Abstract

Title of dissertation: MECHANISMS OF GAZE STABILITY DURING
                           WALKING: BEHAVIORAL AND PHYSIOLOGICAL
                           MEASURES RELATING GAZE STABILITY TO
                           OSCILLOPSIA

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Visual sensory input plays a significant role in maintaining upright posture

during walking. Visual input contributes to control of head, trunk, and leg

motion during walking to facilitate interaction with and avoidance of objects

and individuals in the environment. The vestibular system contributes to

postural control during walking and also to stabilization of the eyes during

head motion which may allow for more accurate use of visual information.

This dissertation reports the findings of five experiments which explore how

the nervous system uses vision to control upright posture during walking and

also whether the act of walking contributes to gaze stability for individuals with

severe vestibular loss. In the first experiment, continuous oscillatory visual

scene motion was used to probe how the use of visual input changes from

standing to walking and also to determine whether the trunk motion response to visual motion was the same in the medio-lateral (ML) and anterior-posterior (AP) directions. In the second experiment, visual feedback (VFB) regarding the approximate center of mass position in the ML and AP directions was used to demonstrate that ML path stability was enhanced by concurrent visual feedback for young and older adults. In the third experiment, adults with vestibular loss and healthy adults were both able to use VFB during treadmill walking to enhance ML path stability and also to separately modify their trunk orientation to vertical. The final two experiments investigated whether gaze stability was enhanced during treadmill walking compared to passive replication of sagittal plane walking head motion (seated walking) for individuals with severe vestibular loss. Individuals with severe bilateral vestibular hypofunction displayed appropriately timed eye movements which compensated for head motion during active walking compared to seated walking. Timing information from the task of active walking may have contributed to enhancement of gaze stability that was better than predictions from passive head motion. This dissertation demonstrates: 1) the importance of visual sensory input for postural control during walking; 2) that visual information can be leveraged to modify trunk and whole body walking behavior; and 3) that the nervous system may leverage intrinsic timing information during active walking to enhance gaze stability in the presence of severe vestibular disease.

MECHANISMS OF GAZE STABILITY DURING WALKING:
BEHAVIORAL AND PHYSIOLOGICAL MEASURES RELATING GAZE
STABILITY TO OSCILLOPSIA

By

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Dedication

To Amber,

your love and support keeps me going each and every day

To Connor and Dylan,

who daily inspire me to be better at everything

To Chad,

your mentorship inspired me to pursue a research oriented career to advance patient care

Acknowledgements

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List of Abbreviations

A – Anterior

Abn – Abnormal

Ant – Anterior Semi-Circular Canal

AP – Anterior-Posterior

BVH/H – Bilateral Vestibular Loss / Hypofunction

CNS – Central Nervous System

COM – Center of Mass

COP – Center of Pressure

COR – Cervico-ocular reflex

CPG – Central Pattern Generator

CSD – Cross Spectral Density

DVA – Dynamic visual acuity

F – Female

FRF – Frequency Response Function

GVS – Galvanic vestibular stimulation

H – Horizontal

HIT – Heat Impulse Test

Lat – Lateral Semi-Circular Canal

L – Left

M – Male

ML – Medio-Lateral

Nor – Normal

n/t – Not tested

n/a – Not applicable

OFI – Oscillopsia Functional Impact scale

OSQ – Oscillopsia Severity Questionnaire

OS VAS – Oscillopsia Visual Analogue Scale

P – Posterior

Post – Posterior Semi-Circular Canal

PSD – Power Spectral Density

R – Right

UVL – Unilateral vestibular loss

VAT – Vestibular Autorotation Test

vHIT – Video Head Impulse Test

VOR – Vestibulo-ocular reflex

Chapter 1

Introduction

1.1 Problem Statement

The perception that the environment is stable as we interact with and move through it is largely due to a phenomenon known as gaze stability. The ability to clearly see our environment as we move through it is important for humans. This ability to stabilize the visual world is important for daily tasks such as shopping, obstacle avoidance and manipulation, identification of our location through the ability to read signs, and driving. Gaze stability is a multi-faceted task that requires integration of multiple sensory systems (vision, vestibular, proprioception) and coordination of ocular muscles with postural muscles that control movement of the head (Allison et al., 1996; Della Santina et al., 2002; Mamoto et al., 2002). The profound impact of unstable gaze on daily function is readily observed in individuals with bilateral vestibular disease who often complain of gaze instability and often self-restrict activity as a result (Herdman et al., 2007).

When the biological systems that enable gaze stability fail, the result is oscillopsia (Goldberg et al., 2012). Ford and Walsh first described oscillopsia symptoms as "loss of ocular fixation during movements of the head" (Ford & Walsh, 1936). The term oscillopsia is credited to Brickner in 1936, which he described as apparent motion of a stationary visual scene during head motion or during walking. Gaze stability is traditionally described related to function of the vestibular system and the visual following systems. Bilaterally reduced function of the vestibular system

results in oscillopsia during all head motions, while unilateral vestibular hypofunction only results in oscillopsia with head motions in the direction of the impaired labyrinths.

Oscillopsia is a frequent complaint for individuals with bilateral vestibular loss /hypofunction(BVL/H), but not all individuals with BVH report the same severity of oscillopsia (Baloh et al., 1984). Additionally, oscillopsia severity does not consistently correlate with physiological (i.e. vestibulo-ocular reflex [VOR] and cervico-ocular reflex [COR]) or behavioral assessments (i.e. dynamic visual acuity [DVA]) of vestibular function (Bronstein, 1992; Guinand et al., 2012; Badaracco et al., 2010). There is a disconnect between diagnostic tests and the negative impact of oscillopsia on quality of life. A possible explanation for the inconsistent relationship between subjective and physiological/behavioral measures is that most current physiological measures evaluate vestibular function in the yaw plane using passive head/body rotations (for example rotational chair testing). During most natural movements, there is considerable head motion in the sagittal plane. It may be that stabilization of eye motions with respect to head motions in the sagittal plane is more closely tied to oscillopsia.

There are two aims of this dissertation. The primary aim was to investigate how the task of walking influences gaze stability and to determine whether gaze stability during walking is better than predicted by traditional testing methods for individuals with BVH. The second aim was to investigate the relationship between subjective complaints of oscillopsia and both physiological and behavioral measures of gaze stability using a novel subjective questionnaire.

1.2 Study Objectives

The objectives of this dissertation are to investigate the following specific aims:

1) Characterize eye movements during locomotion with respect to standard physiological and behavioral assessments of vestibular function in individuals with BVH.

