compared to initial assessment.

VOR gain differences between left and right HSCC remained across assessment points (Table 6.11). No VOR differences were noted for the vertical canals across the twelve-month period. Ear differences remained for HSCC condition across the twelve months, no ear effect was noted between assessment points for the vertical canals.

**Table 6.11.** Twelve-month comparisons for VOR gain in each vHIT condition

| *vHIT* | N | Time point | VOR gain Mean (SD) | Range | Adj P |
|---|---|---|---|---|---|
| ***HSCC*** | 30 | 1 | 0.95 (0.05) | 0.82-1.02 | .764 |
| | 30 | 2 | 0.94 (0.06) | 0.81-1.05 | |
| | 30 | 3 | 0.95 (0.09) | 0.79-1.26 | |
| ***ASCC*** | 30 | 1 | 0.93 (0.14) | 0.67-1.20 | .472 |
| | 29 | 2 | 0.90 (0.13) | 0.67-1.18 | |
| | 28 | 3 | 0.90 (0.12) | 0.69-1.12 | |
| ***PSCC*** | 29 | 1 | 0.94 (0.11) | 0.69-1.19 | **.008** |
| | 29 | 2 | 0.88 (0.11) | 0.70-1.18 | |
| | 28 | 3 | 0.85 (0.09) | 0.64-1.00 | |

Significant values in bold (p<.05). Abbreviations: vHIT = video head impulse test; HSCC = horizontal semicircular canal; ASCC = anterior semicircular canal; PSCC = posterior semicircular canal; VOR = vestibulo-ocular reflex.

### 6.11.2 Saccule function as measured by cVEMP: twelve-month comparisons

cVEMP latencies did not change significantly over a twelve-month period, but cVEMP amplitudes did. cVEMP thresholds showed a significant increase in amplitudes between six- and twelve-month comparisons, with no differences noted between baseline and twelve-month measures. A significant decrease in cVEMP amplitudes was noted at maximum presentation levels across time points, for unrectified amplitudes. Table 6.12 outlines descriptive statistics for all conditions including at maximum presentation level and threshold level.

**Table 6.12.** Twelve- month comparisons for cVEMP data.

| *cVEMP latencies (ms)* | | N | Time point | Mean (SD) | Range | Adj P |
|---|---|---|---|---|---|---|
| ***Presentation at 113 dB SPL*** | *p13* | 28 | 1 | 13.62 (0.77) | 12.38-15.40 | .532 |
| | | 28 | 2 | 13.93 (1.10) | 11.86-16.96 | |
| | | 30 | 3 | 13.72 (1.25) | 10.85-16.58 | |
| | *n23* | 28 | 1 | 19.78 (1.12) | 16.55-21.44 | .367 |
| | | 28 | 2 | 19.87 (1.40) | 17.09-22.79 | |
| | | 30 | 3 | 19.73 (1.51) | 15.02-22.10 | |
| ***Presentation at threshold (88 – 113dBSPL)*** | *p13* | 28 | 1 | 13.86 (1.20) | 11.65-16.55 | .881 |
| | | 28 | 2 | 14.19 (1.28) | 12.00-16.96 | |
| | | 30 | 3 | 13.72 (1.11) | 11.69-16.55 | |
| | *n23* | 28 | 1 | 19.68 (1.28) | 16.55-21.44 | .859 |
| | | 28 | 2 | 19.82 (1.29) | 17.09-22.79 | |
| | | 30 | 3 | 19.68 (1.54) | 15.02-22.41 | |
| ***cVEMP amplitudes*** | | | **Time point** | **Mdn (IQR)** | **Range** | **Adj P** |
| ***Presentation at 113 dB SPL*** | *p13-n23 (µV)* | 28 | 1 | 123.9 (83.1-178.0) | 47.60-273.95 | **.032** |
| | | 28 | 2 | 109.6 (55.7-138.6) | 22.62-241.43 | |
| | | 30 | 3 | 75.7 (55.7-120.5) | 35.42-224.08 | |
| | *p13-n23 (rectified)* | 28 | 1 | 12.73 (9.56-17.57) | 6.68-27.51 | .086 |
| | | 28 | 2 | 11.94 (7.11-16.51) | 3.76-23.39 | |
| | | 30 | 3 | 12.42 (9.37-16.65) | 4.98-26.25 | |
| ***Presentation at threshold (88 – 113dBSPL)*** | *p13-n23 (µV)* | 28 | 1 | 69.03 (52.98-90.66) | 37.44-158.49 | **.032** |
| | | 28 | 2 | 63.03 (44.50-73.16) | 22.62-138.51 | |
| | | 30 | 3 | 69.05 (50.47-87.28) | 26.43-188.63 | |
| | *p13-n23 (rectified)* | 28 | 1 | 11.07 (8.42-15.69) | 4.73-28.73 | **.023** |
| | | 28 | 2 | 8.08 (6.67-11.57) | 3.76-17.23 | |
| | | 30 | 3 | 11.82 (7.29-15.45) | 3.14-26.25 | |

Significant values in bold (p< .05). Abbreviations: cVEMP = cervical vestibular evoked myogenic potentials; ms = milliseconds; µV = microvolts; dB SPL = decibels sound pressure level

### 6.11.3 Utricle function as measured by oVEMP: twelve-month comparisons

No significant differences in oVEMP metrics were noted over a twelve-month period. Table 6.13 outlines the mean and standard deviation, along with median and amplitude range for all conditions at maximum presentation level and threshold level.

### 6.11.4 Postural sway: Longitudinal comparisons

Mixed effects modelling was used to compare log transformed postural sway data across conditions with path velocity as the response (EO, EC, FEO, FEC), assessment point as factor, and height, weight and age considered as covariates.

No significant differences were noted for postural sway across a twelve-month period. Table 6.14 outlines median path velocity and IQR across each of the assessment points for each standing balance condition.

**Table 6.13.** Twelve-month comparisons for oVEMP data.

| ***oVEMP latencies (ms)*** | | **N** | **Time point** | **Mean (SD)** | **Range** | **Adj P** |
|---|---|---|---|---|---|---|
| ***Presentation at 128 dB pFL*** | *n10* | 28 | 1 | 10.06 (0.87) | 7.38-11.24 | .703 |
| | | 26 | 2 | 10.21 (1.19) | 7.38-12.69 | |
| | | 28 | 3 | 10.02 (0.60) | 8.63-11.13 | |
| | *p16* | 28 | 1 | 12.97 (1.17) | 10.82-14.88 | .775 |
| | | 26 | 2 | 13.00 (1.67) | 10.51-16.13 | |
| | | 28 | 3 | 12.78 (1.13) | 11.24-15.19 | |
| ***Presentation at threshold (113-128 dB pFL)*** | *n10* | 28 | 1 | 10.12 (0.69) | 8.01-10.92 | .873 |
| | | 26 | 2 | 10.21 (0.87) | 8.01-11.44 | |
| | | 28 | 3 | 10.32 (0.59) | 9.36-11.44 | |
| | *p16* | 28 | 1 | 12.92 (1.03) | 10.92-14.67 | .457 |
| | | 26 | 2 | 12.25 (1.02) | 9.88-14.26 | |
| | | 28 | 3 | 12.69 (0.75) | 11.24-14.15 | |
| ***oVEMP amplitudes (µV)*** | | | **Time point** | **Mdn (IQR)** | **Range** | **Adj P** |
| ***Presentation at 128 dB pFL*** | *base-n10* | 28 | 1 | 7.29 (5.31-14.09) | 3.30-20.96 | .334 |
| | | 26 | 2 | 6.73 (4.34-10.29) | 2.15-22.31 | |
| | | 28 | 3 | 6.53 (4.75-10.60) | 3.5-16.27 | |
| | *n10-p16* | 28 | 1 | 12.02 (9.06-18.72) | 2.71-31.74 | .100 |
| | | 26 | 2 | 9.96 (6.40-18.09) | 1.53-30.05 | |
| | | 28 | 3 | 10.43 (6.44-20.01) | 1.90-33.50 | |
| ***Presentation at threshold (113-128 dB pFL)*** | *base-n10* | 28 | 1 | 8.08 (4.55-10.80) | 3.61-20.96 | .836 |
| | | 26 | 2 | 5.99 (3.42-7.77) | 2.15-19.79 | |
| | | 28 | 3 | 4.65 (2.94-7.25) | 1.04-21.94 | |
| | *n10-p16* | 28 | 1 | 11.06 (7.00-15.37) | 2.71-31.74 | .339 |
| | | 26 | 2 | 6.95 (4.31-10.73) | 1.53-18.05 | |
| | | 28 | 3 | 7.48 (5.42-10.49) | 3.19-14.84 | |

Abbreviations: oVEMP = ocular vestibular evoked myogenic potentials; ms = milliseconds; µV = microvolts; dB pFL = decibels peak force level

**Table 6.14.** Twelve-month comparisons for path velocities across each standing balance condition.

| *Standing balance condition* | N | Time point | Path velocity Mdn (IQR) | Range | Adj P |
|---|---|---|---|---|---|
| *Eyes Open (Firm)* | 15 | 1 | 1.53 (1.20-1.66) | 1.09-2.60 | .507 |
| | 15 | 2 | 1.61 (1.20- 2.41) | 0.95-4.00 | |
| | 15 | 3 | 1.27 (1.02-1.56) | 0.85-2.69 | |
| *Eyes Closed (Firm)* | 15 | 1 | 1.87 (1.61-2.29) | 1.32-3.54 | .928 |
| | 15 | 2 | 2.09 (1.50-2.51) | 0.87-4.41 | |
| | 15 | 3 | 1.80 (1.47-2.07) | 1.16-4.46 | |
| *Eyes Open (Foam)* | 15 | 1 | 2.12 (1.84-2.44) | 1.46-4.04 | .389 |
| | 15 | 2 | 2.43 (1.93-3.47) | 1.37-6.23 | |
| | 15 | 3 | 1.97 (1.72-2.11) | 1.40-4.67 | |
| *Eyes Closed (Firm)* | 15 | 1 | 4.13 (3.42-4.58) | 2.44-7.07 | .599 |
| | 15 | 2 | 4.16 (3.42-5.37) | 2.69-8.03 | |
| | 15 | 3 | 3.82 (2.87-4.66) | 2.27-6.11 | |

# PART III: Relationship between functional balance, postural sway and vestibular function

Multiple regression was used to explore the relationship between functional balance measures and tests of peripheral vestibular function including SCC, and otolith function at maximum presentation levels for baseline measures. Age, height and weight were covariates for analyses.

## 6.12 Functional balance measures and vestibular function

There was no relationship between BOT-2 scores (percentile rank, BC scale score and Bal score) and measures of peripheral vestibular function (Table 6.15). On the other hand, there was a significant relationship between PBS scores and some measures of vHIT, but not with otolith function. ASCC gain predicted PBS scores ($\beta$=18.39, $t(34)$ =

9.46, $p<.01$); and explained a significant proportion of variance in PBS scores, $R^2=.37$, $F(1, 34) = 9.46$, $p<.01$. This was also evident for PSCC gain ($\beta=21.96$, $t(34) = 3.96$, $p<.01$) and also explained a significant proportion of the variance in PBS scores, $R^2=.47$, $F(1, 34) = 15.68$, $p<.001$.

## 6.13 Standing balance measures and vestibular function

When standing with eyes open, significant relationships were noted between postural sway and otolith function as measured by VEMP latencies. Increased postural sway was correlated with an increase in p13 latency for eyes open on firm ($\beta=7.04$, $t(34) = 3.39$, $p<.01$) and also explained a significant proportion of the variance in p13 latencies, $R^2=.22$, $F(1, 34) = 11,52$, $p<.01$. This was also evident when on a foam surface; $\beta=5.44$, $t(32) = 2.87$, $p<.01$; with a significant proportion of variance in p13 latencies scores, $R^2=.26$, $F(1, 32) = 8.22$, $p<.01$. No other significant relationships were noted between tests of peripheral vestibular function and standing balance (Table 6.16).

**Table 6.15.** Relationship between functional balance measures and tests of peripheral vestibular function.

| *Tests of peripheral vestibular function* | | | PBS (Log transformed data) | | | BC Scale Score | | | Bal Scale Score | | | % rank | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | **β** | **95% CI** | **p** | **β** | **95% CI** | **p** | **β** | **95% CI** | **p** | **β** | **95% CI** | **p** |
| ***vHIT*** | *VOR gain* | *HSCC* | 0.07 | (-2.10, 2.24) | .951 | -0.00 | (-0.01, 0.00) | .688 | -0.00 | (-0.01, 0.00) | .612 | -0.00 | (-0.00, 0.00) | .850 |
| | | *ASCC* | 18.39 | (6.18, 30.61) | **.004** | 0.01 | (-0.02, 0.05) | .514 | 0.03 | (0.01, 0.06) | .129 | 0.00 | (-0.00, 0.01) | .372 |
| | | *PSCC* | 21.96 | (10.64, 33.29) | **<.001** | 0.02 | -0.03, 0.05) | .576 | 0.03 | (-0.01, 0.06) | .110 | 0.00 | (-0.00, 0.01) | .335 |
| ***cVEMP (113 dB SPL)*** | *Latencies* | *p13* | 30.07 | (-21.86, 81.99) | .246 | 0.03 | (-0.11, 0.16) | .687 | -0.03 | (0.16, 0.10) | .644 | -0.00 | (-0.02, 0.02) | .899 |
| | | *n23* | -2.10 | (59.09, 54.93) | .941 | 0.08 | (-0.07, 0.22) | .286 | -0.06 | (-0.09, 0.20) | .431 | -0.01 | (-0.01, 0.3) | .195 |
| | *Amplitudes* | *p13-n23* | -4.23 | (-16.94, 8.47) | .501 | 0.02 | (-0.01, 0.05) | .253 | 0.13 | (-0.02, 0.05) | .399 | 0.00 | (-0.00, 0.01) | .298 |
| | | *p13-n23 (rectified)* | 0.88 | (-0.628, 8.03) | .804 | 0.01 | -0.00, 0.03 | .133 | 0.00 | (-0.02, 0.02) | .802 | 0.00 | (-0.00, 0.00) | .177 |
| ***oVEMP (128 dB pFL)*** | *Latencies* | *n10* | -9.40 | (-55.2, 36.4) | .676 | 0.01 | (-0.09, 0.11) | .834 | 0.22 | (-0.06, 0.15) | .391 | 0.01 | (-0.01, 0.02) | .494 |
| | | *p16* | -13.5 | (-71.0, 43.9) | .633 | 0.00 | (-0.12, 0.13) | .947 | 0.10 | (-0.03, 0.22) | .126 | 0.01 | (-0.01, 0.03) | .269 |
| | *Amplitudes* | *base-n10* | 1.12 | (-12.13, 14.37) | .864 | -0.00 | (-0.03, 0.03) | .822 | -0.00 | (-0.03, 0.03) | .944 | -0.00 | (-0.01, 0.00) | .811 |
| | | *n10-p16* | 1.54 | (-11.6, 14.68) | .812 | 0.01 | (-0.02, 0.03) | .569 | 0.01 | (-0.02, 0.04) | .359 | -0.00 | (-0.00, 0.01) | .359 |

Significant values in bold (p< .05). Abbreviations: vHIT = video head impulse test; VOR = vestibulo-ocular reflex; HSCC = horizontal semicircular canal; ASCC = anterior semicircular canal; PSCC = posterior semicircular canal; cVEMP = cervical vestibular evoked myogenic potentials; dB SPL = decibels sound pressure level; oVEMP = ocular vestibular evoked myogenic potentials; dB pFL = decibels peak force level.

**Table 6.16.** Relationship between postural control measures and tests of peripheral vestibular function.

| *Tests of peripheral vestibular function* | | | Standing Eyes Open (Firm) | | | Standing Eyes Closed (Firm) | | | Standing Eyes Open (Foam) | | | Standing Eyes Closed (Foam) | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | **β** | **95% CI** | **p** | **β** | **95% CI** | **p** | **β** | **95% CI** | **p** | **β** | **95% CI** | **p** |
| ***vHIT*** | *VOR gain* | *HSCC* | -0.14 | (-0.33, 0.05) | .137 | -0.01 | (-0.18, 0.16) | .873 | -0.00 | (-0.18, 0.17) | .972 | -0.07 | (-0.24, 0.10) | .416 |
| | | *ASCC* | 0.29 | (-0.97, 1.56) | .639 | -0.35 | (-1.45, 0.74) | .513 | -0.08 | (-1.05, 1.22) | .880 | 0.27 | (-0.85, 1.40) | .624 |
| | | *PSCC* | 0.18 | (-1.08,1.45) | .768 | -0.69 | (-1.76, 0.37) | .194 | 0.04 | (-1.10, 1.17) | .947 | 0.23 | (-1.11, 1.15) | .968 |
| ***cVEMP (113 dB SPL)*** | *Latencies* | *p13* | 7.04 | (2.80, 11.28) | **.002** | 2.06 | (-1.98, 6.10) | .305 | 5.54 | (1.59, 9.49) | **.008** | -0.05 | (-4.32, 4.22) | .981 |
| | | *n23* | 2.31 | (-3.00, 7.61) | .381 | -0.98 | (-5.38, 3.41) | .651 | 1.71 | (-3.05, 6.46) | .469 | -0.65 | (-5.23, 3.92) | .772 |
| | *Amplitudes* | *p13-n23* | 0.30 | (-0.90, 1.50) | .611 | -0.47 | (-1.45, 0.50) | .329 | 0.38 | (-0.69, 1.45) | .469 | -0.28 | (-1.31, 0.74) | .576 |
| | | *p13-n23 (rectified)* | -0.49 | (-1.14, 0.16) | .134 | -0.17 | (-0.72, 0.38) | .533 | -0.38 | (-0.97, 0.20) | .194 | 0.02 | (-0.56, 0.59) | .954 |
| ***oVEMP (128 dB pFL)*** | *Latencies* | *n10* | 0.07 | (-3.76, 3.91) | .969 | -0.91 | (-4.04,2.22) | .555 | -0.25 | (-4.45, 3.94) | .903 | -0.48 | (-3.68, 2.72) | .760 |
| | | *p16* | 0.98 | (-3.82, 5.77) | .680 | 0.49 | (-3.47, 4.44) | .803 | -0.19 | (-3.53, 3.15) | .907 | -1.72 | (-5.68, 2.24) | .381 |
| | *Amplitudes* | *base-n10* | 0.60 | (-0.49, 1.68) | .268 | 0.25 | (-0.65, 1.16) | .571 | 0.59 | (-0.35, 1.52) | .210 | 0.43 | (-0.48, 1.34) | .344 |
| | | *n10-p16* | 0.45 | (-0.62, 1.55) | .388 | 0.11 | (-0.79, 1.02) | .796 | 0.11 | (-0.84, 1.07) | .812 | 0.06 | (-0.86, 0.98) | .895 |

Significant values in bold ($p < .05$). Abbreviations: vHIT = video head impulse test; VOR = vestibulo-ocular reflex; HSCC = horizontal semicircular canal; ASCC = anterior semicircular canal; PSCC = posterior semicircular canal; cVEMP = cervical vestibular evoked myogenic potentials; dB SPL = decibels sound pressure level; oVEMP = ocular vestibular evoked myogenic potentials; dB pFL = decibels peak force level.

Regression coefficients reflect the mean difference in vestibular test outcomes across the four standing balance conditions (adjusted for age, height and weight).

# PART IV: Age effects on vestibular assessment and postural sway outcomes

## 6.14 Age effects across peripheral vestibular assessments

The effects of age on peripheral vestibular test results were determined using linear regression applied to the baseline measures (N = 35) (Table 6.17). Increasing age was significantly associated with reduced VOR gain for the PSCC condition. Other vHIT conditions demonstrated no significant age effects.

Age was not a predictor of cVEMP p13, n23 latencies for most conditions; but was a predictor of cVEMP amplitudes, with older ages associated with larger amplitude responses. cVEMP amplitudes in all conditions (rectified and unrectified conditions, at maximum and at threshold presentation levels) showed a significant increase in cVEMP amplitude associated with increasing age. Shorter p13 latency was also associated with decreased ages for one cVEMP condition (when performed at threshold). Age did not predict oVEMP latencies or amplitudes.