Preliminary results indicate stable pitch plane eye movements during walking in individuals with bilateral vestibular loss. We investigated whether the gain-phase characteristics of such eye movements are related to the impact of oscillopsia on activity using a new oscillopsia functional impact scale. Results from diagnostic testing were used to inform the interpretation of gaze stability measured during walking.

Hypothesis: Individuals with more severe complaints of oscillopsia impacting daily life function demonstrated lower gain and a less compensatory eye:head timing relationship in pitch. I predicted that subjective oscillopsia complaints will be more strongly related to eye movement control during walking than to standard vestibular testing results due to the more functional aspect of walking. Degradation of dynamic visual acuity during "passive seated walking" compared to walking will mirror changes in gain and phase relationships across conditions.

2) To determine whether gaze stability during walking in individuals with bilateral vestibular loss is better than would be predicted by traditional vestibular function measures in isolation.

If gaze stability during walking is better than predicted by conventional vestibular testing, it might simply be because the conventional tests do not measure how well residual vestibular function or other mechanisms contribute to gaze stability. Here we will isolate the vestibular contribution to gaze stability during walking by presenting the identical sagittal plane vestibular input that individuals experienced during walking in a passive condition while sitting on a motion platform.

Hypothesis: Gaze stability during active locomotion is better than what would be predicted by passive head motion that replicates walking head movement and is isolated to vestibular stimulation via a head restraint, suggesting a locomotion specific contribution.

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1.3 Dissertation Organization

Chapter 2 will present a systematic review of the literature relating vision to walking and the mechanisms that facilitate stable gaze during head motion. The structural organization presented below demonstrates the systematic progression of experiments (Chapters 3-6, Part 1 through Part 2b below) leading up to the final experiment of this dissertation (Part 3, below).

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│                    Walking                        │
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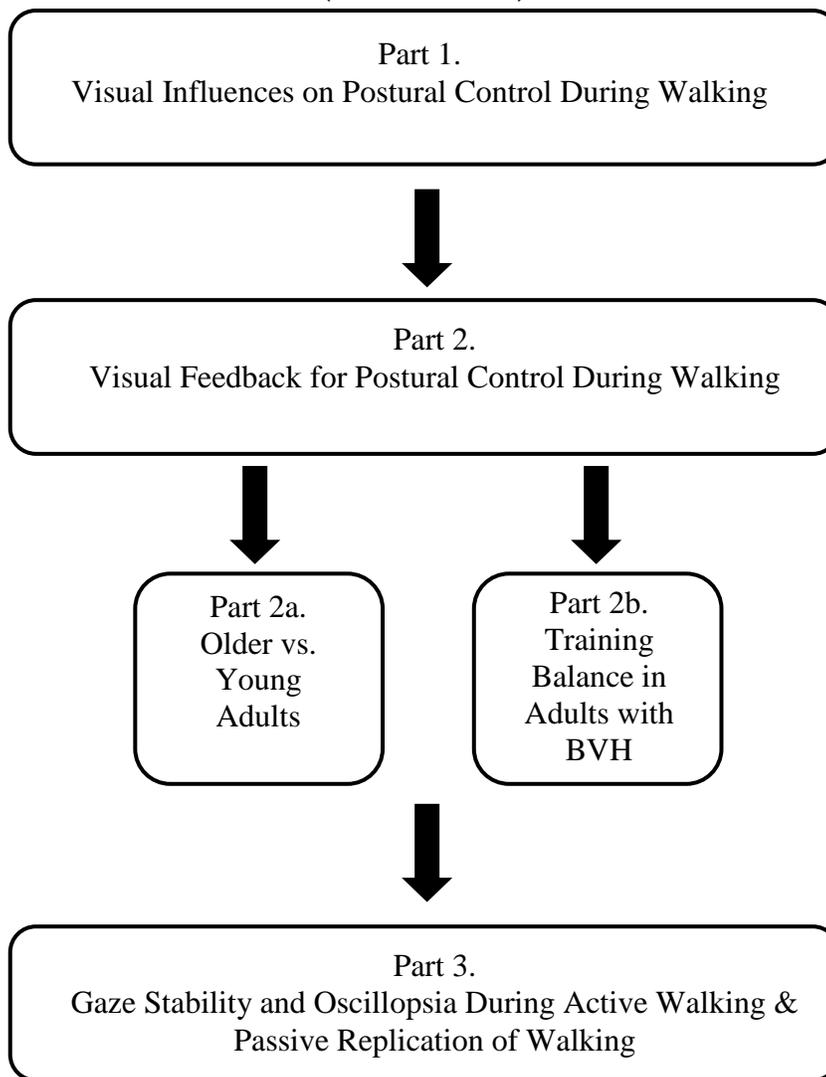
Figure 1-1 Structural organization of the dissertation

Chapter 2

A Review of the Literature

2.1 Introduction

The perception that the environment is stable as we interact with and move through it is largely due to a phenomenon known as gaze stability. When the biological systems that enable gaze stability fail, the resulting apparent motion of non-moving objects during head motion is known as oscillopsia (Goldberg et al., 2012). Ford and Walsh first described symptoms that have become known as oscillopsia as "'jumping' of objects… due to bobbing up and down of the head" (Ford & Walsh, 1936; Wist et al., 1983). Gaze stability is traditionally described as related to function of the vestibular system and the visual following systems (Herdman et al., 2007; Demer, 1995). Reduced reactivity of the vestibular system bilaterally results in subjective complaints of oscillopsia with head motion in any direction, while unilateral vestibular hypofunction only results in oscillopsia with head motions in the direction of the weak labyrinth.

Gaze stability during head motion is largely attributed to combined input from the vestibulo-ocular reflex (VOR), the cervico-ocular reflex (COR), optokinetic nystagmus (OKN), and both pursuit and saccadic eye movements (Gresty et al., 1977; Della Santina et al., 2002; Schubert & Zee, 2010; Borel et al., 1994). Individuals with bilateral loss of vestibular reflexive function (BVH) often complain of apparent motion of the environment with head movement (Ford & Walsh, 1936; Dandy, 1941; Crawford, 1952). In addition to the apparent environmental motion, there is also a degradation of visual acuity that makes recognizing faces or reading signs/labels difficult or impossible

(Crawford, 1952). The smooth pursuit and COR gaze systems are not able to

adequately compensate for high frequency head motion such as that which occurs

during walking (Bronstein, 1992; Grossman & Leigh, 1990; Gresty et al., 1977).