**Table 6.17.** Age effects on tests of peripheral vestibular function.

| ***Tests of peripheral vestibular function*** | | | **β** | **95% CI** | **p** |
|---|---|---|---|---|---|
| ***vHIT*** | *VOR gain* | *HSCC* | .003 | (-0.00, 0.01) | .305 |
| | | *ASCC* | .001 | (-0.02, 0.02) | .602 |
| | | *PSCC* | -.018 | (-0.03, -0.00) | **.029** |
| ***cVEMP (113 dB SPL)*** | *Latencies* | *p13* | .083 | (-0.07, 0.23) | .269 |
| | | *n23* | .098 | (-0.08, 0.27) | .264 |
| | *Amplitudes* | *p13-n23* | .052 | (-0.02, 0.08) | **.002** |
| | | *p13-n23 (rectified)* | .024 | (0.00, 0.05) | **.020** |
| ***cVEMP (threshold)*** | *Latencies* | *p13* | .182 | (0.01, 0.35) | **.035** |
| | | *n23* | .104 | (-0.07, 0.28) | .247 |
| | *Amplitudes* | *p13-n23* | .033 | (0.01, 0.06) | **.013** |
| | | *p13-n23 (rectified)* | .027 | (0.01, 0.05) | **.014** |
| ***oVEMP (128 dB pFL)*** | *Latencies* | *n10* | .001 | (-0.11, 0.11) | .984 |
| | | *p16* | .100 | (-0.03, 0.23) | .136 |
| | *Amplitudes* | *base-n10* | .001 | (-0.03, 0.03) | .938 |
| | | *n10-p16* | .017 | (-0.01, 0.05) | .272 |
| ***oVEMP (threshold)*** | *Latencies* | *n10* | -.002 | (-0.09, 0.09) | .963 |
| | | *p16* | .093 | (-0.03, 0.22) | .150 |
| | *Amplitudes* | *base-n10* | .014 | (-0.01, 0.04) | .304 |
| | | *n10-p16* | .009 | (-0.02, 0.04) | .568 |

Significant values in bold ($p < .05$). Abbreviations: vHIT = video head impulse test; VOR = vestibulo-ocular reflex; HSCC = horizontal semicircular canal; ASCC = anterior semicircular canal; PSCC = posterior semicircular canal; cVEMP = cervical vestibular evoked myogenic potentials; dB SPL = decibels sound pressure level; oVEMP = ocular vestibular evoked myogenic potentials; dB pFL = decibels peak force level.

## 6.15 Age effects across postural sway

General linear modelling for postural sway with age, height and weight as covariates showed significant effects of age across most postural sway conditions: that is, age predicted postural sway, with a consistent decrease in path velocities associated with increasing age when standing with eyes open (on firm and foam surfaces) and when standing on foam with eyes closed. Height did not affect any postural sway condition; weight affected standing with eyes closed on a firm surface. For each standing balance condition, Table 6.18 outlines the general linear modelling and multiple regression analyses, and Figure 6.7 represents each participant's median path velocity across standing balance conditions.

**Table 6.18.** Age effects on postural sway measures.

| *Postural control* | | Age | | | Height | | | Weight | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | **β** | **95% CI** | **p** | **β** | **95% CI** | **p** | **β** | **95% CI** | **p** |
| ***Path Velocity*** | *Eyes Open (Firm)* | -0.053 | (-0.095, -0.016) | **.007** | 0.010 | (0.000, 0.014) | .054 | -0.006 | (-0.013, 0.000) | .077 |
| | *Eyes Closed (Firm)* | -0.034 | (-0.077, 0.009) | .120 | 0.006 | (-0.001, 0.014) | .124 | -0.001 | (-0.01, 0.002) | **.015** |
| | *Eyes Open (Foam)* | -0.005 | (-0.09, -0.01) | **<.0001** | 0.002 | (-0.01, 0.01) | .592 | -0.000 | (-0.01, 0.01) | .956 |
| | *Eyes Closed (Foam)* | -0.054 | (-0.096, -0.012) | **.014** | 0.004 | (-0.004, 0.012) | .305 | -0.001 | (-0.008, 0.007) | .860 |

Significant values in bold (p< .05).

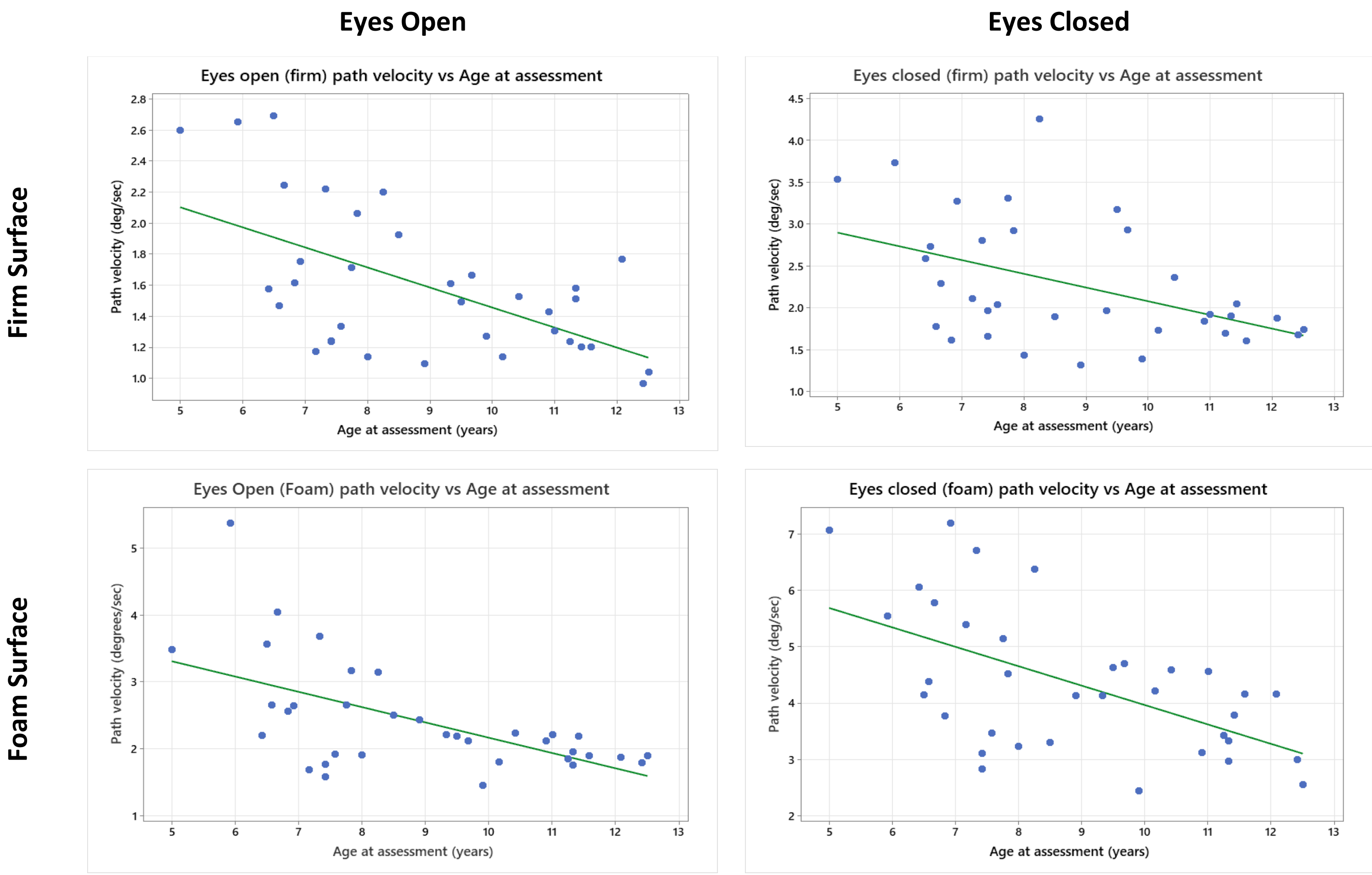



**Figure 6.7.** Postural sway across the four standing conditions as a function of age. In all conditions, increasing age was associated with decreasing postural sway.

## 6.16 Discussion

### Part I: Normative data for peripheral vestibular function and postural control

Tests of peripheral vestibular function and postural control are well tolerated by children 5-12 years, given adherence to the test protocol for the initial assessment. Findings suggest that this test battery may be a feasible approach to quantify vestibular function and motor proficiency in the growing child.

Normative findings must be interpreted with caveats, and for some assessments, there are limitations in generalising test findings to a broader group of typically developing children. One reason relates to the use of EMG monitoring for cVEMP testing; while SCM contraction was visually monitored by the examiner, due to device limitations active EMG monitoring was not performed during assessment. Instead, post stimulus rectification was applied to the waveforms for analysis. While VEMP findings from this study may be generalised to the equipment used (Natus BioLogic Nav Pro), and the typical clinical processes utilised in Australian settings (bilateral SCM contraction from a semi-recumbent position), one must interpret and contrast findings for other equipment and processes which may utilise different monitoring or rectification methods.

Initial exploration of vHIT data showed left HSCC VOR gain was significantly less than the right HSCC VOR gain; this finding likely due to camera location on the vHIT goggles, with other studies substantiating this observation (Bachmann et al., 2018; L. McGarvie et al., 2015). VOR gain for normative vHIT comparisons were averaged VOR gain values, taken across a range of peak head velocities (100-250deg/sec) rather than discrete head velocities. Peak head velocities were not accounted for in analyses given the small number of impulses performed for each condition (minimum of ten for each plane across a range of velocities, rather than ten impulses across several specified velocities). This may have influenced overall findings; while all efforts were taken to ensure a range was consistent across participants, there may have been inherent variability across the participants studied.

Furthermore, there is evidence to suggest that for children, a slower range of head velocities may relate to anatomical variations in cervical spine flexibility, with younger children having a more flexible cervical spine, thereby reducing the examiner's ability to manipulate the head to generate the appropriate velocity of the head impulse (Ross & Helminski, 2016). This was not observed in the present project across the child group; a sufficient range of head velocities was achieved. Increased head velocities may also contribute to larger variability in responses (L. McGarvie et al., 2015). Head impulse velocities were conducted across a consistent range (100-250 deg/sec) in the current study, with vertical impulses marginally (but not significantly) slower but still within the range.

Larger variability in VOR gain for vertical impulses was noted in the current study, and has been reported in the literature (Bachmann et al., 2018). Bachmann noted this difference when comparing VOR gain for children and adults in vertical planes and related this to pupil size of the individual. Pupil size can impact on the quality of head impulses collected particularly in vertical conditions where the eyelids can obscure the pupil from being optimally recorded (Curthoys et al., 2023). While pupil size was not explicitly considered in the study, this may be a factor to consider for future research, particularly when measuring vHIT in younger children.

Cut-off values for quantifying VOR gain in children have varied across the literature. Hamilton (Hamilton et al., 2015) used a value of <0.7 across all SCC based on receiver operating characteristic (ROC) curve comparing vHIT results to abnormal rotational chair results. The normative range determined by Janky and Givens (Janky & Givens, 2015) was based on 1.5 standard deviations from the mean, with cut-off values for abnormal VOR gain at ≤0.85 for HSCC, and ≤0.65 for vertical SCC. These normative values are not dissimilar to those obtained in the current project with cut-off values for abnormal VOR gain at ≤0.84 for HSCC, and ≤0.66 for vertical SCC, based on two standard deviations from the mean. The presence of corrective saccades should also be used in conjunction with VOR gain to quantify dysfunction.

Postural sway varied significantly across most standing balance conditions; generally, complex standing conditions where vision or somatosensory information was compromised were associated with greater amounts of postural sway. However, similar postural sway was observed between conditions two (standing with eyes closed on a firm surface) and three (standing with eyes open on a foam surface). Theoretically, for condition two where vision is compromised, reliance on somatosensory and vestibular information is required to maintain balance, in addition to other sensorimotor processes utilised to ensure the limits of stability are not violated. For condition three, where vision is available but somatosensory information in compromised, reliance on vision and vestibular information increases. This pattern of responses has been observed in the literature (Barozzi et al., 2014), but other authors have noted more consistent increases in postural sway across conditions of increasing complexity (Hsu, Kuan, et al., 2009). Postural sway was only analysed for the anteroposterior plane, as most sway occurs in this plane for bipedal stance (Baloh et al., 1998; Collins & De Luca, 1993).

DWT comparisons of frequency bands corresponding to visual, vestibular, cerebellar and somatosensory information varied across all standing balance conditions. More complex standing balance conditions had greater contributions from all DWT frequency bands, which is not unexpected given path velocities generally increased in these contexts. DWT vestibular contributions for eyes closed (firm surface) and eyes open (foam surface) were significantly different, despite overall path velocities and other DWT frequency bands being similar. This suggests some element of vestibular inputs to postural control when somatosensory inputs are compromised, when standing on foam with eyes open.

## Part II: Longitudinal comparisons of postural sway and peripheral vestibular function

Postural sway did not change significantly over a twelve-month period, but comparisons of vestibular measures across three time points showed some significant findings.

cVEMP amplitudes significantly changed over a six-month and twelve-month period. Amplitudes were similar at baseline and twelve months, but significantly smaller at the six-month data point. Given that there is not a progressive shift in amplitudes (either consistently increasing or decreasing), this finding must be interpreted with caution. Rather than a documented change in VEMP amplitudes, these findings may reflect the inherent variability in response amplitudes which may be the result of re-testing or relate to procedural parameters such as maintaining adequate head elevation or SCM contraction across assessments. No differences were noted across VEMP latencies (p13, n23, n10, p16) or oVEMP amplitudes. Good to fair test-retest reliability for adults has been reported for cVEMP amplitudes evoked using 500Hz pure tones (Nguyen et al., 2010), with better test-retest reliability noted for oVEMP amplitudes and latencies. Fuemeller (Fuemmeler et al., 2020) found better reliability in cVEMP amplitudes for children when compared to adults. Thus, the findings from the project do not substantiate current evidence in the literature.

Over a twelve-month period, there was a progressive, significant decrease in PSCC VOR gain. However, other SCC did not show this pattern of findings. Exploration of SCC measures over time are sparse in the literature, particularly in the context of normal SCC function. Longitudinal comparisons have typically focused on children at risk of vestibular impairment to monitor progression over time (Dhondt et al., 2021).

Overall findings suggest that some clinical assessments of the peripheral vestibular system remain stable over time, while others change over a six- or twelve-month period. While these changes are small, some of these factors must be considered in the context of clinical findings, particularly when using consistent protocol and equipment setups. The relevance of developmental changes may also be greater for children <5 years, and thus future research exploring developmental trajectories should focus on this younger age group.

## Part III: Relationship between functional balance, postural sway and vestibular function

The relationship between vestibular function and postural control measures was not robust. A positive relationship was evident between variables cVEMP latencies and postural sway when standing with eyes open: longer p13 latencies were associated with larger postural sway. This is somewhat counterintuitive to the other findings related to peripheral vestibular function and postural control observed in Study 1, and part II of Study 2. Findings from Study 1 show that p13 latencies in children are shorter than adults, and this is supported by existing literature (Nicole et al., 2020; Rodriguez et al., 2019). Furthermore, the present PhD project and other literature provide substantial evidence that children show larger postural sway than adults (Barozzi et al., 2014; de Sá et al., 2018; Ferber-Viart et al., 2007). Therefore, this relationship, if it truly exists, is proposed to be a negative relationship, rather than positive as observed in the current study. This suggests that for typically developing children with normal vestibular function, test outcomes may not be sensitive to predict postural control scores due to wide variability in responses, and potential small changes in function that may lie within the normative range.

There was a relationship between functional balance performance and VOR gain for vertical SCC (for ASCC and PSCC): a larger VOR gain was associated with higher PBS scores. While this relationship may be small, other studies have shown a relationship between similar constructs of HSCC and functional balance outcomes in children with vestibular impairment (Janky et al., 2022).

## Part IV: Age effects on peripheral vestibular function and postural control

Overall, postural sway measures varied as a function of age, with smaller postural sway associated with increasing age. This finding was evident even when anthropometric correlates (height and weight) were accounted for. This finding did not persist over a twelve-month period, suggesting that perhaps the substantive changes seen over this time period are not sensitive enough to detect, and longer time comparisons are warranted to determine the change over time. No differences were noted at the six-month and twelve-month data points. Thus, considering regression equations to document age related changes are more suitable than using a mean and normative range.

VOR gain for PSCC function was influenced by age: younger children had larger VOR gain values. It is important to note that for children sampled across all assessment points they had a higher overall VOR gain than the pooled data of 35 children to begin with, but this pattern of difference was still notable. cVEMP amplitudes across all conditions (rectified and unrectified, at maximum and at threshold presentation levels) showed a significant increase in cVEMP amplitude associated with increasing age. p13 latency was also associated with age for one cVEMP condition (when performed at threshold). Age did not predict oVEMP latencies or amplitudes.

Despite some vestibular outcome measures showing age related effects, the use of regression may not be that applicable in a clinical context. For VOR gain, it is widely accepted to use a normative range to compare values for both horizontal and vertical canal assessment, despite recording parameters and apparatus setup potentially influencing results (L. McGarvie et al., 2015). Regression is typically used when comparing slower and faster head impulse speeds, but not considered clinically when comparing responses. Additionally, cVEMP normative ranges may be more clinically applicable than regression to determine the expected amplitudes. Overall, findings from this study suggest that VOR does not seem to be affected by age in childhood, which is consistent with other literature (Bachmann et al., 2018; Hamilton et al., 2015). VOR differences have consistently been observed with older adults (L. McGarvie et al., 2015).

## 6.17 Summary

This chapter provides a comprehensive review of peripheral vestibular function, functional balance, and postural control comparisons for typically developing children between 5 and 12 years of age. The findings have implications for clinical practice: the range of clinical assessments explored provide a cohesive protocol for children in this age group, in addition to normative data ranges that can be applied in a clinical setting using the similar equipment.

# Chapter 7: VESTIBULAR FUNCTION AND POSTURAL CONTROL IN CHILDREN WITH SENSORINEURAL HEARING LOSS

This chapter presents the findings of a study exploring postural control and otolith function in children between 5-12 years of age, with bilateral, sensorineural hearing loss. The manuscript was submitted to the International Journal of Audiology in February 2023, and following peer review, resubmitted in revised form in June, 2023.

## 7.1 Abstract


**Objective:** Balance difficulties are common in children with sensorineural hearing loss. For some of these children, concomitant vestibular deficits may impact postural control. This study aimed to explore vestibular function, functional balance and postural control, and the relationship between these measures in children with sensorineural hearing loss.
**Design:** Cross sectional study quantifying peripheral vestibular function (vestibular evoked myogenic potentials, video head impulse test), functional balance (Bruininks-Oseretsky Test of Motor Proficiency) and postural control (static posturography with modified sensory inputs). The relationship between degree of vestibular impairment, functional balance and postural control was explored.

**Study Sample:** Eleven with sensorineural hearing loss, and eleven with normal sound detection between 5-12 years of age.

**Results:** Children with sensorineural hearing loss had varying degrees of vestibular dysfunction and differences in overall balance performance. Across all children, greater degrees of vestibular impairment was associated with significantly poorer functional balance and postural control performance for complex standing conditions (BOT percentile rank p=.001; compliant surface eyes open: p=0.027; compliant surface eyes closed: p=0.048).

**Conclusions:** Vestibular dysfunction in children with sensorineural hearing loss was variable. Vestibular impairment predicted poorer functional balance performance and postural control abilities, including differences in postural sway patterns.

## 7.2 Introduction

For children with sensory loss affecting the vestibular system, balance issues can be evident in early life, when typical motor milestones of sitting, crawling and walking emerge. Failure to meet motor milestones is one such flag for onward referral or intervention (Verbecque et al., 2017).

Mastery of motor milestones is often considered formative elements of childhood development. Sensory dysfunction has developmental consequences for motor milestone mastery and integration of sensory input required for postural control, a fundamental requisite for maintaining balance in daily life. For children with sensorineural hearing loss (SNHL), typical milestones of head control, crawling and walking can be significantly delayed (Leen Maes et al., 2014; Wiener-Vacher, 2008), and there is some evidence to suggest that these delays have repercussions for later childhood, when differences in motor performance persist (Rine et al., 2000). Motor delays can also cause an increased risk of falls, clumsiness and longer-term impact on physical participation and activity (Cushing et al., 2013; Cushing & Papsin, 2018).

Children that are most at risk for vestibular dysfunction are those with conditions affecting auditory structures, where hearing loss is evident (Cushing et al., 2013; De Kegel et al., 2012). In children the most common causes of SNHL are related to Connexin 26 mutations, cochleovestibular anomalies occurring in isolation (enlarged vestibular aqueduct), related to a syndrome (Usher, CHARGE syndrome), or acquired (meningitis, cytomegalovirus) (Cushing et al., 2013; Martens et al., 2022). Greater degrees of SNHL are associated with the increased likelihood of vestibular impairment, and vestibular dysfunction is more closely correlated with conditions related to structural anomalies of the inner ear (Janky & Givens, 2015; Leen Maes et al., 2014). Conditions affecting the auditory and vestibular structures can have functional and consequential impacts if left undiagnosed.

If underlying mechanisms for motor delay remain unidentified this can affect timely assessment and the success of interventional approaches. In these instances, consequences of undiagnosed vestibular impairment mean that non-specific rehabilitation approaches may cause a plateau of intervention outcomes or prolong intervention unnecessarily (Rine et al., 2004). And while this is clearly not life-threatening, it can have a negative impact on quality of life and enjoyment of diverse physical activities at a formative time in development.

One way to ensure that the underlying mechanisms are adquately assessed is to consider all constructs for motor milestone mastery and postural control including sensory integration from the proprioceptive, visual and vestibular systems. This includes postural control measures, which can determine sensory integration processes, functional balance measures to determine motor skill performance on a range of daily activities (Deitz et al., 2007), and assessment of the peirpheral vestibular system to provide quantifying information about vestibular function.

Postural control measures can be particularly useful for establishing postural abilities in children who have motor delay or show differences in motor behaviour. Static posturography documents the amount of postural sway over a specified time period using a force plate and can indicate integration of visual, vestibular and somatosensory systems. Various metrics can be obtained, including centre of pressure (CoP) path length, path velocity or area (Clark et al., 2010). Differentiating CoP measurement into discrete frequency bands, known as discrete wavelet transform (DWT) analyses, provides a more nuanced representation of movement patterns not typically observed during traditional measures, and has been valuable for various clinical populations (Rhine et al., 2017). DWT analyses can be a useful indicator of the relative sensory contributions to postural control; with certain frequency components thought to represent different physiological mechanisms: vision (<0.1Hz), vestibular (0.1-0.39Hz), cerebellar (0.39-1.56Hz) and somatosensory (1.56-6.25Hz)(Liang et al., 2014). Evaluation of postural control in children with SNHL has shown greater amounts of postural sway in more challenging balance conditions (De Kegel et al., 2012).These measures quantify postural control abilities and sensory integration during static activity, but do not capture balance performance during daily activities. Thus, an understanding of daily balance performance is better represented by functional balance measures.

Motor skill performance including fine manual control, body coordination and balance can be determined using functional balance measures (Deitz et al., 2007). Some measures of functional balance can be used to indicate motor delay and are useful clinical assessments without the need for specialised equipment. Typically, these assessments are well tolerated and have shown to be sensitive to delay (Bruininks, 2005). However, functional balance tasks must be sufficiently difficult to identify vestibular impairment, as easier tasks may not rely on vestibular inputs (Cushing et al., 2008). Additionally, functional balance measures do not clearly delineate underlying mechanisms of motor performance and thus assessment of sensory processes used for balance control should be considered in children who are at risk of vestibular or motor impairments.

Vestibular assessment in children has become an area of interest for many researchers. Assessment of the semicircular canals involves measurement of the vestibulo-ocular reflex (VOR). Various methods of semicircular canal assessment including caloric, rotational chair and video head impulse testing have been performed in children, yet all have some degree of limitation. Caloric testing can be difficult to complete and is not well tolerated even when air calorics are chosen over water calorics (Cushing et al., 2008). Rotational chair is limited in providing localising information of the horizontal semicircular canal (HSCC) and is less sensitive to a unilateral deficit in a compensated state. Video head impulse testing (vHIT) uses goggles that are often a poor fit to paediatric patients and fit is critical for accurate assessment. In addition, they have been shown to be insensitive to some pathologies in the adult population (L. A. McGarvie et al., 2015). However the benefits of vHIT outweigh the liabilities as vHIT is quick, simple, well tolerated and can measure function for all SCC (Hamilton et al., 2015; Hülse et al., 2015), and have been shown to be sensitive in quantifying SCC dysfunction in children with SNHL(Janky & Givens, 2015).

Otolith function is commonly measured using vestibular evoked myogenic potentials (VEMP); cervical VEMP (cVEMP) measures saccule function, and ocular VEMP (oVEMP) measures utricle function, as well as the associated reflex pathways. VEMP are short latency potentials evoked by an auditory or vibratory stimulus and modulated by myogenic activity (Rosengren et al., 2019). A biphasic waveform is typically generated, with two latency measures and a peak-to-peak amplitude calculated to infer otolith function. VEMP assessments have been reported to be well tolerated in the paediatric setting, as both are relatively quick and non-invasive (Fuemmeler et al., 2020). VEMP have most commonly been explored in school aged children, however responses have been recorded in infants (Martens et al., 2022). For children with SNHL, VEMP measurements have either been absent (Cushing et al., 2013; Zhou et al., 2009) or in cases where they are present, have similar latencies but smaller inter-amplitudes, which can be indicative of dysfunction of the relevant structures assessed (Zhou et al., 2009). Typically, clinical assessment of the peripheral vestibular system is only considered for children when there are functional balance concerns, or complaints of dizziness or vertigo in children who are able to articulate this accurately.

While the literature has established children with SNHL and vestibular impairment can have delays in motor skill development or postural control differences, these constructs have typically been explored in isolation. Breaking down postural sway data into discrete frequency bands may provide further insight into understanding movement patterns and sensory system reliance that traditional postural control measures do not necessarily provide (Rhine et al., 2017). Furthermore, comprehensive assessment of peripheral vestibular structures, functional balance and postural control data may be useful adjuncts to inform rehabilitation approaches (Leen Maes et al., 2014). Elements of peripheral vestibular function, functional balance and postural control have been explored in children with SNHL, yet the relationship between these constructs has not been widely considered.

The aim of this study was to explore vestibular function, functional balance and postural control, and relationship between these measures in children with SNHL. It was hypothesised that children with SNHL would have differences in peripheral vestibular function, functional balance measures and postural control compared to children with normal sound detection thresholds. Furthermore, it was hypothesised that peripheral vestibular dysfunction would influence motor skill performance and postural stability.

## 7.3 Materials and Methods

***Participants***

Two groups of children, one group with sensorineural hearing loss (SNHL), and one group with normal sound detection (NSD), between 5 and 12 years of age were recruited via otolaryngologists, pediatricians, and audiologists in community based and private clinical settings in Melbourne, Australia. Guardians provided written consent and children provided verbal assent prior to assessment. All procedures were conducted according to the tenets of the Declaration of Helsinki, and ethical approval was obtained (17-1348H).

Twenty-two children were recruited into the study, n=11 in each group, with group demographics presented in Table 7.1 and hearing loss aetiologies for the SNHL group in Table 7.2. Children in each group were age matched within three months. Those with normal sound detection were characterized by a four-frequency pure tone hearing level average of ≤20dB, and no recent history of middle ear disease (< six months). Children in the SNHL group had a confirmed diagnosis of bilateral SNHL (characterized by a four-frequency pure tone hearing level average of >20dB), had at least 12 months device experience (hearing aids or cochlear implants), and no recent history of middle ear disease (<6 months). Ten participants had congenital SNHL, one acquired SNHL in infancy. All participants understood simple instructions and had no known neurodevelopmental diagnoses. Children with SNHL had optimized auditory devices at the time of assessment and wore their auditory devices for all assessments.

**Table 7.1.** Group demographics for children with normal sound detection and children with sensorineural hearing loss including anthropometric correlates, hearing levels, and proportion of normal peripheral vestibular structures (expressed as a percentage). Normal responses were defined by the following criteria: vHIT VOR gain values of ≥0.81 for HSCC, or ≥0.75 for ASCC/PSCC, present cVEMPs, or present oVEMPs.

| | | | | | | Audiometry | | vHIT | | | | | | cVEMP | | oVEMP | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | 4FA HL | | HSCC | | ASCC | | PSCC | | Saccule | | Utricle | |
| | N | M:F ratio | Mean Age (range) | Height (cm) (SD) | Weight (kg) (SD) | Left (SD) (Range) | Right (SD) (Range) | Left | Right | Left | Right | Left | Right | Left | Right | Left | Right |
| **NSD** | 11 | 7:4 | 8.8 (5.9-11.3) | 135.4 (12.7) | 33.7 (0.6) | 8.4 (5.2) (1.3-13.8) | 7.7 (4.7) (1.3-12.5) | 100% | 100% | 100%[a] | 100%[a] | 100%[a] | 100%[a] | 91% | 100% | 100% | 100% |
| **SNHL** | 11 | 9:2 | 8.8 (5.8-11.5) | 134.5 (16.0) | 32.8 (9.7) | 106.6 (25.0) (51.3-120) | 91.9 (35.7) (25-120) | 63% | 72% | 77%[b] | 55%[b] | 67% [b] | 67%[b] | 60%[a] | 60%[a] | 70%[a] | 70%[a] |

Abbreviations: NSD = normal sound detection; SNHL = sensorineural hearing loss; 4FAHL = Four frequency average hearing level; vHIT = video head impulse test; HSCC = horizontal semicircular canal; ASCC = anterior semicircular canal; PSCC = posterior semicircular canal; cVEMP = cervical vestibular evoked myogenic potentials; oVEMP = ocular vestibular evoked myogenic potentials

[a] denotes responses from 10 children

[b] denotes responses from 9 children

**Table 7.2.** Hearing loss aetiology, proportion of normal vestibular responses, and amplification type for children with sensorineural hearing loss. Normal responses were defined by the following criteria: vHIT VOR gain values of ≥0.81 for HSCC, or ≥0.75 for ASCC/PSCC, present cVEMPs, or present oVEMPs.

| **Participant** | **Aetiology** | **Amplification type** | **Proportion of normal SCC responses (/6)** | **Proportion of normal otolith responses (/4)** |
|---|---|---|---|---|
| **SN01** | Cytomegalovirus | Cochlear Implant | 2 | 0 |
| **SN02** | Enlarged Vestibular Aqueduct | Cochlear Implant | 5 | 4 |
| **SN03** | Ushers Type 1 | Cochlear Implant | 0 | 0 |
| **SN04** | Enlarged Vestibular Aqueduct | Hearing Aids | 6 | 4 |
| **SN05** | Connexin 26 | Bimodal | 6 | 4 |
| **SN06** | Connexin 26 | Hearing Aids | 6 | 4 |
| **SN07** | Enlarged Vestibular Aqueduct | Hearing Aids | 6 | 4 |
| **SN08** | Ushers Type 1 | Cochlear Implant | 0 | 0 |
| **SN09** | Connexin 26 | Cochlear Implant | 6 | 3 |
| **Sn10** | Meningitis | Bimodal | 6 | 3 |
| **SN11** | Branchio-Oto-Renal | Cochlear Implant | 0 | 0 |

### *Assessment*

All children underwent auditory, vestibular and functional balance assessment. Hearing and middle ear status was documented using pure tone audiometry and immittance testing. Vestibular assessments documented peripheral vestibular organ function via the vHIT and VEMP tests. Functional balance measures including the Bruininks-Oseretsky Test of Motor Proficiency (BOT) and static posturography provided an evaluation of body coordination and balance, as well as sensory system integration, involving assessment of standing (static) balance with modified environmental inputs.

### *Audiometry and immittance*

Pure tone audiometry was performed in a sound treated booth using an Interacoustics Affinity PC based audiometer (Interacoustics, Denmark). Behavioural thresholds were obtained at octave frequencies, and four-frequency pure tone averages (4FA) - calculated from 500Hz, 1kHz, 2kHz and 4kHz. Immittance testing using a GSI Tympstar (Grason-Stadler Instruments) included tympanometry and ipsilateral acoustic reflex assessment at 1kHz; tympanometry findings were classified according to Jerger's proposed guidelines (Jerger, 1970). Middle ear status was confirmed prior to advancing to vestibular assessments.

***Semicircular canal assessment***

Assessment of high frequency semicircular canal (SCC) function was performed using the GN Otometrics ICS impulse system (GN Otometrics, Taastrup, Denmark). Participants were required to visually fixate on a small static target, located approximately 1m distance at eye level, directly in front of them. Each coplanar SCC pair was assessed: lateral (left and right HSCC), left anterior/right posterior SCC (LARP) and right anterior/left posterior SCC (RALP). Head impulse magnitude ranged between 15-20 degrees, and head impulse peak velocities ranged between 150-250 degrees per second for the lateral condition, and 100-250 degrees per second for the vertical conditions. To minimise recording errors and artifacts, goggles were fit firmly to participants, calibration was performed in between each condition. All efforts were made to ensure there was no eyelid interference (for vertical conditions) and participants remained focused on the visual target thought testing (Mantokoudis et al., 2015). A minimum of ten head impulses were performed for each condition. The slow phase eye velocity of the eye movement was compared to the velocity of the head impulse to determine overall VOR gain and was processed and analysed using the GN Otometrics statistical software. Each trial was visually inspected by the examiner, and any artifacts caused by goggle slippage, blinking, or pupil tracking difficulties were manually removed (Mantokoudis et al., 2015). Head impulses that showed reduced VOR gain and clear, high amplitude corrective saccades were retained for analysis.

***Otolith assessment***

VEMPs were recorded using Bio-Logic AEP Version 7.0.0 software on the Natus Bio-Logic NavPro (Natus, Pleasanton, CA, USA). For cVEMP, a 500Hz tone burst stimulus of condensing polarity was presented monaurally at 113 dB SPL via air conduction (50-ohm ERA insert phones).

Four electrodes were placed on the participant: one common electrode at naison (Nz) on the lower forehead, one non-inverting electrode at the sternoclavicular junction, and two inverting electrodes placed on the belly of each sternocleidomastoid muscle (SCM). Participants lay semi-recumbent with their head and torso positioned approximately 20 degrees from supine. From this position, participants were instructed to lift their head towards their toes and hold this position until the stimulus stopped (Rosengren et al., 2019). Real time electromyographic (EMG) rectification was not possible due to device limitations but SCM contraction was visually monitored by the examiner for each trial, and post stimulus rectification was applied to waveforms. To minimise fatigue effects stimuli were presented alternately between ears, and breaks were provided between presentations. Conventional cVEMP labelling (p13, n23 latencies), and p13-n23 interamplitude were determined for all traces.

For oVEMP a 500Hz stimulus was presented at 128 dB pFL via bone conduction (B&K minishaker), with the minishaker placed at the midline of the upper forehead (Fz). Four electrodes were placed on the participant: one common electrode at the sternoclavicular junction, one non-inverting electrode on the chin, and two inverting electrodes placed on lower orbits of the eyes (left and right) and aligned with the centre of each pupil. Participants lay semi-recumbent and maintained an upward gaze of approximately 15 degrees for the stimulus duration. Conventional oVEMP labelling (baseline, n10, p16) and two interamplitude calculations (baseline to n10, and n10-p16) were determined for all traces. For both VEMP assessments, a minimum of two traces per condition were conducted in all to ensure repeatability. Responses were averaged and labels assigned to the average waveform which was then used for statistical analysis.

***Functional balance assessment***

Functional balance was measured using two subtests of the Bruininks Oseretsky Test of Motor Proficiency 2nd Edition (BOT-2) (Bruininks, 2005); bilateral coordination and balance. The standardised test battery was used according to BOT-2 guidelines (Bruininks, 2005); each task was taught to the child via physical demonstration, verbal instruction, or instructional pictures (via the BOT task easel). Bilateral coordination tasks included jumping in place and walking in a straight line; these were scored based on the number of responses correct. Balance tasks included standing on one leg and standing on a balance beam; these were scored based on the maximum duration the participant was able to maintain their balance for. For each task, a maximum of two trials were administered. Sex specific norms were used to determine scale scores, percentile ranks, and an overall composite body coordination score for each subtest.

***Postural control assessment***

The Nintendo Wii Balance Board (WBB) was used to perform computerised static posturography which has been validated against traditional force plate measures (Clark et al., 2010). The board was connected to a laptop via Bluetooth and data were recorded at the native frequency (≈40Hz) using customised software (LabVIEW Version 8.5, National Instruments, Austin Tx, USA). System calibration and data processing were conducted using established methods (Clark et al., 2010).

Centre of pressure (CoP) information was measured across four standing balance conditions: standing on a firm surface with eyes open (EO) and eyes closed (EC); and standing on a compliant (foam) surface with eyes open (FEO) and eyes closed (FEC). A 5cm high-density thermoplastic polyurethane cushion was placed over the WBB platform for compliant conditions (Vitkovic et al., 2016).

All participants were instructed to stand barefoot (feet 10cm apart) on the WBB and remain as still as possible with hands by their sides. For each condition (EO, EC, FEO, FEC), three 30 second trials were completed and the median score of the three trials were used for statistical analyses. Trials were discontinued if the participant lost balance, opened their eyes (for eyes closed conditions), or moved their arms; if this occurred the participant was given one additional trial for the same condition. Height and weight were used as covariates in statistical analyses.

CoP measures included path velocity (cm/s) and DWT analyses, which corresponded to very slow to fast moving components of the CoP data. The DWT frequency bands comprised of ultralow (<0.10Hz), very low (0.10 to 0.39Hz), low (0.39 to 1.56Hz), and moderate frequency bands (1.56 to 6.25Hz) and were extracted from the CoP data using the methods described elsewhere (Clark et al., 2018). These are thought to represent different physiological mechanisms: the visual system (ultralow) (Friedrich et al., 2008), the vestibular system (very low)(Oppenheim et al., 1999), cerebellar system (low) and somatosensory system (moderate) (Liang et al., 2014).These measures were analysed across all standing balance conditions for the anteroposterior plane.

***Statistical analysis***

Path velocity, DWT measures, BOT measures and VEMP latencies (p13, n23, n10, p16) were assumed to be normally distributed based on the Anderson Darling Test of Normality; VEMP amplitudes (p13-n23, Base-n10, n10-p16), and vHIT measures (HSCC, ASCC, PSCC) were observed to be not normally distributed.

Outcome measures included latencies and amplitudes (for VEMP), VOR gain (for vHIT), BOT percentile ranks, BOT Balance scale score, BOT bilateral coordination scale score and CoP data (path velocity, DWT analyses for ultralow, very low, low and moderate frequency bands). CoP analyses included height, weight and age as covariates. Group comparisons for each assumed normally distributed outcome measures and were performed using general linear modelling, and Mann Whitney U tests used for non-parametric data (vHIT gain and VEMP amplitudes). The significance level for post-hoc Tukey analyses was set at $p<0.05$. Regression and Pearson correlations were conducted to explore the relationship between clinical vestibular assessments, functional balance, and postural sway measures across all children.

## 7.4 Results

All children completed postural control and peripheral vestibular function assessments. Three children (one with normal sound detection, two with SNHL) underwent vHIT for the lateral condition only due to reluctance with completing LARP/RALP conditions. One child with SNHL did not complete VEMP testing due to assessment contraindications.