However, not all individuals with a diagnosis of BVH complain about oscillopsia to the

same extent (Bhansali et al., 1993). It has been suggested that a reason for

inconsistent oscillopsia complaints is due to learned anticipatory mechanisms (Lehnen

et al., 2009) which would include feed-forward saccades that occur during head motion

(Schubert & Zee, 2010). It is also possible that due to limitations in vestibular diagnostic

testing, individuals diagnosed with BVH may have substantial residual vestibular

function (Brantberg & Löfqvist, 2007; Agrawal et al., 2013). Canal function is impaired

in 100% of individuals with BVH, but ~60% of those individuals demonstrate some

degree of preserved otolithic function (Agrawal et al., 2013). Canal function evaluated

by head impulse test (HIT) does not require complete absence of function in order to be

identified as pathologic (Perez-& Rama-Lopez, 2003); therefore, there may also be

some preserved canal function in individuals with a diagnosis of BVH based on head

impulse tests. Any preserved vestibular function may allow an enhancement of gaze

stability that would not be predicted by the diagnostic tests used to identify BVH. An

additional mechanism that may contribute to enhanced gaze stability during walking

could be specifically related to the act of walking itself. Recent animal investigations

have identified spinal efference copy mechanisms as primary mechanisms which

stabilize gaze during locomotion (Lambert et al., 2012; von Uckermann et al., 2013).

Since all traditional diagnostic tests for vestibular function are performed with the

individual sitting or lying down, the presence of the specific contribution of walking has

yet to be demonstrated in humans. Development of a method for evaluating

physiological gaze stability during walking will not only enhance diagnostic capability,

but also narrow the gap between artificial testing and normal functional activities.

2.2 The visual system and walking

Of the three primary sensory systems that contribute to walking (vision,

somatosensation, vestibular), vision is the only one capable of providing exteroceptive

information about environmental motion and distance with respect to the body

(Sherrington, 1906). However, the contributions of vision as a sensory system also

include information about body motion with respect to the environment (Gibson, 1958).

As such, vision is a unique sensory system and the same sensory input is used

differently for navigation and postural control during walking (Logan et al., 2010). Vision

has long been known to provide important information that allows humans to walk

through and interact with their environment (Gibson, 1958; Patla, 1998; Rossignol et al.,

2006). As an exteroceptor, the visual system facilitates the detection and recognition of

obstacles to avoid and targets to intercept. Following an appropriate path requires

visual input in both feedforward and feedback capacity, which has been demonstrated

for obstacle clearance, direction changes, and precision stepping (Patla et al., 1991;

Reynolds & Day, 2005).

Motion of objects in the environment with respect to the observer's eye results in

image motion across the retina, known as optic flow. Optic flow contributes to several

aspects of walking: foot placement, gait speed, and trunk motion (Gibson, 1958;

O'Connor & Kuo, 2009; Prokop et al., 1997; Warren et al., 1996; Kay & Warren, 2001).

Parallax is an additional visual cue that provides depth information and is defined by the relative size of two or more objects in the visual field based on two distinct viewpoints (i.e. two eyes). Parallax allows an estimate of target distance to be made and contributes to determination of egocentric path direction (Warren et al., 2001). Visual sensory input contributes to control of both sub-tasks of locomotion: 1) navigation; and 2) equilibrium.

2.2.1 Navigation

During goal oriented locomotion, optic flow has a radial component that emanates from the goal object (i.e. the focus of expansion) and a linear component at the periphery (Warren et al., 1996; Bardy et al., 1999). The visual system decomposes optic flow into a forward motion signal used for navigation and a postural cue to stabilize upright equilibrium (Woolacott et al., 1986). The visual system is capable of interpreting movement direction and velocity from the optic flow field (Warren & Kurtz, 1992). Detection of heading direction was more accurate when the focus of expansion was presented on the fovea, compared to the peripheral retina (Warren & Kurtz, 1992; Crowell & Banks, 1993). A rich visual environment (i.e. optic flow and motion parallax) facilitates more accurate navigational control (Warren et al., 2001). The combination of optic flow and motion parallax not only indicates heading but also obstacle distance and size; all necessary to control limb (foot) placement for obstacle clearance or change in path direction (Patla, 1998; Marigold, 2008; Prévost et al., 2002; Bruggeman et al., 2007). Removal of vision during the last step or two while approaching an obstacle resulted in increased toe clearance over the obstacle, demonstrating a visual

feedforward component to obstacle avoidance (Patla et al., 1991; Patla, 1998). The

increase in toe clearance compared to trials with normal vision reflects the importance

of vision for estimating body location with respect to the environment. Precision foot

placement to stationary targets also includes an online visual feedback component

responsible for increased accuracy (Reynolds & Day, 2005).

Spatio-temporal components of locomotion are easily modulated by optic flow

(Konczak, 1994; Prokop et al., 1997). Optic flow and not polarity of objects in the visual

scene (i.e. trees grow up from the ground) dictated stepping trajectory deviations

following exposure to optic flow that simulated walking around the edge of a curved

room (Nomura et al., 2005). During walking, the location of visual stimuli on the retina

was found to be less important than the structure of the optic flow (Bardy et al., 1999), in

contrast to previous descriptions of differential effects for peripheral retinal versus

central retinal stimulation (Brandt et al., 1973; Berencsi et al., 2005). Optic flow that

appeared to be shifted 15° off vertical in the roll plane using prisms resulted in direction

specific trajectory deviations that were larger at slow speeds (Jahn et al., 2001). During

goal directed locomotion, changes in path direction are precipitated by eye and head

movements that serve to orient the head in the new path direction (Hollands et al.,

2002). This has also been demonstrated for individuals with UVL and BVH during

triangle walking to a target position (Glasauer et al., 2002). For individuals with BVH,

the head motion that precedes a change in direction could be destabilizing due to an

impaired vestibular perception of heading (Fitzpatrick et al.,2006), or due to inaccurate

directional optic flow due to unstable gaze.

Separate from the postural control deficits known to exist for individuals with BVH during standing and walking, pathologic function of the VOR resulting in unstable gaze may also contribute to the staggering gait pattern often observed in individuals with BVH. The fovea can only tolerate retinal slip image velocities of $\leq 2°$ before image acuity begins to be degraded (Demer et al., 1994). A perceived increase in vection speed occurs when a 1 Hz (±2°) "jitter" is superimposed on a constant velocity optic flow signal regardless of whether the observer remained motionless or actively moved their head in a synchronous manner with the "jitter" (Kim & Palmisano, 2008). Poorly compensated eye movements result in the perception of a "jittering or bouncing" environment which could be alter the perceived optic flow velocity. This altered perception could have a destabilizing effect on the gait cycle and on postural control during walking, both of which are influenced by optic flow (Prokop et al., 1997; Warren et al., 1996).