***Peripheral vestibular function between groups***

Interpretation of peripheral vestibular function was dependent on the presence or absence of responses for each assessment. For vHIT, all children had measurable responses and thus, all comparisons were included in analysis. Based on normative data obtained from the control group (cut off values for normal VOR gain were based on two standard deviations from the normal sound detection group mean, equating to <0.81 for HSCC, and <0.75 for ASCC/PSCC), five children with SNHL had reduced VOR gain for one or more SCC (19/58, 33%). All impulses with reduced VOR gain were associated with corrective saccades. A proportion of children with SNHL had absent VEMPs which meant that their findings were removed from comparative analyses. Table 7.1 outlines the proportion of normal vestibular responses between the groups for each vestibular assessment, and Table 7.2 outlines individual findings for children with SNHL.

Children with SNHL (who had recordable VORs) showed overall lower gain values in all vHIT conditions (Table 7.3). Large variability for the SNHL group was observed with some children demonstrating significantly reduced VOR gain, while others showed clinically normal VOR gain. When absent VEMP responses were excluded from analyses, cVEMP latencies, amplitudes and oVEMP latencies, amplitudes were similar between groups (Table 7.3).

**Table 7.3.** Group comparisons for all measures of peripheral vestibular function (vHIT**,** cVEMP, and oVEMP).

| | | SNHL | | | NSD | | | |
|---|---|---|---|---|---|---|---|---|
| | | N | Median (IQR) | Range | N | Median (IQR) | Range | Adj P |
| vHIT VOR gain | HSCC | 22 | 0.87 (0.59) | 0.14-1.10 | 22 | 0.94 (0.11) | 0.87-1.11 | **.035** |
| | PSCC | 18 | 0.86 (0.63) | 0.11-1.01 | 20 | 0.90 (0.14) | 0.80-1.13 | **.048** |
| | ASCC | 18 | 0.84 (0.23) | 0.16-1.06 | 20 | 0.96 (0.12) | 0.76-1.05 | **.013** |
| **cVEMP** | | | **Mean (SD)** | **Range** | | **Mean (SD)** | **Range** | **Adj P** |
| **Latencies (ms)** | **p13** | 12 | 14.20 (0.89) | 13.11-16.13 | 21 | 13.40 (1.36) | 10.44-15.75 | .080 |
| | **n23** | | 20.28 (1.12) | 17.48- 21.96 | | 19.46 (1.42) | 17.2-22.10 | .101 |
| **oVEMP** | | | **Mean (SD)** | **Range** | | **Mean (SD)** | **Range** | **Adj P** |
| **Latencies (ms)** | **n10** | 14 | 10.13 (0.65) | 9.05-11.37 | 22 | 10.30 (1.21) | 7.38-12.07 | .634 |
| | **p16** | | 13.31 (1.23) | 10.51-15.40 | | 13.09 (1.27) | 10.82-15.5 | .607 |
| **cVEMP** | | | **Median (IQR)** | **Range** | | **Median (IQR)** | **Range** | **Adj P** |
| **Amplitude (µV)** | **p13-n23** | 12 | 10.02 (12.86) | 4.07-29.82 | 21 | 13.29 (8.83) | 5.39-49.2 | .359 |
| **oVEMP** | | | **Median (IQR)** | **Range** | | **Median (IQR)** | **Range** | **Adj P** |
| **Amplitude (µV)** | **base-n10** | 14 | 9.5 (6.03) | 4.50-16.45 | 22 | 6.81 (3.51) | 3.62-31.71 | .263 |
| | **n10-p16** | | 16.74 (20.68) | 3.00-32.48 | | 9.62 (4.72) | 3.53-41.19 | .485 |

Significant values in bold ($p < 0.05$). Abbreviations: SNHL = sensorineural hearing loss; NSD = normal sound detection; vHIT = video head impulse test; HSCC = horizontal semicircular canal; PSCC = posterior semicircular canal; ASCC = anterior semicircular canal; cVEMP = cervical vestibular evoked myogenic potentials; oVEMP = ocular vestibular evoked myogenic potentials.

***Postural stability and functional balance between groups***

Decreased postural stability was observed in children with SNHL for conditions requiring greater reliance on the vestibular system, as illustrated by Figure 7.1. Faster path velocities indicative of decreased postural stability was observed for children with SNHL when on compliant surfaces (FEO: NSD mean [SD] = 2.40 [0.60] vs. SNHL mean [SD] = 3.84 [2.16], p=0.046; FEC: NSD mean [SD] = 4.34 [1.22] vs. SNHL mean [SD] = 6.41 [2.84], p=0.038). Path velocity was similar between groups when standing on a firm surface (EO: NSD mean [SD] = 1.59 [0.55] vs. SNHL mean [SD] = 2.35 [1.36], p=0.100; EC: NSD mean [SD] = 1.92 [0.49] vs. SNHL mean [SD] = 2.78 [1.54], p=0.108).

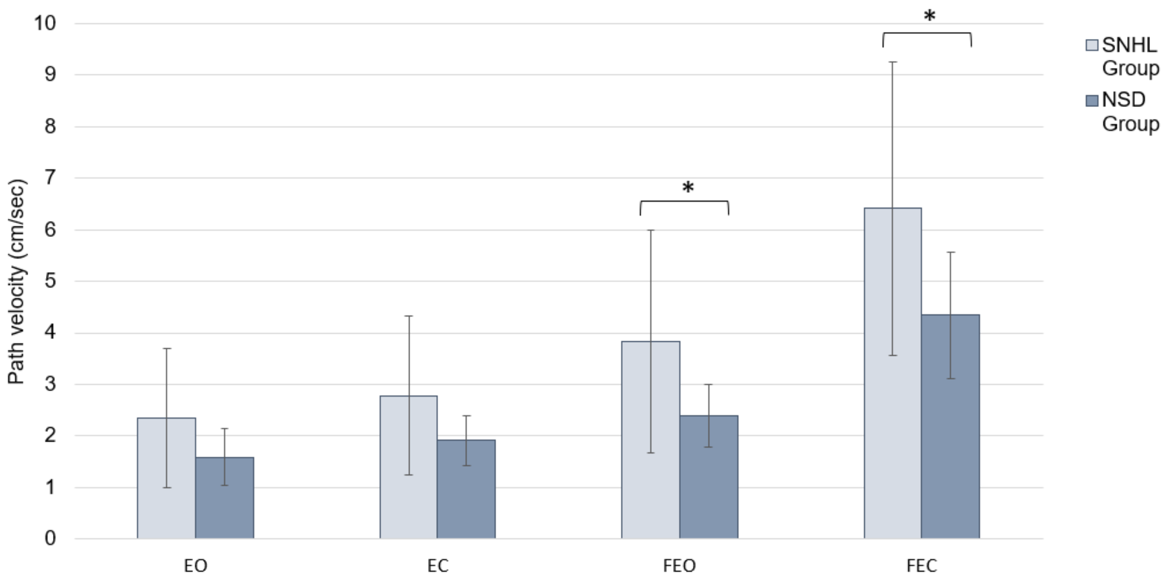



**Figure 7.1.** Mean path velocity across the four standing conditions for children with normal sound detection and children with sensorineural hearing loss. Children with sensorineural hearing loss showed reduced postural stability, as indicated by increased path velocities, in conditions where somatosensory information was modified (FEO, FEC conditions). Additionally, large variability in standing balance was observed in children with SNHL across all conditions when compared to children with normal sound detection. *denotes $p<0.05$

When the postural sway data were broken down into discrete frequency bands, different patterns of postural sway emerged between the groups. For the frequency band thought to correlate to vestibular information (DWT very low), children with SNHL showed overall greater sway across some standing conditions (EO: $p=0.030$; EC: $p=0.050$; FEO: $p=0.040$; FEC: $p=0.267$; Table 7.5). Greater postural sway was also noted in compliant surface conditions (FEO, FEC) across frequency bands thought to be correlated with cerebellar (FEO: $p=0.040$; FEC: $p=0.031$) and somatosensory (FEO: $p=0.033$, FEC: $p=0.038$) information (Table 7.4) for children with SNHL.

**Table 7.4.** Group comparisons for DWT path velocity across frequency bands for all standing balance conditions

| | Standing balance condition | EO | | | | EC | | | | FEO | | | | FEC | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | **SNHL Mean (SD)** | **NSD Mean (SD)** | **ES** | **Adj P** | **SNHL Mean (SD)** | **NSD Mean (SD)** | **ES** | **Adj P** | **SNHL Mean (SD)** | **NSD Mean (SD)** | **ES** | **Adj P** | **SNHL Mean (SD)** | **NSD Mean (SD)** | **ES** | **Adj P** |
| **DWT path velocity (cm/sec)** | **Ultralow** | 0.11 (0.06) | 0.09 (0.04) | 0.56 | .204 | 0.10 (0.03) | 0.10 (0.04) | 0.09 | .827 | 0.13 (0.06) | 0.11 (0.05) | 0.40 | .374 | 0.16 (0.06) | 0.13 (0.04) | 0.71 | .110 |
| | **Very Low** | 0.47 (0.25) | 0.28 (0.09) | 1.00 | **.030** | 0.56 (0.27) | 0.38 (0.09) | 0.89 | .050 | 0.78 (0.42) | 0.46 (0.16) | 0.94 | **.040** | 1.20 (0.76) | 0.90 (0.33) | 0.51 | .267 |
| | **Low** | 1.05 (0.70) | 0.74 (0.25) | 0.60 | .174 | 1.28 (0.79) | 1.12 (0.43) | 0.26 | .545 | 1.87 (1.06) | 1.14 (0.31) | 0.94 | **.040** | 3.21 (1.17) | 2.24 (0.74) | 0.99 | **.031** |
| | **Moderate** | 1.04 (0.59) | 0.74 (0.26) | 0.67 | .135 | 1.30 (0.76) | 0.92 (0.25) | 0.67 | .150 | 1.82 (1.06) | 1.06 (0.29) | 0.98 | **.033** | 3.19 (1.32) | 2.18 (0.76) | 0.94 | **.038** |

Significant values in bold ($p < .05$). Abbreviations: DWT = discrete wavelet transform; cm/sec = centimetres per second; EO = eyes open, EC = eyes closed, FEO = foam eyes open, FEC = foam eyes closed; SNHL = sensorineural hearing loss; NSD = normal sound detection; ES = effect size (calculated using Hedges g); Adj P = adjusted p value (Tukey post hoc analysis).

***Relationship between vestibular function, functional balance and postural control***

The degree of vestibular loss was categorised based on the number of abnormal responses observed for each vestibular structure (utricle, saccule, HSCC, ASCC, PSCC) in both ears (Janky & Givens, 2015). A score of 0 indicated abnormal function of all peripheral vestibular structures, and score 10 indicated normal function of all peripheral vestibular structures.

A significant relationship between the degree of peripheral vestibular function and BOT was observed, with a larger number of abnormal peripheral vestibular structures associated with lower percentile ranks, bilateral coordination and balance scale scores (Table 7.5). Peripheral vestibular dysfunction also predicted performance when standing on a compliant surface with eyes open (FEO) and closed (FEC); those with larger postural sway had greater degrees of peripheral vestibular dysfunction. When eyes were open, peripheral vestibular function predicted DWT performance relating to ultralow, very low and low frequency bands. Those with greater postural sway in these frequency bands had reduced peripheral vestibular function, with a stronger negative correlation noted for more complex standing balance conditions (FEO).

Functional balance and path velocity measures were negatively correlated indicating that children with lower functional balance measures had larger path velocity scores which is overall consistent with reduced postural stability. Lower percentile ranks were significantly associated with larger path velocity measures for all conditions except for when standing with eyes closed on a firm surface (EO path velocity: r(22) = -0.454, $p$=0.034; EC path velocity: r(22) = -0.329, $p$=0.145; FEO path velocity: r(22) = -0.692, $p$<0.001; FEC path velocity: r(22) = -0.661, $p$<0.001). This pattern also extended to balance scale scores (EO path velocity: r(22) = -0.478, $p$=0.024; EC path velocity: r(22) = -0.338, $p$=0.134; FEO path velocity: r(22) = -0.704, $p$<0.001; FEC path velocity: r(22) = -0.655, $p$=0.001), yet bilateral coordination scale scores were only significantly correlated with more complex standing balance conditions (EO path velocity: r(22) = -0.270, $p$=0.225; EC path velocity: r(22) = -0.206, $p$=0.371; FEO path velocity: r(22) = -0.492, $p$=0.020; FEC path velocity: r(22) = -0.508, $p$=0.016).

**Table 7.5.** Relationship between standing balance measures and degree of vestibular loss, calculated based on the number of normal responses from each vestibular organ.

| ***Outcome measure*** | **$R^2$** | **F-value** | **p** | **Coefficient Degree of vestibular loss** |
|---|---|---|---|---|
| ***BOT-2*** | | | | |
| Percentile Rank | 0.424 | 14.69 | **.001*** | 4.50 |
| Balance Scale Score | 0.439 | 15.66 | **.001*** | .747 |
| Bilateral Coordination Scale Score | 0.326 | 9.66 | **.006*** | .438 |
| ***Path velocity*** | | | | |
| Eyes open: firm surface (EO) | 0.018 | 0.36 | .557 | -.039 |
| Eyes closed: firm surface (EC) | 0.007 | 0.14 | .714 | -.028 |
| Foam eyes open: compliant surface (FEO) | 0.223 | 5.74 | **.027*** | -.219 |
| Foam eyes closed: compliant surface (FEC) | 0.140 | 4.42 | **.048*** | -.274 |
| ***DWT path velocity*** | | | | |
| EO: DWT moderate | 0.028 | 0.56 | .461 | -.021 |
| EO: DWT low | 0.007 | 0.14 | .711 | -.012 |
| EO: DWT very low | 0.181 | 4.41 | **.049*** | -.023 |
| EO: DWT ultra-low | 0.230 | 5.97 | **.024*** | -.006 |
| EC: DWT moderate | 0.008 | 0.16 | .696 | -.014 |
| EC: DWT low | 0.008 | 0.16 | .698 | .015 |
| EC: DWT very low | 0.069 | 1.47 | .239 | -.015 |
| EC: DWT ultra-low | 0.037 | 0.77 | .391 | -.001 |
| FEO: DWT moderate | 0.147 | 3.28 | .086 | -.085 |
| FEO: DWT low | 0.294 | 8.31 | **.009*** | -.124 |
| FEO: DWT very low | 0.358 | 11.16 | **.003*** | -.055 |
| FEO: DWT ultra-low | 0.080 | 1.75 | .201 | -.004 |
| FEC: DWT moderate | 0.142 | 3.30 | .084 | -.119 |
| FEC: DWT low | 0.166 | 3.99 | .060 | -.118 |
| FEC: DWT very low | 0.117 | 2.51 | .129 | -.055 |
| FEC: DWT ultra-low | 0.006 | 0.11 | .743 | -.001 |

Significant values in bold (p<.05). Abbreviations: BOT-2 = Bruininks-Oseretsky Test of Motor Proficiency; DWT = discrete wavelet transform

## 7.5 Discussion

The aim of this study was to explore peripheral vestibular function and postural control in children with SNHL. As such, it is one of few studies to explore the relationship between functional balance, postural control and comprehensive peripheral vestibular function in this population. Most studies in this area have focused on functional balance measures coupled with one to two measures of peripheral vestibular function(Singh et al., 2022). Children with SNHL in this study had varying degrees of peripheral vestibular dysfunction, with reduced vestibular function consequently influencing postural control and functional balance ability. There was a significant relationship between peripheral vestibular function and functional balance measures, which has implications for daily activities. Measures of postural control reveal that postural control strategies are different for greater degrees of vestibular loss. This is relevant because these different strategies are used where eyes are open, akin to general daily activity. These findings highlight the importance of routinely performing a range of clinical assessments to measure balance function for all children with SNHL, to understand the likely implications for balance performance and to consider potential remediations.

When considering all peripheral vestibular organs, peripheral vestibular function was significantly different between groups, with large variability in peripheral deficit for children with SNHL. This variability is due to the range of aetiologies, only some of which have known association with vestibular impairment (including Usher syndrome and cytomegalovirus) (Cushing et al., 2013; Martens et al., 2022). Some children with SNHL had partial or complete dysfunction of peripheral vestibular structures, whereas others had similar peripheral vestibular function to children with normal sound detection.

Interpretation of clinical vestibular assessments varied according to presence or absence of vestibular function. Previous cut offs for vHIT in children included a fixed value to determine abnormal function (Hamilton et al., 2015) or values which differed depending on the plane assessed (Janky & Givens, 2015). Using the normative VOR range based on children with normal sound detection in this study, children with SNHL showed a large range of variability in SCC function. Children with SNHL and absent saccule function were excluded from the statistical comparison; yet those with saccule function had similar

VEMP latencies and amplitudes to children with normal sound detection, in agreement with other findings (L. Maes et al., 2014).

There is no clear consensus in the literature regarding the degree and extent of vestibular dysfunction impacted with SNHL. Few studies have looked at function of all vestibular organs; the current study showed similar proportions of SCC and otolith abnormalities consistent with other studies that have assessed all vestibular structures (Janky & Givens, 2015). The overall incidence of abnormal vestibular responses was lower in the current study; 30-40% of vestibular function tests were abnormal in children with SNHL compared to 45-55% (Cushing et al., 2008; Janky & Givens, 2015; Leen Maes et al., 2014), although this estimate can be far greater, up to 90% depending on the vestibular organ assessed (Zhou et al., 2009). This difference may also relate to the types of aetiologies and likelihood of associated structural abnormalities.

Overall peripheral vestibular function predicted performance on functional balance measures, with greater degrees of vestibular impairment related to poorer balance. This indicates that functional balance and motor performance are directly influenced by vestibular contributions and this is supported in studies with younger and older children previously published (De Kegel et al., 2012; Janky & Givens, 2015).

Greater degrees of vestibular impairment correlated with more postural sway, most evident for conditions requiring complex sensory system integration, when standing on a compliant surface with eyes open and closed. This has been reported in other studies where differences in balance performance for people with vestibular impairment occur when conditions become more difficult (Cushing et al., 2008; Enbom et al., 1991). Different patterns emerged when postural sway was broken down into discrete frequency bands. When somatosensory information was modified (standing on a compliant surface with eyes open and closed), movement patterns of CoP data showed greater postural sway for frequency bands corresponding to cerebellar and somatosensory information. Significantly more postural sway was also noted in the frequency band corresponding to vestibular information in eyes open conditions (eyes open on firm, and compliant surfaces). This suggests that overall, children with SNHL may be utilising sensory processes effectively, but in cases where peripheral vestibular function is compromised, incoming sensory information from the vestibular system compromises postural control, resulting in greater reliance on somatosensory information. Furthermore, this pattern of responses might be related to the integrative processes required for postural control: this may be related to a motor delay, as motor delays have been widely documented in children with SNHL (De Kegel et al., 2012; Leen Maes et al., 2014), or related to the integration of incoming sensory information, which may take longer due to the compensatory strategies (adaptive or substitution) occurring to maintain balance. Specifically, there is evidence to suggest that younger children place greater reliance on visual information for postural control, and the sensory system re-weighting adjusts in later childhood to be more reliant on somatosensory and vestibular information before reaching adult form (Schmid et al., 2005).

Postural stability measures were performed in conditions whilst standing stationary. Maintaining postural stability when still should be easier than during dynamic movement as less task demands on the sensory systems are required (Hatzitaki et al., 2002). For children with vestibular impairment, postural control challenges may be amplified for scenarios in daily life where dynamic movement is required, which can have a negative impact on physical activity, general mobility and also causing greater falls risk. Moderate to strong correlations were observed between functional balance and postural stability, indicating that those with larger postural sway had decreases in functional balance. Therefore, in the absence of computerised postural stability measures, functional balance measures may serve as an alternative assessment method in the clinical environment.

While not explicitly considered as a factor in the statistical analyses, most children with SNHL in this study had undergone some form of physical therapy in their preschool years to address motor milestone delays, and regularly participated in sporting activities. Despite physical therapy these group deficits remain, highlighting that potentially children with vestibular impairment will be at greater risk of motor delay or falls in future. Cross sectional comparisons from this study have demonstrated differences in various aspects of balance performance. Yet longitudinal comparisons may unveil greater differences, with evidence to suggest that motor delay can progress for children with vestibular impairment, particularly if they do not undergo vestibular rehabilitation (Rine et al., 2004; Rine et al., 2000).