2.2.2 Equilibrium

The visual system contributions to navigation are better understood than the equilibrium specific contributions. Complicating this is the known variable response to visual stimulation which results in either a navigational or equilibrium response (Keshner and Kenyon, 2000). Warren et al. (1996) suggested that the visual system decomposes afferent information into a forward motion signal and a postural cue necessary to maintain upright control. This is consistent with the ideas of Winter (1995) and Wollacott (1986) that locomotion is actually two separate tasks: navigation and postual equilibrium. The visual system is the primary sensory system capable of providing

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exteroceptive information regarding the environment. Visual stimuli during walking affect stride-to-stride foot position, which is thought to contribute to medio-lateral (ML) trunk stability (O'Connor & Kuo, 2009; McAndrew et al., 2010). Variability of upper trunk translation increases in the ML direction compared to control conditions with mediolateral visual scene motion (McAndrew et al., 2010). Logan et al. (2010) recently suggested that trunk postural control over a moving base of support (walking) has two components: trunk position in space (translation) and trunk orientation with respect to vertical, which are separately controlled or influenced by vision during walking.

2.3 The vestibular system and walking

The vestibular system also contributes to both sub-tasks of locomotion (Fitzpatrick et al., 2006). Vestibular sensory information contributes to maintaining the upright orientation of the head on the trunk in order to maintain a stable egocentric reference frame (Pozzo et al., 1990). A stable egocentric reference frame would be important for accurate "spatial navigation" (Cohen, 2000). The head on trunk relationship is no longer stable for individuals with BVH (Pozzo et al., 1991). When walking towards a remembered target, individuals with chronic unilateral vestibular loss (UVL), acute UVL following acoustic neuroma resection, and BVH all demonstrated larger lateral path deviations earlier in the path than healthy individuals (Cohen, 2000; Glasauer et al., 1994). Although total distance walked with eyes closed did not differ between healthy individuals and those with BVH for linear or triangular goal oriented paths (Glasauer et al., 1994; Glasauer et al., 2002); larger end point errors were observed during triangle path walking for individuals with BVH (Glasauer et al., 2002).

This effect was attributed to greater errors in turning magnitude for individuals with BVH, indicating that the vestibular system is only necessary for path integration during turns (Glasauer et al., 2002).

Galvanic vestibular stimulation (GVS) results in trunk and head tilt in the frontal plane during locomotion (Bent et al., 2004) and lateral path deviation (Deshpande & Patla, 2005; Kennedy et al., 2003; Brandt et al., 1999). Fitzpatrick et al. (1999) suggested that GVS during walking may have influenced the perceived trajectory, as individuals consistently deviated toward the side of the anode with eyes closed (Kennedy et al., 2003). They reported two consistent responses; individuals either continued their turn in the direction of the anode or corrected for their initial anode directed path deviation. Caloric irrigation during slow walking on a split belt impairs the ability of healthy subjects to match the speed of a variable speed belt (i.e. right leg) to that of a fixed speed belt (i.e. left leg), but the speed errors were not consistent in direction (Marques et al., 2007). Caloric irrigation during fast walking did not result in speed matching errors (Marques et al., 2007), suggesting a velocity dependent vestibular contribution to the walking pattern (Fitzpatrick et al., 2006; Brandt et al., 1999).

When visual information is altered using prisms in combination with GVS, the magnitude of lateral path deviation was greater than that for GVS or prisms alone but less than GVS with eyes closed (Kennedy et al., 2003). During combined prism and GVS stimulation, individuals always displayed path deviation in the direction of the prism more than with the prism alone (Kennedy et al., 2003). This visual vestibular

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interaction during locomotion is not consistently reported and likely depends on the availability of a visual target (Deshpande & Patla, 2005; Kennedy et al., 2003).

2.4 Gaze stabilization: A mechanistic approach

Often gaze stability is measured or described strictly in terms of the angular VOR, however Crane & Demer (1999) argued that since natural human walking included both angular and linear head motion that the gaze stability system should be modeled with terms that describe both angular and linear contributions. More recently, the combined effect of linear and angular inputs to the pitch VOR was reported to enhance the low frequency VOR (Wood et al., 2009). In this experiment subjects lay on their side in the dark while attempting to fixate an imagined target in the laboratory and the axis of rotation was either aligned with the inter-aural axis or was offset by 0.5 meters. The rotation axis eccentricity resulted in linear acceleration in the direction of the long axis of the body (constant acceleration), as well as tangential to the arc of rotation which varied with rotation frequency.

2.4.1 Vestibulo-ocular reflexes

The vestibulo-ocular reflex is mediated by a short latency pathway from the peripheral vestibular afferents to the target extra-ocular muscles responsible for control of eye in orbit position. The vestibular system generates both angular (semi-circular canals) and linear (saccule and utricle) VORs that contribute to maintaining visual fixation on a target (Leigh & Brandt, 1993; Fetter, 2007). For rotational frequencies below 0.04 Hz the semicircular canal afferents transmit a signal that corresponds to

head acceleration. For rotational frequencies above 0.04 Hz the semicircular canal

afferents transmit a signal that corresponds to head velocity (Jones & Milsum, 1971;

Baloh & Kerber, 2011).

The simplest case of the VOR, the horizontal gaze center, is depicted in Figure

2-1. The horizontal gaze center includes both excitatory and inhibitory projections

during head rotation about a vertical axis toward the left. Figure 2-1 represents the

angular VOR from the horizontal semi-circular canals, and the eyes are shown to rotate