It is known that different aetiologies of hearing loss can present with varying degrees of peripheral vestibular function (Cushing et al., 2013). We grouped all aetiologies and degrees of hearing loss into one due to small sample size and as a result this study does not allow statistical comparisons. However, it was observed that for certain conditions (Usher Type I, Cytomegalovirus and Branchio-Oto-Renal), children had vestibular impairment of most or all peripheral vestibular structures which has been noted in other studies (Cushing et al., 2013; Verbecque et al., 2017). Additionally, a large proportion of children in this study had at least one cochlear implant. Cochlear implantation has the potential to damage peripheral vestibular structures with an estimated impact of approximately 10% (Jacot et al., 2009), however recent studies suggest this incidence is far lower (Dhondt et al., 2022). True impacts of cochlear implantation on peripheral vestibular function remain unknown without baseline assessment. Furthermore, age differences for cochlear implantation may contribute to the degree or progression of vestibular deficit, and the time taken to centrally compensate. Age of cochlear implantation may also influence central compensatory processes, auditory mapping and sensory integration. While balance performance could potentially be influenced by the amount of auditory input provided by devices in individuals with vestibular impairment (Vitkovic et al., 2016), all children with SNHL in this study had optimised hearing devices worn throughout assessment.

The implications of vestibular impairment can extend beyond balance performance. Depending on the age on the individual, a range of functional implications may be evident, from motor milestone delays in children with congenital vestibular impairment, to activity limitations during sport or other recreational activities. For children with vestibular impairment, there is a body of literature that supports vestibular rehabilitation, including exercises to improve gaze stability, postural control and motor performance (Melo et al., 2019). The vestibular rehabilitation approach is largely dependent on the type and severity of the vestibular impairment but may include adaptation/habituation strategies focusing on central mechanisms, or substitution strategies focusing on increasing reliance of other sensory mechanisms such as vision or somatosensation. Thus, comprehensive vestibular assessment should be considered as a complementary assessment for children with balance difficulties to refine vestibular rehabilitation approaches.

Fundamental motor milestones are achieved by early childhood, but functional balance deficits can remain if underlying mechanisms for balance control are not investigated thoroughly. While some studies have explored these mechanisms in younger age groups (De Kegel et al., 2012) the feasibility of reliable vestibular testing in children <5 years can be challenging, and require specific test protocols, but is important to address the critical need for these assessments to be performed in a timely manner to complement rehabilitation (Martens et al., 2022). Furthermore, future research should aim to document the developmental trajectory and longitudinal changes that peripheral vestibular dysfunction has on motor performance and determine whether deficits remain in adolescence and adulthood. While this has been documented in adolescents and cross-sectionally (Melo Rde et al., 2015), it is not known how balance performances changes over time in the individual.

## 7.6 Conclusion

Outcomes from this study demonstrate that some children with SNHL can have reduced vestibular function and decreased postural stability, which in turn, can negatively impact functional balance. Furthermore, postural control findings for children with vestibular impairment suggest that strategies to maintain balance in more complex environments may be related to a delay of available sensory integration mechanisms. For any child diagnosed with SNHL, vestibular function and functional balance assessment are imperative to identify vestibular deficit and better understand the functional consequences on motor performance so that appropriate mitigating strategies can be implemented.

# Chapter 8: VESTIBULAR FUNCTION AND BALANCE PERFORMANCE IN CHILDREN WITH AUTISM

This chapter presents the findings of a study exploring postural control and vestibular function in children between 5 and 12 years of age with autism. The manuscript presented includes journal specific headings and is planned for submission to Autism Research.

## 8.1 Abstract


**Background**: Postural control deficits have been documented in children with autism, yet vestibular system contributions to postural control have not been widely considered.

**Objective:** The purpose of this study is to explore the relationship between functional balance, postural sway and vestibular function in children with autism.

**Methods:** Ten children with a confirmed diagnosis of autism and ten age-matched children with no known neurodevelopmental or motor delays participated. Bruininks-Oseretsky Test of Motor Proficiency and the Paediatric Balance Scale measured functional balance. Static posturography measured postural sway with modified sensory inputs. Tests of vestibular function included cervical vestibular evoked myogenic potentials and video head impulse testing.

**Results:** With visual cues removed, children with autism demonstrated reduced postural stability and different patterns of postural sway. Functional balance correlated with postural sway for conditions with modified sensory information. Peripheral vestibular function was similar between groups. Functional balance was not correlated with vestibular function.

**Conclusions:** Despite normal vestibular function, postural control differences in children with autism remain, particularly when sensory information is modified. Postural sway patterns suggest sensory system integration is less developed in children with autism. Findings highlight the importance of utilizing a range of clinical tools to quantify balance ability.


## 8.2 Introduction

Autism spectrum disorder is a neurodevelopmental condition with an estimated prevalence of 1 in 40 (Maenner et al., 2020; Randall et al., 2016; Xu et al., 2018), characterised by impairments in communication, social reciprocity and repetitive behaviours (Association, 2013). Differences in motor behaviour have also been documented in autistic children (Green et al., 2009) including postural stability deficits (Fournier, Kimberg, et al., 2010), gross motor skill delays (Mache & Todd, 2016), and functional balance abnormalities.

For children with autism, evidence suggests that underconnectivity between central mechanisms of the cerebellum or general neural circuitry affect postural control (Minshew et al., 2004). This is particularly evident for more complex motor tasks or when sensory information is modified (Minshew et al., 2004). Yet the precise mechanisms of postural stability deficits in children with autism remain unclear.

Functional balance measures typically provide an indication of motor skills including fine manual control, body coordination and balance (Deitz et al., 2007). Static posturography is one way of assessing postural control; a force plate is used to measure the postural sway of an individual over a specified time period. Additionally, static posturography can reflect sensory system contributions (visual, somatosensory, vestibular) and predominance in various sensory conditions (Mache & Todd, 2016; Stins et al., 2015; Travers et al., 2013). For people with autism, postural sway is more pronounced when sensory information is modified via methods such as standing on foam or closing eyes, (Mache & Todd, 2016; Stins et al., 2015; Travers et al., 2013). Some authors have noted deficits across all sensory conditions (Fournier, Kimberg, et al., 2010; Minshew et al., 2004), whereas others have only found deficits in more challenging sensory environments (Doumas et al., 2016; Molloy et al., 2003). Furthermore, these attributes have largely been explored in adults and are yet to be thoroughly explored in children. Evaluating postural control in children is complicated by the fact that individual sensory system contributions to postural control varies across childhood (Sinno et al., 2021).

Postural sway has typically been measured using center of pressure (CoP) measurements including path length, path velocity, and area. However, breaking down CoP measurements into discrete frequency bands based on the speed of postural sway (known as discrete wavelet transform [DWT]) analyses, can provide a more detailed representation of the movement and include an indicator of relative physiological contributions to postural control (Chagdes et al., 2009; Micarelli et al., 2020). It is thought that certain frequency components of the CoP data represent different sensory mechanisms: somatosensory (0.5-1.0Hz), vestibular (0.1-0.5Hz), and vision (<0.1Hz) (Chagdes et al., 2009; Oppenheim et al., 1999). DWT analyses provide additional information compared to regular CoP data in clinical groups including adults with Parkinson's Disease (Holmes et al., 2013) or chronic neck pain (Quek et al., 2014), as well as children with mild traumatic brain injury (Rhine et al., 2017). Typically developing children have also shown larger DWT responses compared to adults (Micarelli et al., 2020).

Vestibular function is fundamental to balance, and in children, peripheral vestibular assessment serves an important role in understanding the mechanisms of motor delay and management of balance difficulties. A range of clinical vestibular assessment tools can be used to quantify vestibular function in children, including assessment of the semicircular canals (SCC) (Abdullah et al., 2017; Hamilton et al., 2015) and otolith organs: the utricle and saccule (Kelsch et al., 2006; L. Maes et al., 2014; Young, 2015; Zhou et al., 2014). Additionally, the role of vestibular function in standing balance relies on central processing mechanisms to assist with providing appropriate motor outputs. Though studies have demonstrated that children with autism have deficits in motor skill development, and that this relates to postural control (Mache & Todd, 2016), the relationship between vestibular function in children with autism and postural control has not been directly evaluated. Furthermore, understanding movement patterns by exploring discrete frequency bands has not been considered in children with autism and may provide further insight into the physiologic mechanisms underpinning movement patterns during standing balance. These assessments may provide a more cohesive overview of balance ability in children with autism and may be useful to consider in the context of diagnosis and management of motor behaviour deficits.

The primary aim of this study was to explore vestibular function and postural control in children with autism. We hypothesised that clinical assessments of vestibular function would be similar between children with and without autism, yet postural sway would be larger for children with autism across conditions where sensory information is modified. Furthermore, we hypothesised that a relationship exists between motor skills and postural sway measures including path velocity and the fast-moving component of the CoP trace.

## 8.3 Methods

***Participants***

Twenty children between 5 and 12 years of age were recruited via paediatricians, speech pathologists and audiologists in clinical settings across Melbourne, Australia. Ethical approval was granted (approval number 17-1348H) and procedures were conducted according to the tenets of the Declaration of Helsinki. Guardians provided written consent and verbal assent was obtained from each child.

Children were age matched within three months and met the following criteria: children in the autism group (n=10) had a confirmed diagnosis of autism spectrum disorder according to DSM-V guidelines (Association, 2013); children in the comparison group (n=10) had no known neurodevelopmental or motor delays. Participants required normal sound detection thresholds and middle ear function at the time of assessment, as both factors can influence peripheral vestibular results (Welgampola & Colebatch, 2005; Zhou et al., 2009). All participants understood simple instructions.

***Audiometry and immittance***

Behavioural thresholds for pure tone audiometry were established at octave frequencies between 250Hz and 8kHz. Tympanometry and ipsilateral acoustic reflex assessment determined middle ear status(Jerger, 1970).

***Semicircular canal assessment***

The video head impulse (vHIT) was performed to assess high frequency semicircular canal (SCC) function. Overall VOR gain was determined by comparing slow phase eye velocity to the head impulse velocity. Task administration was based on standard clinical procedures (L. McGarvie et al., 2015). A minimum of ten head impulses were performed for each condition involving each coplanar SCC pair: lateral, left anterior/right posterior SCC (LARP) and right anterior/left posterior SCC (RALP). Head impulse magnitude ranged between 15-20 degrees from centre, and head impulse peak velocity ranged from 150-250 degrees/sec. Data were processed and analysed using GN Otometrics statistical software. Each trial was visually inspected by an experienced audiologist and any artefacts caused by goggle slippage or pupil tracking difficulties were manually removed prior to analysis.

***Otolith assessment***

Cervical VEMP (cVEMP) was performed using the Natus Bio-logic Navigator Pro (Natus, Pleasanton, CA, USA). A 500Hz tone burst of condensing polarity (with a linear ramp of equal rise, fall and plateau of 1ms), was presented at 113 dB SPL. Acoustic stimuli were delivered via air conduction using 50-ohm ERA-3 insert phones (Etymotic Research, Elk Grove Village, IL, USA) at a stimulus rate 5.1Hz. Electrophysiological responses were recorded using a four electrode-montage setup: a common electrode placed at Nz, non-inverting electrode placed at the sternoclavicular junction, and two inverting electrodes placed on the belly of each sternocleidomastoid muscle. Responses were elicited using the elevation method of bilateral SCM contraction (Papathanasiou et al., 2014); participants lay semi-recumbent and were instructed to lift their head and look towards their toes when they heard the stimuli. EMG rectification was not available during assessment due to system limitations, but post stimulus rectification was applied to the waveforms. Stimuli were presented alternately between ears to minimise fatigue effects on responses, and two traces per condition were conducted to ensure repeatability. Established labelling conventions were used to mark cVEMP latencies (p13, n23) (Papathanasiou et al., 2014; Rosengren et al., 2019) and response amplitudes (p13-n23) calculated.

***Functional balance***

Two subtests from the Bruininks Oseretsky Test of Motor Proficiency 2$^{nd}$ Edition (BOT-2) (Bruininks, 2005), bilateral coordination and balance, were administered to all participants. Standard scores and percentile ranks were determined using sex-specific norms, and an overall composite body coordination score was calculated. The Pediatric Balance Scale (PBS), a supplementary assessment used to quantify motor performance (Franjoine et al., 2010) included fourteen motor tasks subjectively rated by the examiner.

***Standing balance***

Computerised static posturography was conducted using the Nintendo Wii Balance Board (WBB), connected via Bluetooth to a laptop with customised software to enable data recording at the native frequency (≈40Hz) (LabVIEW Version 8.5, National Instruments, Austin Tx, USA). Calibration and data processing were conducted according to established protocols (Clark et al., 2010; Lorefice et al., 2015).

Postural sway was objectively measured using centre of pressure (CoP) information in four sensory conditions: standing with eyes open on a firm surface (EO), eyes closed on a firm surface (EC), eyes open on a foam surface (FEO), and eyes closed on a foam surface (FEC). For two conditions, a 5cm foam cushion fit completely over the platform.

The assessment was conducted barefoot, and a practice trial was performed to ensure task understanding. For each condition, three x 30-second trials were completed and the median score of the three trials used for statistical analyses. Height and weight characteristics were obtained following postural sway assessment.

Centre of pressure (CoP) measures included path velocity (cm/s) and DWT analyses, where the CoP trace is broken down into discrete frequency bands. The frequency bands correspond to ranges from very slow moving to fast moving components of the CoP data and included ultralow (<0.10Hz), very low (0.10-0.39Hz), low (0.39-1.56Hz), and moderate frequency bands (1.56-6.25Hz) using the methods described (Clark et al., 2018). Centre of pressure was analysed across the four standing conditions in the anteroposterior plane, given the task was conducted for bipedal stance. The Romberg quotient was also calculated (EC/EO), with a score >1 indicating larger sway with eyes closed (Rhine et al., 2017).

***Statistical analysis***

All data except for the PBS were normally distributed based on statistical analysis. Outcome measures included latencies and amplitudes (for VEMP), VOR gain (for vHIT), BOT-2 percentile ranks, BOT-2 Balance scale score, BOT-2 body coordination scale core, PBS overall score, and CoP data (path velocity, DWT analyses for frequency bands). Comparisons for each normally distributed outcome measure were performed using general linear modelling and independent t-tests. Mann Whitney U was used to compare PBS data. Participant height and weight were considered as covariates for CoP analyses. Post-hoc Tukey analyses was set at a significance level of $p<0.05$. Effect sizes were calculated using Hedges's $g$ (Lakens, 2013). Pairwise Pearson correlations explored the relationship between vestibular, functional balance, and postural sway measures across all children.

# 8.4 Results

All children completed standing balance and peripheral vestibular function assessments. One child from the autism group did not complete the PBS and body coordination subtest of BOT-2. Left and right responses for tests of peripheral vestibular function were not significantly different and therefore averaged for statistical analysis. Group demographics are presented in Tables 8.1 and 8.2.

**Table 8.1.** Group demographics for children with and without autism.

| Group | N | Male: Female ratio | Mean Age (years) | Height (cm) | Weight (kg) | Audiometry<br>4FAHL Left (dB HL) | <br>4FAHL Right (dB HL) |
|---|---|---|---|---|---|---|---|
| **Autism Group** | 10 | 7:3 | 7.62 (5.42-9.92) | 132.20 (13.89) | 31.86 (6.51) | 11.25 (2.82) | 10.75 (2.37) |
| **Comparison Group** | 10 | 6:4 | 7.77 (5.92-9.92) | 130.45 (10.11) | 30.08 (11.6) | 6.38 (5.91) | 8.25 (1.55) |

Abbreviations: 4FAHL = four frequency hearing level average across 500Hz, 1kHz, 2kHz and 4kHz; dB HL = decibels hearing level.

**Table 8.2.** Participant demographics for assessments used in autism diagnosis.

| Participant | Gender | Age at assessment (years) | Assessments used in autism diagnosis |
|---|---|---|---|
| **1** | F | 5.42 | DSM-V, CELF-P, WPPSI-IV |
| **2** | M | 9.33 | DSM-V, WISC-V, CELF-4 |
| **3** | F | 7.50 | DSM-V, WISC-V, CELF-5 |
| **4** | M | 6.92 | DSM-V, WPPSI-IV, CELF-P2, DBC, ADOS |
| **5** | M | 7.17 | DSM-V, CELF-5, ADOS, Mullen, ADI-R |
| **6** | M | 8.67 | DSM-V, PEP-3, ABC, CARS, CELF-5 |
| **7** | M | 8.25 | DSM-V, CELF-4 |
| **8** | M | 6.92 | DSM-V, WPPSI-IV, ADOS, ABC, CELF-4 |
| **9** | F | 6.08 | WPPSI-IV, ADOS, CELF-5 |
| **10** | M | 9.92 | DSM-V, CELF-5, ADOS, VABS, WNV |

ABC Autism Behaviour Checklist
ADI-R Autism Diagnostic Interview-Revised
ADOS Autism Diagnostic Observation Scale
CARS Childhood Autism Rating Scale
CELF-P, CELF-4, CELF-5 Clinical Evaluation of Language Fundamentals (Preschool, Edition 4,5)
DBC Developmental Behaviour Checklist
DSM-V Diagnostic and Statistical Manual of Mental Disorders (Edition V)
PEP-3 The Psychoeducational Profile (Version 3)
VABS Vineland Adaptive Behaviour Scales (Version 3)
WISC Wechsler Intelligence Scales for Children (Version V)
WPPSI Wechsler Pre-School and Primary Scale of Intelligence (Version IV)
WNV Wechsler Nonverbal Scale of Ability

Overall functional balance measures varied; children with autism had lower PBS scores when adjusted for ties (Autism group mdn[IQR]= 53[2] vs. Comparison group mdn[IQR]= 54[1] vs., p=0.044), but BOT-2 body coordination percentile ranks were similar (Autism group mean[SD]= 42.8[24.8] vs. Comparison group mean[SD]= 58.0[24.9], p=0.201). However, exploration of the BOT-2 subtests demonstrated that children with autism showed significantly lower Balance scores (Autism group mean[SD]= 11.9[3.18] vs. Comparison group mean[SD]= 15.4 [3.69], p=0.036), but no differences were observed between groups for Bilateral Coordination (Autism group mean[SD]= 16.33[3.32] vs. Comparison group mean [SD] = 17.30 [3.27], p=0.532).

While functional balance measures were different between children with neurotypical development and children with autism, peripheral vestibular function was similar, with findings reported in Table 8.3. No significant differences in cVEMP latencies or amplitudes were observed between groups, indicating similar saccule function. vHIT findings showed comparable VOR gain across conditions suggesting that high frequency semicircular canal function was similar. These findings demonstrate that peripheral vestibular function is normal in children with autism.

**Table 8.3.** Group comparisons for peripheral vestibular function including cVEMP and vHIT.

| | | Autism Group | | Comparison Group | | | |
|---|---|---|---|---|---|---|---|
| ***cVEMP*** | | **Mean (SD)** | **Range** | **Mean (SD)** | **Range** | **ES** | **Adj P** |
| ***Latencies (ms)*** | ***p13*** | 13.90 (1.50) | 11.37-16.65 | 13.42 (1.32) | 10.44-15.75 | 0.34 | .290 |
| | ***n23*** | 19.73 (1.68) | 15.54-21.54 | 19.76 (1.37) | 17.5-22.1 | 0.02 | .942 |
| ***Amplitude (µV)*** | ***p13-n23*** | 12.59 (4.72) | 3.90-20.28 | 9.97 (3.87) | 4.73-21.67 | 0.61 | .063 |
| ***vHIT*** | | | | | | | |
| | ***HSCC*** | 0.98 (0.09) | 0.83-1.2 | 0.93 (0.05) | 0.85-1.03 | 0.69 | .051 |
| ***VOR gain*** | ***PSCC*** | 0.95 (0.09) | 0.75-1.05 | 0.96 (0.20) | 0.71-1.34 | 0.07 | .828 |
| | ***ASCC*** | 0.97 (0.13) | 0.70-1.16 | 0.94 (0.14) | 0.76-1.22 | 0.22 | .578 |

Abbreviations: cVEMP = cervical vestibular evoked myogenic potentials; p13 = p13 latency; n23 = n23 latency, p13-n23 = peak to peak cVEMP amplitude; vHIT = video head impulse test; VOR = vestibulo-ocular reflex; HSCC = horizontal semicircular canal; PSCC = posterior semicircular canal; ASCC = anterior semicircular canal; ES = effect size (calculated using Hedges *g*); Adj P = adjusted p value (Tukey post hoc analysis).