in the opposite direction of the head motion.
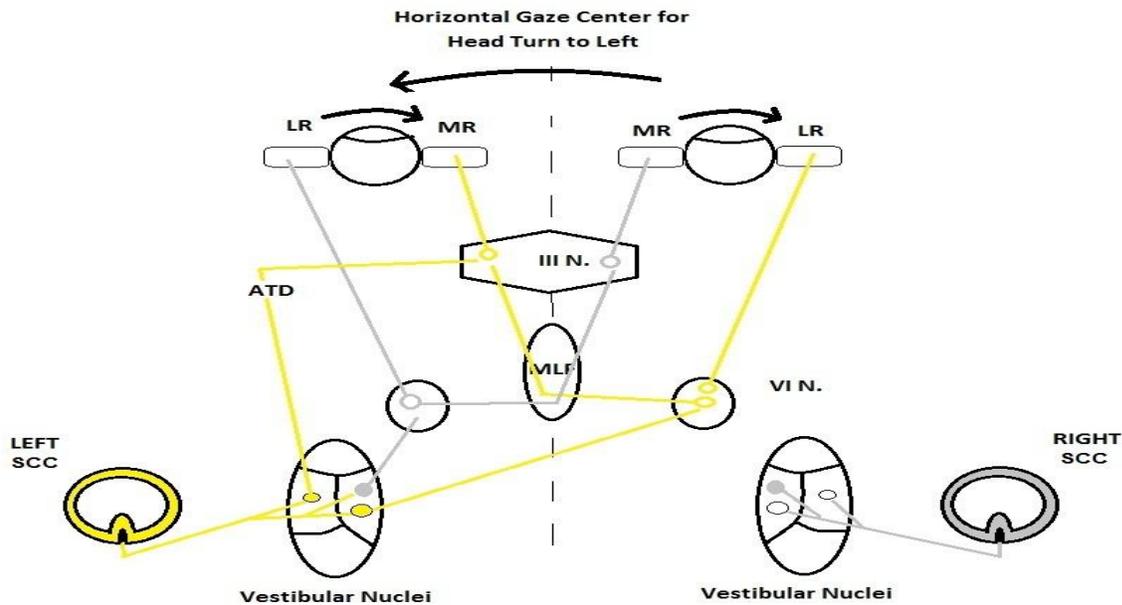
Figure 2-1. Schematic of the horizontal gaze center and neural activations during head rotation to the left with excitatory VOR connections indicated in yellow and inhibitory connections indicated in gray. SCC- semi-circular canal, LR – lateral rectus, MR – medial rectus, ATD – ascending tract of Deiter's, MLF- medial longitudinal fasciculus, III N. – Oculomotor nuclei, VI N.-Abducens nuclei

The linear component of the VOR provides corrections for target distance and head tilt

(Leigh & Brandt, 1993; Gresty et al., 1992; Moore et al., 2001). The ability of the

angular and linear VOR to work synergistically is important during walking since the

head motion is a combination of angular and linear paths (Crane & Demer, 1999). Each

semicircular canal is capable of detecting rotation to either side; ipsilateral rotation

results in excitation (increased firing rate) of Type I secondary vestibular neurons and

simultaneous inhibition (decreased firing rate) of Type II neurons while contralateral

rotation has the opposite effect (Leigh & Zee, 2006). This mechanism allows for

contralateral rotation signals to be sent through the vestibular commissural pathway to

the contralateral vestibular nuclei to facilitate gaze stabilization (Baloh & Kerber, 2011).

This mechanism may be responsible for aspects of adaptation following injury to the

vestibular system.

2.42 Cervico-ocular reflexes

Neck proprioception can also play a role in stabilizing gaze via the cervico-ocular

reflex (Bronstein, 1992). In healthy individuals the gain of the cervico-ocular reflex

(COR) is very low and may not contribute significantly to gaze stability (Bronstein et al.,

1991; Carmona & Nieto, 2005). However, for individuals with vestibular deficits the

COR demonstrates plasticity and the gain of eye motion to neck motion increases

(Carmona & Nieto, 2005; Bronstein, 1992). Neuro-plastic changes in the COR can be

observed in healthy individuals after training that requires tracking of a visual target that

moves in-phase with the trunk while the trunk is rotated under the head (Mandellos et

al., 2006). The limitation for the COR is that, like the optokinetic mediated response, it

saturates as velocity increases making it only functional for very low frequency

movements of the head with respect to the trunk (Mergner et al., 1998). This would not

make the isolated COR a good candidate for stabilization of gaze during natural head movements that occur during walking and may explain the poor relationship between COR gain and complaints of oscillopsia (Bronstein, 1992). It may be that during active walking the COR contributes to gaze stability to improve low frequency gaze stability.

2.4.3 Optokinetic & Oculomotor

Full field motion of the visual environment is known to elicit eye movements that allow temporary fixation on a portion of the moving visual field (Baloh & Kerber, 2011). The method of tracking allows intermittently stable gaze on an object(s) as it moves past the observer's eye. Optokinetic eye movements can easily be seen by observing the eyes of another person as they look out the window of a moving train. This results in a perception of vection or apparent rotation during stationary viewing (Brandt et al., 1973) and also has effects on postural sway (Keshner & Kenyon, 2000; Clément & Lathan, 1998). A major limitation to relying on optokinetic eye movements to stabilize gaze is that limited velocity information could be derived from the visual scene since the eyes would track the environments. Since visual scene velocity is used primarily for postural control this would result in posture and walking impairments (Jeka et al., 2004; Prokop, 1997), which would effectively destabilize the head, providing a further challenge to gaze stability mechanisms (Pozzo et al., 1990).

Pursuit eye movements allow a moving object of interest to be maintained on the fovea, reducing retinal slip. Pursuit movements are triggered primarily by target velocity, which results in retinal slip when the target velocity exceeds the eye velocity (Robinson, 1968). Latency of smooth pursuit eye movements is about 100-125

milliseconds when following a moving target after a trajectory change (Robinson, 1968; Orban de Xivry & Lefèvre, 2007). This latency makes tracking fast moving objects difficult, particularly if the object rapidly changes velocity or moves in an unpredictable manner. For predictable target movements, anticipation of the target velocity may be used to initiate pursuit movements prior to onset of target motion, reducing the initial tracking error (Orban de Xivry & Lefèvre, 2007). The pursuit system also contributes to gaze stability during combined head and target motion, when the head follows the target motion (Gordon et al., 2008). During relatively slow and predictable head motions, the pursuit system may allow for greater gaze stability; however, head motions during walking are not entirely predictable despite having some rhythmic qualities and include velocities ~90 degrees/second (King et al., 1992; Demer et al., 1994). When relying on smooth pursuit to maintain visual acuity while tracking an object with the head still, visual acuity is degraded to a clinically measurable degree when the target moves at 20 degrees/second and visual acuity degrades to 20/200 (legal blindness) for target velocities of 100 degrees/second (Demer et al., 1994).

Another way around an inability to keep up with fast moving targets is to incorporate the saccade system, which acts to supplement the pursuit system under such conditions (Orban de Xivry & Lefèvre, 2007). A position error of the image on the retina will trigger a saccade to allow re-fixation of the target. The combined action of the pursuit and saccade systems and the failure of the pursuit system during high velocity head motion can best be exemplified by re-fixation saccade(s) following a HIT for an individual with acute UVL or BVH (Halmagyi & Curthoys, 1988). In this case, eye motion during head motion is not compensatory in magnitude or timing, and the eyes

end up not looking at the target. This position error triggers a corrective saccade back to the original target. Individuals that are well compensated following an insult to the vestibular system demonstrate corrective saccades during head motion, known as covert saccades (Schubert & Zee, 2010). These covert saccades contribute to gaze stability by reducing the gaze position error and/or the gaze velocity error of the target image projected on to the retina (Peng et al., 2004).