When measuring postural stability, children with autism demonstrated significantly faster path velocities when visual cues were removed (EC: Autism group mean[SD]= 3.24[1.25] vs. Comparison group mean[SD]= 2.09[0.71], p=0.024; FEC: Autism group mean[SD]= 6.41[2.04] vs. Comparison group mean[SD]= 3.95[1.06], p=0.005). Figure 8.1 illustrates path velocities between groups; faster path velocity is indicative of poorer postural control. In contrast, path velocity was similar between groups when visual information was available (EO: Autism group mean[SD]= 2.25[1.13] vs. Comparison group mean[SD]= 1.78[0.59], p=0.253; FEO: Autism group mean[SD]= 3.06[1.09] vs. Comparison group mean[SD]= 2.76 [1.22], p=0.577). This also corresponded to a significantly larger Romberg ratio in children with autism (Autism group mean[SD]= 1.58[0.42] vs. Comparison group mean[SD]= 1.12[0.23], p=0.009).

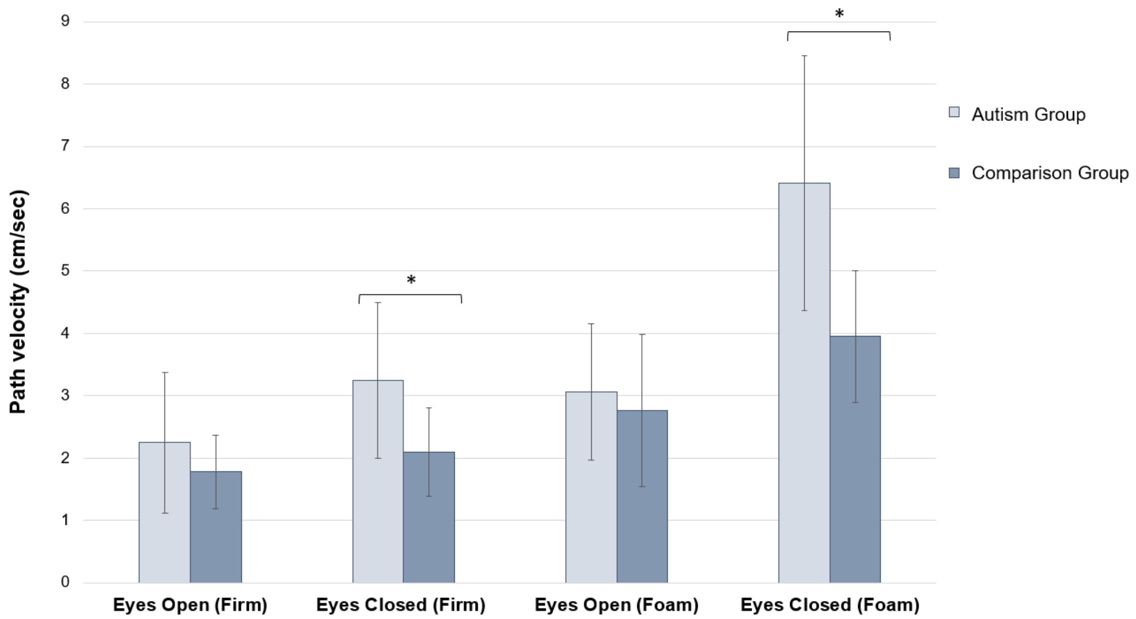



**Figure 8.1.** Mean path velocity across four standing conditions for children with and without autism. Children with autism showed reduced postural stability, as indicated by increased path velocities, in conditions where visual information was removed (eyes closed conditions on firm and foam surfaces).

Post hoc comparisons of DWT analyses showed that children with autism had significantly larger contributions in moderate and low DWT frequency bands when visual information was removed (EC, FEC), and somatosensory information was modified (FEC). No significant differences between groups across EO and FEO conditions were noted, as demonstrated in Table 8.4.

**Table 8.4.** Group comparisons for discrete wavelet transform bandwidth velocities across frequency bands for all standing balance conditions.

| **Standing balance condition** | | **Eyes Open** | | | | **Eyes Closed** | | | | **Foam Eyes Open** | | | | **Foam Eyes Closed** | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | **Autism** | **Comparison** | | | **Autism** | **Comparison** | | | **Autism** | **Comparison** | | | **Autism** | **Comparison** | | |
| | | **Mean (SD)** | **Mean (SD)** | **ES** | **Adj P** | **Mean (SD)** | **Mean (SD)** | **ES** | **Adj P** | **Mean (SD)** | **Mean (SD)** | **ES** | **Adj P** | **Mean (SD)** | **Mean (SD)** | **ES** | **Adj P** |
| ***DWT path velocity (cm/sec)*** | ***Ultralow (vision)*** | 0.13 (0.08) | 0.09 (0.37) | 0.15 | .182 | 0.14 (0.04) | 0.11 (0.06) | 0.59 | .119 | 0.10 (0.04) | 0.12 (0.05) | 0.44 | .425 | 0.17 (0.03) | 0.14 (0.05) | 0.73 | .200 |
| | ***Very Low (vestibular)*** | 0.39 (0.29) | 0.30 (0.09) | 0.42 | .365 | 0.54 (0.26) | 0.41 (0.15) | 0.61 | .087 | 0.57 (0.32) | 0.54 (0.22) | 0.11 | .808 | 1.04 (0.40) | 0.92 (0.47) | 0.28 | .573 |
| | ***Low (cerebellar)*** | 0.96 (0.70) | 0.79 (0.23) | 0.33 | .320 | 1.51 (0.72) | 1.08 (0.33) | 0.77 | **.018** | 1.33 (0.39) | 1.33 (0.60) | 0.51 | .817 | 2.92 (1.15) | 2.03 (0.62) | 0.96 | **.013** |
| | ***Moderate (somatosensory)*** | 0.86 (0.42) | 0.79 (0.25) | 0.20 | .480 | 1.43 (0.53) | 1.02 (0.37) | 0.90 | **.019** | 1.35 (0.73) | 1.25 (0.56) | 0.65 | .646 | 3.16 (1.21) | 2.07 (0.81) | 1.06 | **.011** |

Significant values in bold ($p<.05$). Abbreviations: DWT = discrete wavelet transform; cm/sec = centimetres per second; ES = effect size (calculated using Hedges *g*); Adj P = adjusted p value (Tukey post hoc analysis).

Postural stability was correlated with functional balance. Significant, negative correlations were observed with standing balance and functional balance measures, particularly where visual and somatosensory input was modified (FEC condition). Lower PBS scores indicative of poorer functional balance were associated with larger path velocities (r(19) = -.799, $p$<.001), and larger contributions from the faster components of CoP data (Moderate DWT: r(19) = -.634, $p$=.004; Low DWT: r(19) = -.737, $p$<.001). Lower balance scale scores from BOT-2 indicative of poorer balance function were also associated with larger path velocities (r(20) = -0.597, $p$=0.005), and larger contributions from DWT moderate and DWT low frequency bands (Moderate DWT: r(20) = -.585, $p$=.007; Low DWT: r(19) = -.453, $p$= .045). Larger path velocities from the moderate DWT frequency band were correlated with lower body coordination scores and overall percentile ranks (BOT-2 body coordination: r(19) = -.497, $p$=.030; BOT-2 percentile rank: r(19) = -.504, $p$=.028). No correlations were observed between vestibular function (which was typically normal) and functional balance.

# 8.5 Discussion

This study quantified peripheral vestibular function, motor proficiency and standing balance ability in children with autism. Children with autism show compromised functional balance, which in turn has repercussions for balance during daily activities. Despite normal peripheral vestibular function, reduced postural stability was observed when visual inputs were compromised, suggesting greater reliance on visual information. Furthermore, children with autism showed greater postural sway for the faster moving components of the CoP data, illustrating that sensory system integration may be different for children with autism when compared to children with neurotypical development.

Functional balance and postural stability can be influenced by the vestibular system, as demonstrated in other groups of individuals with documented peripheral vestibular dysfunction (Inoue et al., 2013; Ionescu et al., 2020). In this study, peripheral vestibular function is normal in children with autism and therefore is not the primary factor for differences in functional balance and overall postural control.

The cerebellum and vestibular system are intricately linked (Faan et al., 2010). Measures of peripheral vestibular function provide an overall representation of several elements: the integrity of the peripheral end organs, their corresponding neural reflex pathways, and to a lesser extent the structures involved in producing the output. In addition to detecting motion, the vestibular system contributions to postural control are predominately for head and body stabilization (Faan et al., 2010; Herdman & Clendaniel, 2014; Welgampola & Colebatch, 2001b). In instances where proprioceptive and visual cues are reduced, reliance on the vestibular system and vestibular reflexes increases. Therefore, given that peripheral vestibular function is normal in children with autism, the differences observed with postural stability and functional balance suggests that the central processing mechanisms may be underdeveloped, which in turn may influence the processing of sensory information during standing balance (Lim et al., 2017).

Postural stability was similar between groups when eyes were open, but different when eyes were closed. For children with autism, increased postural sway, indicative of reduced postural stability was most notable once visual information was removed. This finding suggests that children with autism have greater reliance on visual cues to maintain balance, and to an extent, may indicate developmental differences in sensory system integration (Molloy et al., 2003; Stins et al., 2015). Visual system predominance during standing balance is dependent on the nature of the balance task and whether movement is involved. For younger children, the visual system is the main contributor to balance control due to insufficient multimodal sensory integration (Forssberg & Nashner, 1982; Woollacott & Shumway-Cook, 1990), even with static balance tasks, but there is evidence to suggest that there is less reliance on vision with increasing age. Children with autism in this study showed a similar pattern of visual predominance which may suggest immaturity of sensory system integration.

Greater sensory integration is required for more complex standing conditions. In this study, the most difficult standing balance condition (FEC) was more challenging for children with autism. Children with autism showed greater postural sway for the fast-moving components of the CoP data (moderate and low frequency bands) when visual and somatosensory information were modified. While these frequency bands are thought to correlate with somatosensory and cerebellar information, this may be due to greater difficulties with postural control integration as demonstrated by larger amounts of sway. Furthermore, these faster moving components were correlated with poorer functional balance; those with lower balance scores on PBS and BOT-2 had postural stability which had more faster moving components than children who were more stable. It is known visual predominance for postural control occurs in younger children, and there is a readjustment of sensory system predominance as the vestibular and somatosensory systems become better integrated in the overall process of postural control (Hirabayashi & Iwasaki, 1995; Shumway-Cook & Woollacott, 1985). These findings suggest that sensory integration processes are underdeveloped in children with autism, thereby corresponding to poorer functional performance.

The cerebellum is considered the central mechanism for multimodal sensory integration and serves an important role in refining and executing vestibular mediated reflexes and motor outputs, or motor coordination (Morton & Bastian, 2004). Sensory system information is received by the central processing mechanisms, where the information is processed and results in a motor or reflexive output. Previous studies have identified differences in the cerebellum in autism, related to reduced Purkinje cells (Courchesne, 1995; Kemper & Bauman, 1993), but also decreased functional connectivity between the connective structures involved in integrative processes within the brain (Catani et al., 2008; Just et al., 2004; Khan et al., 2015). These differences could be linked to the observations noted in this study; for children with autism, greater reliance on visual information was observed, and for more complex standing balance conditions the fast-moving components of postural sway were predominant. These findings were in the context of normal vestibular input during standing balance conditions. Thus, these findings may unveil difficulties with integrating more complex sensory information, rather than sensory impairment in isolation.

## 8.6 Conclusion

Postural control deficits in children with autism may be related to a maturational deficit in sensory system integration or related to cerebellar underconnectivity. Further research is required to better understand the relationship between postural control, vestibular function and sensory system reweighting in children with autism. Utilising a range of clinical assessments for children with balance or motor development concerns can reveal potential functional consequences, and aid in addressing balance concerns more comprehensively.

Clinically, vestibular function was similar between children with autism and neurotypical development. For children with autism presenting with balance concerns, formal vestibular function assessment would still be useful to rule out an additional peripheral vestibular disorder. In instances where no peripheral deficits are identified, the balance concerns may be related to sensory integration issues based on deficits identified in this study. Physical rehabilitation may be beneficial in these circumstances, with focus on motor integration and learning to use sensory feedback to improve balance (Baker et al., 2008). Further research is required to understand if the deficits identified in this study are resolved throughout childhood or continue to adulthood, and whether specific physical rehabilitation may be useful in these circumstances. If a peripheral vestibular deficit is identified, these findings would be useful to guide management and ensure that deficits are holistically addressed via inclusion of vestibular rehabilitation (Rine, 2018).

This study also highlights the importance of considering alternative postural control measures such as fast-moving components of postural sway data. This movement analysis of postural control may be a more comprehensive way to quantify postural stability in children with autism and provide the clinician with a broader understanding of underdeveloped areas for postural control. In turn, these measures may supplement intervention options so therapists can provide specific exercises to address the deficits identified.

# Chapter 9: DISCUSSION

This final chapter discusses findings from the research conducted in the PhD project.

The four studies from this PhD validate the use of a range of assessment tools to determine peripheral vestibular function in school aged children and confirm that children's measures do change as a function of age, which in turn necessitates paediatric-focused normative data to determine overall peripheral vestibular functional and postural control. Furthermore, these studies highlight the importance of utilising a range of tools for children who have additional motor control or balance concerns; the benefit from these assessments would assist with differential diagnosis and inform intervention outcomes based on the clinical presentation and findings of whether vestibular function is affected. The four studies illustrate the importance of peripheral vestibular function in overall postural control, but also highlight other mechanisms such as higher order processing that can impact on postural control in childhood.

The PhD project has demonstrated that postural control and functional balance deficits can exist for children with and without peripheral vestibular impairment. Impacts of peripheral vestibular function on postural control in children with SNHL was also explored (Aim 3). Children with vestibular dysfunction showed more postural sway for conditions where greater reliance on the vestibular system was required. These findings were also observed with functional balance ability; peripheral vestibular function predicted functional balance performance. Children with autism showed normal peripheral vestibular function but impaired functional balance and postural control (Aim 4); these findings suggest that higher order processing or sensory integration required for balance control is immature, presenting in a similar way to a motor delay.

Assessing peripheral vestibular function can be a useful way to determine prognosis and formulate a management plan for children that present with a motor delay or dysfunction, or delays in motor skill development. This chapter concludes with some considerations for optimal balance assessment for children at risk of vestibular or motor impairment, and future directions for clinical practice.

# 9.1 Summary of key findings

## 9.1.1 Balance in typically developing children and adults

Aim 1: For typically developing children between 5-12 years of age: a) compare measures of otolith function, and b) compare postural sway measures and postural sway strategies to a young-middle aged adult cohort.

Hypotheses:

1) Otolith function will differ between adults and children, with children showing smaller responses and shorter latencies across assessments.

2) Postural sway will be larger in children across all measures of standing balance and will demonstrate greater reliance on visual and somatosensory information to maintain balance.

3) In children, shorter VEMP latencies and smaller VEMP amplitudes would be associated with more postural sway.

The hypotheses for this PhD aim were partially supported. Elements of otolith function differed between adults and children. Children in both groups (<8 years, and ≥8 years) showed significantly shorter cVEMP latencies (p13, n23) compared to adults, but no differences in child groups were noted. Younger children also had smaller amplitude cVEMP responses (p13-n23) compared to older children and adults for both rectified and unrectified responses. Shorter oVEMP p16 latencies, and n10-p16 amplitudes were also noted in both groups of children compared to adults.

Children in this study show reduced postural stability when compared to adults across all standing balance conditions; but greatest differences were observed when sensory information was modified, in agreement with existing literature (Barozzi et al., 2014; de Sá et al., 2018; Ferber-Viart et al., 2007; Franjoine et al., 2010; Sakaguchi et al., 1994).

Grouping children in younger and older age brackets showed significant differences across all standing balance conditions, rather than demonstrating a linear change in postural control as a function of age. Younger children show increased postural sway compared to older children. The change in sensory system re-weighting was delineated in DWT analyses, where children showed no difference in use of visual information to maintain postural sway, but younger children showed greater postural sway across the frequency bands corresponding to vestibular and somatosensory information, suggesting a less integrated postural control system.

A plausible explanation for postural sway differences observed may be related to how sensorimotor mechanisms influence postural control. Between 7-8 years of age, children may undergo a transition from open-loop to closed-loop predominance, which could relate to the turning point observed in various studies exploring standing balance (Riach & Starkes, 1994; Steindl et al., 2006). Therefore, we have evidence of sensory system integration for postural control, and as this changes the integration or reweighting of information may need to adapt as various closed loop feedback systems are introduced and refined.

There was a relationship between otolith function and postural sway data where p13 latencies predicted postural sway for conditions with eyes open. However, this relationship was observed for conditions with eyes open where traditionally, there is less reliance on vestibular information. This relationship was also unexpected; longer latencies associated with increased postural sway and may be attributed to the dataset and outliers. The significance of these findings is uncertain in explaining the relationship between these constructs, given the other observations in this study.

### 9.1.2 Balance function in typically developing children: normative data and longitudinal comparisons

Aim 2: To describe the vestibular and motor proficiency development in typically developing children 5-12 years of age through a) peripheral vestibular assessment, functional balance and postural sway measures, and b) monitoring vestibular function and postural control at three intervals over a twelve-month period.

Hypotheses:

1) Peripheral vestibular function will be positively correlated with increasing age; postural sway will be negatively correlated with increasing age.

2) Typically developing children will show no substantive changes in peripheral vestibular function over a twelve-month period but will show an improvement in postural sway performance.

The hypotheses for this PhD aim were partially supported. Normative data for each peripheral vestibular assessment and postural sway condition was also considered as part of this PhD aim.

Increasing age was significantly correlated with elements of peripheral vestibular function and postural sway measures across most conditions, however the associations varied according to assessment. Larger cVEMP amplitudes were associated with increasing age, lower PSCC VOR gain were associated with increasing age. Overall, other measures of peripheral vestibular function were not correlated with age. For postural sway, a consistent decrease in path velocities was associated with increasing age across most conditions (standing with eyes open on firm surface, standing with eyes open and closed on a foam surface).

Some measurements of peripheral vestibular function changed over a six- or twelve-month period. cVEMP amplitudes varied across both assessment points, although there was no consistent trend across the twelve-month period. On the other hand, a progressive reduction in PSCC VOR gain was noted over twelve months. These factors should be considered in the context of clinical findings.

Postural sway did not change substantially over a twelve-month period, suggesting that the twelve-month period of observation may not be sensitive enough to document changes over time, or longer time comparisons are needed to observe this. Furthermore, child age may have influenced this observation; greater changes in postural control over the twelve-month period may have been observed in younger children, however this was not explicitly explored.

### 9.1.3 Balance function in children with sensorineural hearing loss

Aim 3: For children between 5-12 years of age with bilateral sensorineural hearing loss: a) compare functional balance, postural sway, and vestibular function to typically developing children with normal hearing between 5-12 years of age, and b) determine the relationship between these measures.

Hypotheses:

1a) Postural sway measures will be larger for children with sensorineural hearing loss across conditions where sensory information is modified.

1b) Children with sensorineural hearing loss will show reduced peripheral vestibular function when compared to children with normal hearing.

2) The degree of peripheral vestibular function will influence motor skill performance and postural stability.