2.4.4 Active vs. Passive head movement

Vestibular assessments that involve head motion are generally performed in a passive way; the patient is asked not to help. Passive rotational testing either via head impulse testing or rotational chair testing are the primary examples of this. Differences in VOR performance are known to occur when self-generated head rotation is compared to passively received head rotation. Gaze stability is enhanced during active head rotation, even in the presence of vestibular disease (Della Santina et al., 2002). Feed-forward behavior or efference copy information is thought to play a role in this augmentation of the VOR for self-generated predictable motion (Della Santina et al., 2002; Schubert & Zee, 2010). Substitution from the somatosensory system (i.e. the cervico-ocular reflex) may also contribute to gaze stability, although the absolute perception thresholds are both greater and more variable when the vestibular system is absent (Valko et al., 2012).

Greater retinal slip should be expected when relying solely or dominantly on visual tracking mechanisms, such as during a head still visual tracking task of a fast moving object. Phase delay and retinal slip increased with frequency and decreased

with target distance (Gielen et al., 2004). Phase delay and retinal slip improved with active self-motion compared to passive tracking of a moving visual target (Gielen et al., 2004). This is consistent with the difference in response latency of the VOR (~12 ms) and pursuit latency (~125 ms) of the visual system (Baloh & Kerber, 2010; Ackerly & Barnes, 2011). For low frequency head rotation, the visual tracking system and feed-forward contributions to gaze stability would be greater than the VOR contributions. Small phase delay for low frequency head rotation likely represents an enhancement from feed-forward extra-retinal contributions and to a lesser extent the VOR for low frequency head motions (Ackerly & Barnes, 2011). During head free tracking of an extinguished visual target the gain of eye velocity to target velocity was closer to ideal than during head fixed conditions (Ackerly & Barnes, 2011). These extinguished target experiments demonstrate the importance of expectation of target motion, the VOR, and tracking systems working together such that an intact VOR facilitates tracking of moving objects during head motion. This is important as the point of regard during free walking changes via gaze shifts to different targets, and we need to be able to see clearly when fixating both moving and non-moving targets.

Walking has been described as a periodic limit cycle (McGeer, 1990; Bauby & Kuo, 2000). The periodicity of the limit cycle suggests that in the absence of perturbations or noise the cyclic head motions could be predicted by a feed-forward system which could contribute to gaze stability. As with seated active head movements (Ackerly & Barnes, 2011), gaze behavior may be enhanced during active walking in ways that are not captured by passive diagnostic tests. Active head rotation in freely behaving guinea pigs with BVH results in eye movements that are compensatory for the

head rotations (Shanidze et al., 2010). The latency of those eye movements (~1ms) suggests an anticipatory behavior mediates those eye movements rather than sensory feedback contributions. Despite head motion during walking being semi-periodic, it also displays unpredictable characteristics (Grossman et al., 1989). The pseudo-random head motion during walking is poorly compensated for in conditions of vestibular loss, or altered vestibular calibration. Exposure to prolonged micro-gravity is known to alter head and trunk coordination (Bloomberg et al., 1997). Astronauts returning from space often experience transient oscillopsia which may be related to more random, less predictable head motions during walking, which could be attributed to the sudden change in otolith input on return to earth (Berthoz et al., 1986). The less predictable head motions would affect the stability of the head in space (Pozzo et al., 1991). Thus, a feed-forward system alone may not adequately stabilize gaze during walking when the VOR is impaired.

2.4.5 Locomotion Specific Control

The importance of gaze stability during locomotion can best be explained by the report of a physician with bilateral vestibular disease who reported that he had to stop walking in order to read the print on signs or recognize faces (Crawford, 1952). It has been suggested that the VOR developed for the purpose of allowing stable vision specifically during locomotion (Walls, 1962; Leigh & Brandt, 1993). The inability of smooth pursuit and optokinetic systems to adequately compensate for the higher frequency head movements that occur during walking supports this view (Gresty et al., 1977).

The vestibular system also contributes to walking through mechanisms other than the VOR. During over-ground walking individuals with an intact vestibular system demonstrate head pitch rotations that are compensatory in direction and timing to counter vertical head translation (Pozzo et al., 1990; Demer & Crane, 2001). This compensatory head pitch and head translation relationship during natural movements has been described as a mechanism to improve gaze stability during walking by reducing the overall head pitch in space (Demer & Crane, 2001). Individuals with BVH have lost the consistent head pitch and vertical translation relationship seen in healthy individuals (Pozzo et al., 1991). Individuals with BVH also demonstrated a decrease in head pitch amplitude when walking with eyes closed compared to eyes open (Pozzo et al., 1991). The absence of a consistent covariation between vertical head translation and head pitch during walking would result in a more unstable platform for the eyes. These alterations in the timing relationship of head pitch and vertical translation would limit the effectiveness of anticipatory compensation strategies to enhance gaze instability when the VOR does not function.

Vestibular afferents also contribute to leg muscle activation during walking which could influence head stability in space and via small perturbations to course trajectory. Leg muscle activity demonstrates a gait cycle phase dependent response to stochastic electrical stimulation (SVS) of the vestibular system (Isles et al., 2006; Blouin et al., 2011). This SVS modulation to muscle activity occurred early in stance and was interpreted to provide stability to the stance ankle which would also contribute to the medio-lateral placement of the swing leg (Blouin et al., 2011; Bent et al., 2004). Greater control of the medio-lateral swing leg placement and increased stability of the stance leg

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ankle would contribute to overall path consistency. The extent of path deviation due to vestibular stimulation during walking depended on the gait cycle phase when the GVS was applied (Bent et al., 2004). Early step initiation was unaffected by GVS, while lateral COP trajectory at gait termination was significantly greater with GVS than in control trials suggesting a vestibular contribution to trunk on leg movement at gait termination (Bent et al., 2002). Individuals with unilateral or bilateral vestibular loss demonstrate path deviations while walking a remembered path (Glasauer et al., 1994; Glasauer et al., 2002; Borel et al., 2004). A damaged vestibular system negatively impacts walking ability through a combination of altered postural control and impaired external space orientation (Bent et al., 2002; Borel et al., 2014). Overall larger movements of the head in space during walking will further compound the problem of gaze instability that results from BVH.

Individuals with BVH will not be able to rely on the peripheral vestibular afferents to signal head motion, but the vestibular nuclei serve as a connection point between those afferents and the target oculomotor neurons. A walking representation in the vestibular nuclei might contribute to gaze stability during walking, especially in cases of vestibular loss. Both active and passive leg motion is represented in the cat vestibular nuclei from somatosensory projections (Arshian et al., 2014). The leg motion information was integrated with whole body rotational information from the vestibular end organs. This representation of leg motion in the vestibular nuclei may serve to enhance gaze stability in a walking specific manner. The combined leg-head motion representation could serve to indirectly influence gaze stability by contributing to motion of the head in space or to act directly on gaze stability by directing eye motions.

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Mechanistically, leg motion representation in the vestibular nuclei could come from an efference copy and enhance gaze stability during walking via anticipatory contributions. There is evidence of a spinal efference copy that is responsible for locomotion gaze stability in some animal models (Lambert et al., 2012; McCall et al., 2013; von Uckermann et al., 2013). On the other hand, information regarding leg motion found in the vestibular nuclei could represent sensory feedback with inherent time delays that might allow for appropriately sized eye movement responses (gain) but the timing (phase) would be impacted by the feedback delay.

2.5 Gaze instability: impact of oscillopsia

Retinal slip exceeds the 2-4º/sec tolerance during head motion for individuals with BVH accounting for reports of oscillopsia in this population (Demer & Amjadi, 1993). The presence of oscillopsia relates to reduced quality of life measured by reduction in activity participation, elevated economic burden, and self-imposed limitations on driving (Ward et al., 2013; Sun et al., 2014). In order to understand the impact and potential disability that oscillopsia can have on a person's life we must 1) consider the problems that gaze instability produces; and 2) be able to characterize the domains of activity and participation that are restricted (Alghwiri et al., 2011). Imagine that every time you went grocery shopping, you had to stop walking to read the labels on packages. Or when traveling you miss a connecting flight because while walking down the concourse you could not read the gate numbers. JC, a physician who acquired BVH, was unable to distinguish faces or read signs when walking (Crawford, 1952). His compensation strategy to overcome this problem was to greet every person

he walked past. However, the effectiveness of this compensation strategy may not be effective for everyone and it only addresses interpersonal interaction and not problems related to reading street signs or interacting with a cell phone. The problems related to gaze instability occur during all head motions for individuals with BVH, including driving, flying, and riding in a vehicle as a passenger (Hillman et al., 1999; Cohen et al., 2003). The nature of vestibular disease, completeness of vestibular loss, and degree of compensation may also contribute to the severity of complaints with respect to daily tasks (Cohen et al., 2003; MacDougall et al., 2009; Ward et al., 2013).

There are several subjective questionnaires that address the symptoms and functional difficulties for individuals with vestibular disorders including the Dizziness Handicap Inventory (Jacobson & Newman, 1990), Visual Vertigo Analogue Scale (Dannenbaum et al., 2011), and the Activities-Specific-Balance Confidence Scale (Powell & Myers, 1995). Only a few reported questionnaires are specifically designed to capture subjective complaints of oscillopsia. The oscillopsia Visual Analogue Scale (OS VAS) was adapted to measure oscillopsia by Schubert and colleagues (2002). The OS VAS provides a quick assessment of symptom severity, but is limited in that it does not characterize how oscillopsia influences function. A newer subjective scale, the Oscillopsia Severity Questionnaire (OSQ) (Guinand et al., 2012), characterizes the frequency of environmental motion symptoms under several different environment/task contexts. The OSQ includes perception of environmental motion that is not dependent on head motion (i.e. while reading or watching TV) in addition to environmental motion that is dependent on head motion. The OSQ score is the average frequency of all the individual symptom frequency scores. Interpreting scores from the OSQ as a single

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construct for oscillopsia may be an over simplification. This might explain the limited

relationship between DVA and OSQ scores (Guinand et al., 2012). Similar to the VAS,

the OSQ is not able to characterize the functional impact (i.e. activity participation) of

oscillopsia. There is a need for a scale that is able to capture symptom severity as well

as the functional impact (i.e. is activity participation restricted related to symptoms) that

is sensitive and specific to oscillopsia.

2.6 Measures of gaze stability and oscillopsia

Methods for measuring gaze stability can be classified into one of two categories:

physiologic or behavioral. The physiologic category is defined as measurement of

physiologic function (i.e. the VOR). The behavioral category is defined as indirect

measures of physiologic function demonstrated via behavioral assessments (i.e. DVA).

Relying solely on the physiologic or behavioral measures to characterize the gaze

stability system, without including the patient's subjective history of oscillopsia, provides

an incomplete perspective of the gaze stability system (Brandt & Strupp, 2005; Sullivan,

2003). The importance of the subjective complaints regarding gaze stability (i.e.

oscillopsia) should not be overlooked, especially since individuals with similar diagnoses

based on physiologic measurements do not report the same disability from or severity of

oscillopsia (Grunfeld et al., 2000).

2.6.1 Physiologic measures

The primary physiological measurement of gaze stability is the vestibular

reactivity to rotational stimulation which is often assessed using the head impulse test

(HIT), caloric stimulation, or rotational testing (Fetter, 2007; Clarke, 2010). The most common laboratory measure of vestibular reactivity is bi-thermal caloric stimulation (Perez & Rama-Lopez, 2003). Bi-thermal caloric irrigation (air or water) of the ear canal induces a sensation of spinning in individuals with an intact horizontal semicircular canal. The warmer (cooler) temperature gradient introduced to the endolymph fluid in the horizontal semicircular canal results in thermodynamic flow of the endolymphatic fluid which results in displacement of the cupula that acts as an excitatory (inhibitory) stimulus (Barber & Stockwell, 1980). Mono-thermal (only cool or only warm) irrigations have been proposed as methods that could reliably identify unilateral vestibular abnormalities with reasonable false negative (< 1% for cool) but greater than 75% with normal bi-thermal tests were found to be positive using mono-thermal tests (Enticott et al., 2003). Caloric testing has the benefit of identifying laterality in vestibular disease, but the thermal stimuli corresponds to rotations of approximately .003 Hz and is presented with the individual laying down. The artificial nature of a caloric stimulus (very low frequency, no actual rotation) while allowing a lateralization of vestibular reactivity may not be very meaningful with respect to gaze stability requirements during walking due to the frequency range of head movements during walking (King et al., 1992).

Rotational testing often provides a more complete picture of vestibular function, especially when combined with caloric stimulation. Baloh and colleagues reported on preserved vestibular horizontal canal reactivity with rotational testing, with gains that increased with increasing frequency, for individuals with little to no vestibular reactivity from caloric stimulation (Baloh et al., 1984). This demonstrates that low frequency

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caloric tests do not provide a comprehensive picture of vestibular function. Rotational

testing may be the most controlled way to test the VOR at specific frequencies using a

rotational chair or moving platform, where angular rotation is the only stimulus.