The hypotheses for this PhD aim were supported. In addition to difficulties maintaining balance and possible motor developmental delays, children with vestibular dysfunction may also demonstrate other functional consequences. For some children, challenges maintaining balance in certain sensory environments may be further influenced by an individual's motor performance. This can lead to fatigue and increased cognitive load particularly for cases where there is evidence of peripheral vestibular dysfunction. There is evidence that even unilateral vestibular dysfunction in children can have functional impairment (Sokolov et al., 2019). Subsequent impacts can relate to activity restrictions, and reduced participation in physical activities during school. While impacts of vestibular impairment were not explicitly addressed in the PhD project, understanding the impacts of balance issues in day-to-day life should be the focus of future research.

### 9.1.4 Balance function in children with autism

Aim 4: For children between 5-12 years of age with autism: a) compare functional balance, postural sway, and vestibular function to typically developing children between 5-12 years of age, and b) determine the relationship between these measures.

Hypotheses:

1a) Postural sway measures will be larger for children with autism across conditions where sensory information is modified,

1b) Children with autism will show similar peripheral vestibular function to typically developing children,

2) Motor skills are negatively correlated with postural sway measures.

The hypotheses for this PhD aim were supported. Children with autism showed larger postural sway in conditions where visual inputs were modified. Furthermore, postural sway patterns suggest differences in how sensory information is integrated for postural control and suggest that sensory system integration is less developed in children with autism. Postural control findings for modified sensory inputs were negatively correlated with functional balance performance. These findings are in the context of normal peripheral vestibular function, and thus, suggest that underdevelopment of central processing mechanisms or higher order processes contribute to the differences in postural control observed. This is supported by Lim's meta-analysis (Lim et al., 2017).

Children in this study did not show evidence of vestibular impairment, yet some literature suggests vestibular impairment may be evident for children with neurodevelopmental diagnoses. This prevalence ranges widely (Van Hecke et al., 2018) and is largely dependent on assessments performed, as well as the underlying mechanisms for vestibular impairment. To date, it remains unclear whether children with neurodevelopmental disorder have an increased risk of vestibular impairment. It is certainly possible that vestibular deficits identified in previous literature are due to other causes such as concomitant sensorineural hearing loss, or idiopathic vestibular impairment but it is difficult to determine this without a range of assessments. This study is one of the first to utilise a range of clinical vestibular assessments to assess several vestibular structures, and combine this with functional balance performance, and is a recommended approach to consider for a child with neurodevelopmental diagnosis. Given that neurodevelopmental disorders present with a diverse range of clinical presentations, it is not possible to generalise these findings, even to children with autism. Larger scale research is required in this area to better understand the potential manifestations for postural control and vestibular function for children with neurodevelopmental diagnoses more broadly.

## 9.2 Synthesis of findings

The four studies provide a snapshot of peripheral vestibular function and postural control in school aged children. The PhD project has demonstrated that elements of peripheral vestibular function (saccule, utricle) and postural control measures do vary between adults and children, and therefore, using adult normative data for these assessments is not appropriate to describe precise changes in children, as they are simply not applicable.

The findings also highlight that in children, some changes in peripheral vestibular function outcomes and postural control relate to age, and that the differences seem to persist over a twelve-month period. Therefore, for these assessments, it may be useful to consider two approaches for the normative dataset:

1) a range of normative data comparisons (including means, ranges, and confidence intervals) for all children across this age group for measures of peripheral vestibular function.
2) regression equations to predict postural sway performance across each sensory condition as a function of age. Given height and weight were not predictors of postural sway performance, these regression analyses only require age.

An additional consideration is the relationship between vestibular function and postural control/functional balance measures. This relationship was not robust for typically developing children with normal vestibular function, but clearer for children with vestibular impairment, where vestibular impairment predicted poorer postural control and functional balance measures, suggesting the importance of vestibular function for these activities.

## 9.3 Peripheral vestibular function

Findings from the PhD project suggest that most peripheral vestibular outcomes tend to stabilise by school age. The assessments are efficient, easy to perform and are useful to differentially diagnose vestibular dysfunction appropriately. Thus, they are a suitable assessment to consider in the child who is at risk of vestibular impairment (which may be congenital in nature, progressive or acquired) or has general balance concerns.

In Australia, vestibular testing is not part of routine assessment for children who present with hearing impairment, balance concerns, developmental delay, or an acute onset of balance symptoms. For these children, the lack of vestibular assessment can have significant consequences if left undiagnosed, delaying intervention such as vestibular rehabilitation, or influencing optimal management outcomes (Christy, 2019). Specifically, vestibular rehabilitation can be beneficial for improving balance performance if a vestibular impairment is identified, or if there are challenges with sensory integration. Sensory integration strategies can also be achieved using occupational therapy approaches (Rodger et al., 2005). For children with hearing impairment, focus is typically on hearing loss diagnosis and intervention, with few considerations on the impact vestibular impairment can have on motor development and balance.

Clinical comparison of peripheral vestibular test results generally relies on two factors: 1) the presence or absence of a response, and if responses are present bilaterally, 2) a comparison of left vs right values to determine an overall asymmetry ratio. For children presenting with balance concerns or symptoms of dizziness or vertigo, it is important to be able to establish the degree of function of each peripheral vestibular organ. Clear differences in peripheral vestibular function were noted for some children with sensorineural hearing loss and these findings were associated with functional balance and postural control performance.

Although a range of clinical tests were used in the current PhD project, considering an abbreviated assessment profile may be a worthwhile starting point to implement for clinical practice. This may be particularly important for children who have general balance concerns or motor delays. Although SCC and otolith measurement are important in the context of clinical diagnosis and management, vHIT may be a useful screening assessment to determine peripheral vestibular function. It is possible for someone to have an isolated end organ dysfunction, but unless a child is at risk of vestibular impairment (i.e., has a history of hearing impairment, or has an acute onset of vestibular symptoms), vHIT may suffice due to the flexibility of the test procedure, test compliance and ability to assess both portions of the vestibular nerve as well as end organ function. For children at risk of vestibular impairment, considering all peripheral vestibular assessments can help to determine more precise comparisons between peripheral vestibular to guide interventional approaches.

## 9.4 Functional balance

Functional balance measures in the context of a child who has increased likelihood of motor milestone delays is a useful way to identify potential deficits and inform processes for onward referral. The Pediatric Balance Scale (PBS) identified children with mild to moderate motor impairment, but not necessarily the best tool to consider as a comparison in typically developing children due to ceiling effects in this cohort. For a typically developing cohort, the PBS may be more suited to a younger (pre-school) age group (Franjoine et al., 2010).

When measuring functional balance performance, BOT-2 subtests may be more useful to differentiate between balance ability and gross motor skills required for bilateral coordination, and to a lesser extent, determine the challenges that may be encountered in daily activity. The balance subtest of the BOT-2 provides an estimate of static and dynamic physical activities required for good daily balance, and postural control maintenance. The BOT-2 balance subtest has been suggested as a good measure of functional balance, particularly in cases of vestibular impairment (Cushing et al., 2008), Given Studies 3-4 showed poorer functional balance ability in both children with SNHL, and children with autism, this test itself is not sufficient to differentiate between the two groups regarding the presence of underlying vestibular deficits. Both groups of children showed poorer balance scores, reflective of a lower subtest score when age and sex were considered. Yet for children with SNHL, vestibular impairment was correlated with poorer functional balance performance, whereas for children with autism, vestibular function was not correlated with functional balance performance. These differences highlight the need for multiple approaches to assessing balance. What also remains unknown is how functional balance varies between children with SNHL and children with autism, as these groups were not directly compared in the current PhD project, and thus may be an area of future research.

## 9.5 Postural control

The primary use of postural control measures in this project were to provide an understanding of the integrative processes used for balance control during static balance conditions. The patterns measured across four standing balance conditions illustrated that children between 5-12 years have greater postural sway than adults, thought to be due to a combination of continued development of sensorimotor and integrative processes for postural control. Children with evidence of vestibular impairment showed greater sway for conditions where reliance on vestibular information was required, and when proprioceptive information was compromised, similar to existing literature (Enbom et al., 1991). Patterns of postural control were also different for children with balance concerns and autism (as demonstrated by poorer functional balance scores but normal vestibular function), who showed greater postural sway when visual information was not available to them. These findings were observed using a static platform, so findings may be compounded for more complex standing balance conditions or when assessing balance control using dynamic movement.

### 9.5.1 Movement patterns revealed by DWT analyses

Exploration of movement patterns using DWT frequency band information has not been widely used in a paediatric setting (Lorefice et al., 2015; Micarelli et al., 2020), yet provides useful information about sensory strategies to maintain balance in different sensory conditions, based on the physiological mechanisms. In this project exploring DWT highlighted distinct movement patterns, particularly when comparing patterns across different standing balance conditions. Low frequency DWT contributions are thought to represent visual and vestibular mechanisms; higher frequency DWT contributions are thought to represent cerebellar and somatosensory mechanisms.

Children utilised different responses to adults as demonstrated by larger movement patterns across all DWT frequency bands relating to somatosensory, vestibular, and visual information. Younger children also showed larger movement patterns for somatosensory and vestibular information when compared to older children, yet visual inputs were used in a similar manner.

Children with SNHL showed greater amounts of postural sway when standing on foam for high frequency bands corresponding to somatosensory and cerebellar information. In these cases, somatosensory information is compromised, requiring greater reliance on vestibular system information. For eyes open conditions, there was greater postural sway in the frequency band corresponding to vestibular information, which in turn may also relate to processing of vestibular information for these conditions. Overall, this finding suggests the integration of incoming sensory information takes longer due to central compensatory strategies, or related to a motor delay which has been documented in children with sensorineural hearing loss (Leen Maes et al., 2014). For those children with confirmed vestibular impairment, this may present as greater sway as feedback loops are also utilised in the process of balance maintenance.

Children with autism showed greater postural sway in conditions where visual inputs were eliminated. The movement patterns were most significant for moderate and low frequency bands, corresponding to somatosensory and cerebellar information. These findings may also relate to sensory strategies utilised by children with autism, with evidence to suggest sensorimotor impairments may contribute to the larger responses (Fournier, Hass, et al., 2010). In both clinical subgroups, cerebellar and somatosensory processes for postural control were larger, which may reflect the relative immaturity of sensory system integration at the level of the cerebellum either related to cerebellar underconnectivity (in autism) or compensatory strategies (in children with vestibular impairment) used to maintain balance. These findings may also relate to a delay of integrative processing required for standing balance.

## 9.6 Clinical Implications

Across all domains of child development, the importance of early intervention is crucial to maximise clinical outcomes and provide a child with the best chance of meeting milestones (Blauw-Hospers & Hadders-Algra, 2005). In Australia, paediatric vestibular assessment is in its infancy, and to the writer's knowledge, there are no accepted clinical guidelines utilised across the country. For children that are dizzy or experience balance concerns, their experience may consist of seeing a specialist for medical oversight and intervention, referral to an occupational or physical therapist for functional assessment and intervention, or referral to an audiologist for vestibular assessment. Vestibular assessment may be limited due to equipment availability or compliance with testing. Furthermore, testing is typically based on adult protocols due to lack of paediatric normative data. While not formally collected as part of the project, anecdotal experiences of caregivers and children suggest that paediatric balance assessment is a scarce and under-appreciated area of clinical practice, despite the significant impacts balance can have on a child's development. These experiences related to children who had hearing impairment, but also children who had potential motor milestone delays or balance concerns. Therefore, the use of a clinical protocol for children at risk of vestibular impairment or motor delay is important to guide management (Van Hecke et al., 2021).

As explored in chapters six, seven and eight, all children underwent a range of clinical assessments to determine balance function, designed to capture the complexity of balance performance through functional assessment, postural control, and vestibular assessment. Combined with different phenotypes of clinical subgroups assessed, including those with SNHL or autism, significant findings across various balance measures validate the requirement for these assessments to be utilised in clinical settings. The range of clinical assessments helps to differentiate between underlying mechanisms contributing to the balance concerns, resulting in different management approaches utilised by paediatric therapists. For children presenting with documented vestibular impairment, this includes vestibular rehabilitation, which can vary depending on type and extent of dysfunction identified (Rine, 2018). These include substitution strategies in case of bilateral vestibular impairment, where reliance on other sensory mechanisms is used to maintain balance, or adaptation/habituation strategies for unilateral vestibular impairment, where rehabilitation focuses on neuroplasticity and central compensation. For children with no evidence of vestibular impairment but evidence of functional balance concerns or reduced postural stability, occupational therapy approaches can be used to target motor skill development and sensory integration (Case-Smith & Arbesman, 2008; Rodger et al., 2005). Rehabilitation approaches and activities may therefore be adapted based on the underlying mechanisms of the balance concerns.

The use of child-focused normative data is an important first step to quantify balance function in school aged children. Adult normative data is not applicable and using adult normative data as comparative points increases the likelihood of 1) a problem when not expecting one, or 2) assessments may not be sensitive enough to determine functional differences that may relate to functional consequences. This was achieved in the PhD project.

Depending on the primary reason for referral, performing a comprehensive test battery may be unnecessary for all children. An abbreviated assessment profile utilising presenting symptoms, clinical history, and test order to determine deficits may a be more effective way of considering a test battery that is efficient and appropriate for purpose, and address some of the challenges that arise when assessing children.

### 9.6.1 Test compliance

While most children completed the clinical assessments without difficulty, several factors suggest that the clinical protocol may require modifications to suit different subgroups of children. For example, test duration and compliance may impact on extending this test battery to a younger age group, or to children who might find the tasks particularly challenging. Anecdotally, some participants reported difficulties standing still for postural sway measured in complex conditions or completing motor tasks as part of functional balance performance. For a few children, reluctance to undergo peripheral vestibular tests related to electrode placement on the skin, or sensitivity to the acoustic stimulus. Thus, considering a tiered approach to the clinical protocols based on presenting symptoms and case history may be more beneficial. Based on clinical assessments utilised in the project, there may be some that are more suitable than others depending on the age of the individual.

Video head impulse testing requires goggles to be placed on the child to record the VOR; the child then visually fixates on a target while their head is turned quickly. This assessment is generally well tolerated, quick to perform, and can be a useful screening assessment prior to advancing to other peripheral vestibular assessments. Results are not influenced by middle ear pathology unlike other vestibular assessments such as VEMP performed with air conduction, or caloric testing. Yet some children do not tolerate the head-worn goggles, particularly younger age groups. Despite this, vHIT can be achieved in younger age groups, utilising an approach where the VOR gain is monitored using eye tracking software (Dhondt et al., 2019; Martens et al., 2019; Wiener-Vacher & Wiener, 2017). In the current project, test compliance for vHIT was high, with all children able to complete vHIT assessment in at least the horizontal plane. Additionally, most children with vestibular impairment identified in Study 3 had concomitant SCC and otolith dysfunction, the remaining showed isolated vestibular impairment. Thus, vHIT assessment may be most useful as a screening measure to quantify high frequency SCC function, before considering other vestibular assessments.

Electrophysiological assessment for VEMP in the current project was less well tolerated. Yet for younger children, electrophysiological assessment may be easier to perform given less requirement on cognition to perform the task. For example, cVEMP testing can be performed in infants where the SCM contraction can be initiated and sustained by a gentle head rotation (Martens et al., 2019). On the other hand, oVEMP can be performed in young children but responses are not reliably obtained until approximately 3-4 years of age (Dhondt et al., 2019; Wang et al., 2013). Challenges with VEMP test compliance may also arise once children are old enough to understand simple instructions, with electrode tolerance typically lower. In a clinical context, and based on prior experience, this is often encountered when attempting to assess children <5 years, and even for some school aged children. This was observed with some children in the present project despite strategies to mitigate this; electrode placement refusal or reduced tolerance to preparation of recording sites meant that the assessments were not possible. Middle ear pathology or auditory stimulus sensitivity may also preclude responses from being recorded; and may impact on completeness of the test battery if utilising this for diagnosis.

Postural control measures are quick, reliable, and child-friendly, and can provide a discrete understanding of postural control patterns that may be related to a vestibular impairment. Breaking postural sway data into discrete frequency bands is useful to understand different postural control strategies utilised for different standing balance conditions, and this was particularly evident for children who were at risk for motor delay or vestibular impairment. Based on the clinical profile from the DWT postural control measures, not all traditional sensory conditions may be needed to differentiate one group from another, so instead of four conditions performed, the assessment may be abbreviated to two test conditions that may show the greatest difference such as standing with eyes open on firm, then foam surfaces (to identify children with vestibular impairment), or standing with eyes open then closed on firm surfaces (to identify children with adequate vestibular function but remaining balance concerns). However, DWT analysis is performed offline, and therefore is not a measure that is available to the clinician during the clinical assessment task itself. Furthermore, access to force plates can be prohibitively expensive, so may not be an assessment that most clinics utilise. These measures are only possible for children who are able to maintain an upright stance for a short period of time, and therefore may not be suitable for younger age groups or children who are unable to stand independently.

### 9.6.2 Approaches to balance surveillance

Figure 9.1 represents potential assessment protocols for different subgroups of school aged children. For all children, a screening questionnaire should be the first step to identify the subsequent test processes for a child with balance concerns or at risk of vestibular impairment. Ideally, this should include information about vestibular and non-vestibular symptoms, motor milestone development, and clinical diagnoses of various conditions. Vestibular questionnaires are useful to determine presenting symptoms; the Paediatric Vestibular Symptom Questionnaire (Pavlou et al., 2016) is a validated rating scale questionnaire for children between 6-17 years that includes questions regarding symptoms such as vertigo, unsteadiness, loss of balance and nausea. As the name suggests, these questionnaires typically focus on vestibular-related symptoms, and do not include questions that relate to motor delays or other potential confounders that relate to balance difficulties. Thus, incorporating a motor milestone checklist may also help to screen for potential motor milestone delays. While motor milestones are often based on guardian's recollection of their child's motor milestone acquisition, they can still provide valuable evidence of potential motor delays that may necessitate a different approach to measuring balance. Challenges obtaining an accurate description of balance symptoms in a younger child (6 years) generally relates to the child's inability to describe their symptoms accurately. In these instances, parental observations of the child may be more important to inform next steps for assessment.

Using a dizziness scale to quantify the impact of presenting symptoms on daily activities is an important addition to the clinical profile and should be incorporated into a screening questionnaire, particularly for children at risk of vestibular impairment (McCaslin et al., 2015). This was not incorporated in the current project but would have been a useful clinical adjunct to determine the effectiveness of screening for balance concerns and also determine the relationship between balance measures.

Children presenting with vertiginous symptoms should undergo the breadth of peripheral vestibular assessment to quantify any vestibular impairment. If no vestibular dysfunction is identified, then functional balance measures (BOT-2 Balance subtest) may be considered if vertiginous symptoms are impacting on daily activities. For all other children presenting with balance concerns, all should undergo functional balance (BOT-2 Balance subtest) and vHIT screening (measuring HSCC function) as a minimum. The use of the BOT-2 Balance subtest for children presenting with balance concerns (in the absence of motor delay) may also be a good screening tool to quickly identify vestibular impairment (Cushing et al., 2008). Depending on BOT-2 Balance outcome measures and vHIT screening outcomes, further peripheral vestibular assessment may be warranted.

Static posturography should also be considered for children with clinical diagnoses. Based on the findings in this project, assessing three of four postural control conditions (EO, EC and FEO) might yield the most appropriate triaging system for children in the clinical subgroups tested. Standing on a firm surface in eyes open and closed conditions may differentiate children with autism from other groups; and standing with eyes open on a firm or foam surface differentiate those with vestibular impairment from other groups.

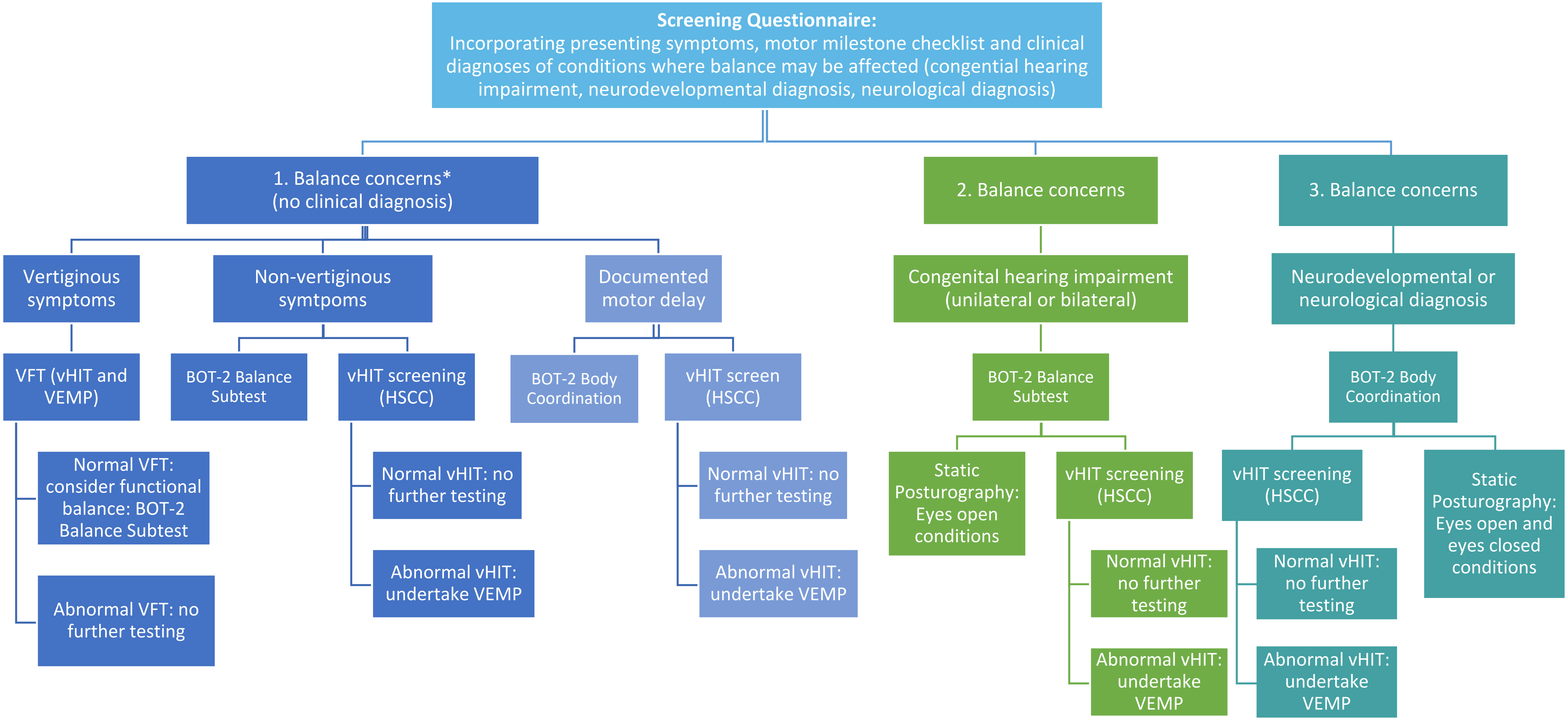



**Figure 9.1.** Abbreviated assessment profile for balance assessment based on screening questionnaire.
Abbreviations: BOT-2= Bruininks-Oseretsky test of motor proficiency; VFT = vestibular function tests, vHIT = video head impulse test, HSCC = horizontal semicircular canal, VEMP vestibular evoked myogenic potentials

To better understand a child's balance ability, one must have knowledge of their balance experience combined with a range of clinical balance measures. These building blocks can assist with onward referral, timely intervention, and management options, but are only useful if management approaches are integrated into the child's care.

Any child with a documented vestibular dysfunction and balance concerns impacting on daily activities would benefit from vestibular rehabilitation. This approach involves a range of activities that may incorporate gaze stabilisation, practice of gross motor skills, work on static and dynamic balance, and in some cases, habituation approaches to improve motion sensitivity (Christy, 2019). In cases of unilateral dysfunction these include strategies to assist with central compensation and activities incorporating vestibular reflexes, particularly gaze stabilisation. For example, VOR exercises may progress from moving the head from side to side with a static visual focus, to performing these visual exercises when walking. For children with documented bilateral vestibular dysfunction, substitution approaches may depend on the extent of the bilateral dysfunction and may incorporate activities which increase the reliance on visual and somatosensory information. However, congenital vestibular impairment may also reduce the effectiveness of visual and somatosensory cues for postural control, thus influencing progression (Rine et al., 2004). Further research is needed to determine the influence of gaze stability exercises on gross motor skills, postural control, and gaze stability for children with vestibular impairment, and whether this is dependent on the type of vestibular impairment (congenital, acquired, unilateral, bilateral) (Hall et al., 2022).

For children with balance concerns in the context of normal vestibular function, rehabilitation approaches may still be valuable. Depending on the impact of presenting symptoms and additional clinical diagnoses, sensory integration strategies may be utilised, in addition to sensory processing skills for children with autism (Baker et al., 2008) motor skill development for documented motor delays, and in some cases, neurodevelopmental treatments for neurological diagnoses (Case-Smith & Arbesman, 2008; Rodger et al., 2005). These approaches utilised by paediatric occupational therapists overcome limitations and promote engagement and participation, with contemporary approaches encompassing improvement in functional balance performance, rather than impairment-based interventions (Novak & Honan, 2019).

## 9.7 Strengths and Limitations

### 9.7.1 Strengths

This project is one of the first to utilise a range of assessments to quantify balance in children between 5-12 years, which included clinical vestibular assessments to assess several vestibular structures combined with measures of functional balance performance and postural control. The normative dataset generated from these assessments can be utilised in paediatric clinical settings as a comprehensive approach to assessing a child with balance concerns or augmented depending on clinical resources. This includes normative data for vHIT, cVEMP, oVEMP and postural sway measured using static posturography. For a subset of typically developing children, this was documented longitudinally to determine developmental trajectories. A combination of these assessments provided unique patterns of balance performance in children with sensorineural hearing loss and those with neurodevelopmental diagnosis.

The studies also provide novel insights to interpreting postural sway data based on the DWT frequency bands thought to correspond to different sensory inputs. The patterns that emerged suggest that for some children, sensory integration was sub-optimal which related to larger responses corresponding to somatosensory and cerebellar mechanisms. The findings also provide a more nuanced understanding of sensory integration strategies in children.

Study outcomes may help to refine referral pathways and inform interventional approaches for children who are at risk of vestibular impairment, motor delay or experience balance difficulties.

### 9.7.2 Limitations

There are several important limitations of the PhD project. Originally, the PhD aims incorporated longitudinal data collection for all clinical subgroups but disruptions throughout the PhD significantly affected the retention and continuity for data collection. Data collection was significantly limited throughout the dissertation (most notably in

2020-2021), impacting on 12- and 18-month comparisons for the typically developing cohort and clinical subgroups.

Clinical comparisons in the project focused on children aged 5-12 years. Given PhD findings show differences in peripheral vestibular function and postural control between this age group and adults, including an adolescent group would have helped to ascertain the developmental trajectory for sensory system integration.

Adequate sample sizes are important to draw robust conclusions from data. For the project, consequences of data collection disruptions between 2020-2021 impacted on overall sample sizes. Adequate sample sizes were achieved for Studies 1 and 2, and despite smaller sample sizes in Studies 3 and 4, significant findings were observed across various balance measures. Replicating these findings for a larger cohort is an important next step before findings can be generalised to a broader group.

Another significant limitation was procedure and interpretation used for cVEMP testing. There is evidence to suggest that neck length can impact on cVEMP responses (Chang et al., 2007), and this was not collected in the project. Due to equipment limitations, cVEMP assessment was performed without active EMG monitoring and rectification. EMG was visually monitored throughout cVEMP assessment, and all participants underwent the same procedure utilising the elevation method of bilateral SCM contraction. Post stimulus rectification applied to all waveforms and analyses included both rectified and unrectified responses. Furthermore, participants were age matched in studies 3 and 4; no significant differences in overall height were noted between groups.

## 9.8 Future directions

Findings from the four studies demonstrate a need for further research in several areas including optimal clinical assessment protocols for measuring balance, expanding assessment to other clinical subgroups and management approaches. While not explicitly explored, understanding the need for balance assessment based on caregiver experiences is another area for future consideration.

Overall balance function can be assessed using a range of measures including peripheral vestibular assessment, functional balance, and postural control. Significant findings across various balance measures were observed across clinical subgroups but should be replicated in larger cohorts to validate these findings. In addition to balance measures, a screening questionnaire should be included to understand a child's primary balance concerns, impact on daily function, and any clinical diagnoses that may increase the risk of vestibular impairment or motor delay.

Future research should include assessment of other subgroups of children who may be at risk of vestibular impairment or motor delay. These include children with confirmed neurological disorder, such as those with Ataxia Telangiectasia, Friedrich Ataxia, or spinal muscular atrophy, all of whom have balance difficulties or gait abnormalities (Maudoux et al., 2020; Rothblum-Oviatt et al., 2016; Wang et al., 2007). For these children, balance impairment is often multifactorial, given changes in motor performance, coordination and muscle strength as the conditions progress. Yet vestibular contributions to balance, as well as postural control measures have not been widely explored and should be an area of future focus. Using DWT analyses as an objective measure of postural sway may also serve as a potential biomarker for disease progression.

Another group of children at risk of vestibular impairment are those who undergo ototoxic treatment, either once off or over a period of time. Some ototoxic medications preferentially affect the vestibular hair cells, in turn causing vestibular impairment to an otherwise healthy system (Selimoglu, 2007; Van Hecke et al., 2017). For these children, establishing baseline measures of balance prior to treatment, and surveillance of balance measures during treatment may help to fast-track optimal management pathways if a vestibular impairment is identified.

Cross sectional data does not adequately capture discrete changes in balance function over time. Longitudinal exploration of balance function should be considered to determine whether balance performance is delayed or progressively worsens. Various clinical subgroups may benefit from balance surveillance, including the clinical subgroups explored in chapters seven and eight, but also children with conditions where balance performance is predicted to change. Longitudinal comparisons may be particularly useful to establish if the deficits can be overcome or effectively managed with tailored rehabilitation, and also serve to educate caregivers by providing insight into changes in balance performance, which may influence the way they support their child. There is evidence that children with sensorineural hearing loss do benefit from vestibular rehabilitation (Melo et al., 2019; Rine et al., 2004), but further research is needed to determine optimal approaches based on aetiology and severity of the vestibular impairment. Longitudinal comparisons of balance performance for individuals with neurodevelopmental or neurological conditions have not been widely reported in the literature (Stins et al., 2015), and even less commonly in children (Zesiewicz et al., 2017).

The importance of early intervention should not be overlooked. Focus of the current projects included children between 5-12 years, but to ensure optimal and timely intervention, diagnosis should be occurring much earlier. Further research used to establish vestibular function in formative years of motor development (<5 years) may yield the most benefit in cases where early intervention is crucial. A combination of questionnaires, checklists, and screening assessments (including vestibular system assessment) may be a reasonable approach to ensure that children are identified early. This approach has been adopted by Martens in a clinical setting for all children with neonatal hearing loss (Martens et al., 2019), yet challenges remain for implementing screening more broadly. Optimal management outcomes may include referral to an occupational therapist for motor skill development, to physical therapy for vestibular rehabilitation in cases of vestibular impairment, or neurological approaches to rehabilitation, in cases of central contributions to balance performance.

Finally, understanding caregivers' perspectives regarding provision of comprehensive balance assessment, including facilitators and barriers to accessing these health care models should be considered. Understanding the journeys taken for their child to receive an appropriate diagnosis, and access intervention is an area that is relatively unexplored but is crucial in patient centred best practice.

## 9.9 Summary

The aims of the PhD project were to describe vestibular function, functional balance and postural control in typically developing children between 5-12 years of age, and in children at risk of vestibular impairment or motor delay. The relationship between these balance constructs was also explored.

Normative data was established across a range of clinical vestibular assessments, as well as postural sway data across sensory conditions and utilising novel approaches to postural sway interpretation. Findings provide new insights into postural sway patterns and the relationship between functional balance measures and peripheral vestibular function across children 5-12 years.

Functional balance can be compromised for children at risk of vestibular impairment or motor delay. For these children, not considering comprehensive assessment of balance performance impacts their provision of care and can have significant consequences for optimising balance outcomes. It is hoped that findings from the PhD project provide a basis for highlighting the importance of routine clinical assessment for children at risk of vestibular important or motor delay, as well as an option for children who present with dizziness or balance concerns. In Australia, the current narrative for paediatric balance assessment must shift to provide children with the necessary assessments to ensure timely diagnosis and management.

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# APPENDICES

## Appendix A-1: HREC approval letter from the Royal Victorian Eye and Ear Hospital

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**HREC Number:** **17/1348H**

**Project Title:** **Vestibular function in children**

**Principal Investigator:** **Ms Donella Chisari**

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I acknowledge receipt of the revised HREA Application Form and Participant Information & Consent Form.

I am pleased to inform you that the above project has now received ethical approval from the Eye and Ear HREC, and meets the requirements of the National Statement. This letter constitutes ethical approval only. You must not commence this research project at any site (including Eye and Ear) until separate research governance authorisation from that site has been obtained.

The HREC approval date is 23 October 2017, the HREC Number is 17/1348H, and approval is valid for five years.

The following documents have been approved:

- Project application, dated 20 Oct 2017
- Patient Information and Consent Form, v2.0 dated 20 Oct 2017

The Royal Victorian Eye and Ear Hospital HREC is constituted and operates in accordance with the National Health and Medical Research Council (NHMRC) National Statement on Ethical Conduct in Human Research (2007 and as updated) and in accordance with the Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95) and the Health Privacy Principles in the Health Records Act 2001(Vic) and Section 95A of the Privacy Act 1988.

In order to comply with the National Statement and Good Clinical Practice requirements you are required to:

- submit an annual progress report for the duration of the project
- submit a comprehensive final report upon project completion
- notify the Secretariat of the project start date
- submit all proposed amendments to the project
- submit any adverse event reports
- report any unexpected developments in the project with ethical implications
- notify any changes of project Principal and all other Investigators
- advise if the project is completed prior to the anticipated date or is withdrawn

- preserve the confidentiality of information and records about research participants and only use information for the purpose specified in the approved protocol

Please note that any researcher named in the application did not participate in deliberations or decision making for this project.

Please use the HREC number in all future correspondence with the HREC Secretariat.

On behalf of the Committee, I wish you every success with your project.

Yours sincerely

Kerryn Baker
Secretary
Human Research Ethics Committee

26 October 2017

the royal victorian eye and ear hospital

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**Research Governance Authorisation**

**HREC Number:** 17/1348H

**Project Title:** Vestibular function in children

**Principal Investigator:** Ms Donella Chisari

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Thank you for submitting the above research project for research governance review. This project was considered by the Eye and Ear Hospital Research Office.

I am pleased to inform you that approval has been granted for the above project to proceed.

The project has been approved to be conducted at the following site:

- Royal Victorian Eye & Ear Hospital

Research governance approval is valid from the date of this letter until 23 October, 2022.

On behalf of the Research Office, I wish you every success with your project.

Yours sincerely

Dr Caroline Clarke
Executive Director Medical Services/Chief Medical Officer

10 November 2017

# Appendix A-2: Amendment to include de-identified adult data

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| | |
|---|---|
| **HREC Number:** | **17/1348H** |
| **Project Title:** | **Vestibular function in children** |
| **Principal Investigator:** | **Ms Donella Chisari** |

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I refer to your amendment dated 27 January 2020 requesting an amendment to the protocol using de-identified data from two previous studies for the above listed project.

The HREC Chair approved the above amendment. This decision will be ratified by the full Human Research Ethics Committee at the next meeting scheduled for 13 February 2020. This amendment can proceed from the date of this letter. No further correspondence will be provided on this amendment unless the HREC requests additional information.

The following document/s were approved:
- Project proposal, incorporating amendment dated 27 Jan 2020
- Project Description Form, v3 dated 23 Jan 2020

Thank you for notifying the Committee.

Yours sincerely

Kerryn Baker
Secretary
Human Research Ethics Committee

4 February 2020

## Appendix A-3: University of Melbourne HESC Registration

THE UNIVERSITY OF MELBOURNE

21 November 2017

Ms D.R. Chisari
Audiology and Speech Pathology
The University of Melbourne

Dear Ms Chisari

I am writing to advise you that this project has been registered at this University as approved by the Royal Victorian Eye and Ear Hospital Human Research Ethics Committee. Please take note of the Human Research Ethics ID number below.

Project title: **Vestibular Function in Children**
Researchers: **Ms D R Chisari**
Ethics ID: **1750810**

Please note the following conditions of registration:

1. The Royal Victorian Eye and Ear Hospital HREC approval must be current for the life of the project
2. You are required to keep the Psychology Health and Applied Sciences HESC informed of any subsequent variations or modifications made to the project and any such changes must be approved by the Royal Victorian Eye and Ear Hospital HREC
3. You are required to submit an annual report to the Psychology Health and Applied Sciences HESC at the end of each year or at the conclusion of the project if it continues for less than this time. Requests for annual reports will be sent out via Themis.

Yours sincerely

Mr Tony Callahan
Secretary, Psychology Health and Applied Sciences HESC
Phone: 8344 2067, Email: t.callahan@unimelb.edu.au

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# Appendix B: Questionnaire

THE UNIVERSITY OF MELBOURNE

**INSTRUCTIONS FOR COMPLETING THIS QUESTIONNAIRE**

*Please read each question and tick the most appropriate response. When asked to specify or provide detail, please write in the given space or in the margin of the page if you require more room. If for any reason there is any question, or part of a question that you do not wish to answer you may leave it blank. If you do not know the answer to all or part of any question please write "unknown".*

| | |
|---|---|
| **Participant ID:** | |
| **Date of Birth:** | |
| **Child's Gender:** | |
| **Your Relationship to the Child:** | |
| **Today's Date:** | |

| **1. General Health** | |
|---|---|
| **1.1** Is your child healthy and well today? | ☐ Yes ☐ No<br>If 'no' please briefly describe concerns: |
| **1.2** Has your child ever had a major illness? | ☐ Yes ☐ No<br>If 'yes' please briefly describe illness/date: |
| **1.3** Does your child have any ongoing health problems? | ☐ Yes ☐ No<br>If 'yes' please briefly describe health problem: |
| **2. General Development** | |
| **2.1** Are there any concerns about your child's overall development? | ☐ Yes ☐ No<br>If 'yes' please briefly describe diagnosis: |
| **2.2** At what age was your child able to: | Sit Age: months ☐ Unsure<br>Crawl Age: months ☐ Unsure<br>Walk Age: months ☐ Unsure |

| | |
|---|---|
| | Descend stairs Age: months ☐ Unsure<br>Run Age: months ☐ Unsure<br>Ride a tricycle Age: months ☐ Unsure<br>Hop on one foot Age: months ☐ Unsure<br>Skip with alternating feet Age: months ☐ Unsure |
| **2.3** Did your child meet motor milestones at the expected ages? | ☐ Yes ☐ No<br>If 'no' please briefly describe: |
| **3. Hearing and Balance Health** | |
| **3.1** Has your child had any history of ear infections or grommets? | ☐ Yes ☐ No<br>If 'yes' please give details: |
| **3.2** Does your child have a permanent hearing loss? | ☐ Yes ☐ No<br>If 'yes' please give details: |
| **3.3** Has anyone related to your child been born with or developed a permanent hearing loss as a child or young adult? | ☐ Yes ☐ No<br>If 'yes' please give details: |
| **3.4** Has your child ever experienced any of the following? | Vertigo ☐ Yes ☐ No<br>Dizziness ☐ Yes ☐ No<br>Frequent falls ☐ Yes ☐ No<br>Clumsiness ☐ Yes ☐ No<br>Fear or panic ☐ Yes ☐ No<br>Strange eye movements ☐ Yes ☐ No<br>Motion sickness ☐ Yes ☐ No<br><br>If 'yes' to any of the above, please give details: |