Sinusoidal or step impulses are used to evaluate either low or high frequency angular

vestibular function in isolation (Jenkins et al., 1982; Honrubia et al., 1985). Traditional

vestibular function testing includes low frequency passive rotation while seated with the

head fixed to the rotating chair (Allison et al., 1996). Individuals with BVH typically

demonstrate lower gains than healthy individuals, but their measured gain increases

with frequency (Honrubia et al., 1985). Vertical axis rotational chair testing can only

evaluate the reactivity of the horizontal semicircular canals, and does not assess the

reactivity of the vertical canals. The use of 6 degree of freedom hexapods has allowed

assessment of vertical canal function (Goumans et al., 2010; Clarke, 2010). The

magnitude of the eye velocity response to head velocity is referred to as gain, with ideal

values being close to 1. The timing of the eye movements in response to the rotational

stimulation is known as phase, and individuals with BVH demonstrate a characteristic

phase advance with vertical axis rotation (Baloh et al., 1984; Honrubia et al., 1985).

Phase lag increased with frequency for active and passive oscillatory head rotation for

individuals with BVH (Gresty et al., 1977). A limitation to extrapolating VOR gain values

derived using this approach is that during human locomotion angular head rotation does

not exist without corresponding linear translation (Demer & Crane, 2001).

     The non-instrumented HIT characterizes the VOR in a binary way as intact

(negative test) or impaired (positive test) by observing for the presence of re-fixation

saccades (Halmagyi & Curthoys, 1988). The HIT has been described as the bedside

criterion test for assessing vestibular function and is described as one of three tests in a battery that are capable of diagnosing severe BVH (Petersen et al., 2013); although others suggest that only when combined with laboratory tests (caloric or rotary chair) can the diagnosis be definite (Kim et al., 2011). The HIT is a brief high acceleration test designed to characterize the high frequency range of head movements where eye movements mediated by the pursuit, cervical afferent, or optokinetic systems can not effectively compensate, and it is thought to be an adequate companion test for caloric tests which correspond to very low frequency head rotation (Clarke, 2010). Canal specific HIT allows characterization of vestibular reactivity for each individual semicircular canal, both horizontal and all four vertical semicircular canals can be tested in this way allowing a much more complete characterization of the angular VOR (Halmagyi et al., 2001). Despite having very high specificity (.91) the non-instrumented HIT has some diagnostic problems; the sensitivity of the HIT is only .45, and the minimum percentage of canal paresis required to correctly identify a positive HIT is 42.5-60% (Perez & Rama-Lopez, 2003; Cohen et al., 2014). An advantage of the instrumented HIT is that similar to rotary testing the VOR can be characterized by the gain of eye velocity with respect to head velocity, with an ideal gain being 1.0 (Leigh & Brandt, 1993; MacDougall et al., 2013). Another advantage to instrumented HIT is the ability to quantify retinal slip. Retinal slip for a non-moving fixation object refers to the motion of the object image across the retina as the eye rotates in space relative to the fixation object (Crane & Demer, 1997). Gaze instability from loss of vestibular function results in retinal image slip that exceeds the tolerable limit of 2-4°/s (Demer et al., 1994; Crane & Demer, 1997).

These methods of probing vestibular reactivity remain artificial in nature, and the relevance of these assessments to natural functional behavior has been questioned (Demer et al., 2001; Badaracco et al 2010). In an effort to address the artificial nature of standard vestibular function tests, the Vestibular Autorotation Test (VAT) was developed. The VAT incorporates metronome cued active sinusoidal head rotational movements while the patient is seated and the VAT has been suggested as a more natural assessment of vestibular function capable of measuring vestibular reactivity at higher frequencies (O'Leary & Davis, 1998). The problem with the VAT is that sinusoidal head rotation is predictable and patients can use efference copies of their rotation, incorporate a cervico-ocular reflex, or generate predictive saccades to stabilize their gaze (Demer & Crane, 2001; Della Santina et al., 2002; Schubert & Zee, 2010). Therefore, interpretation of the VAT as an assessment of vestibular function instead of a composite actively controlled gaze stabilization test may be inappropriate and the utility of the VAT has been questioned (Guyot & Psillas, 1997). A limitation to all of the above tests is that vestibular assessment is triggered by an unnatural stimulus and is not performed during a functional activity (Robinson, 1968).

2.6.2 Perceptual measures

Gaze stability requires the ability to keep an object in the fovea (Orban de Xivry & Lefèvre, 2007), but small drifts of the target on the retina can occur without resulting in gaze impairment (Demer & Amjadi, 1993). Dynamic visual acuity (DVA) is the difference in visual acuity measured on a LogMAR scale between head stationary (i.e. quiet sitting / standing) tasks and dynamic head motion (i.e. head rotation or head

motion during walking) tasks (Schubert et al., 2002). DVA testing characterizes gaze stability impairments with head motion, and is considered a functional measure of gaze stability (Badaracco et al., 2010; Peters et al., 2012; Scherer et al., 2008). This is a behavioral/perceptual test that has greater interpretability compared to tests of physiologic function, particularly because many physiological tests are performed in a more artificial way. DVA testing has similar problems as the VAT, unless it is performed passively with a computer generated optotype that only is presented briefly when head velocity exceeds a threshold (Schubert et al., 2002; Badaracco et al., 2010; Peters et al., 2012). Some reports have used longer optotype presentation periods ~500ms (Hillman et al., 1999; Peters & Bloomberg, 2005), and it has been reported that longer optotype presentations improve discrimination between healthy individuals and those with vestibular disease (Peters et al., 2013). There are also known differences in DVA score depending on whether the head motion is actively or passively generated, with better scores (more stable gaze) found during active head motion (Herdman et al., 2001; Schubert et al., 2008). DVA improvement during active head rotations is thought to be mediated by an efference copy that allows for improved anticipation of head motion and the resulting eye motion. Several reports examined DVA during walking as a more functional method of describing gaze stability (Badaracco et al., 2007; Lambert et al., 2010). Measuring visual acuity ability during walking has promise for characterizing gaze stability in a more functionally meaningful way. Retinal slip in healthy individuals during locomotion on a treadmill has been reported as less than 4°/s, but retinal slip magnitude depends on target distance (Crane & Demer, 1997). Target distance is known to impact visual acuity, as near targets require convergence between

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the eyes in addition to definite contributions from angular and linear VOR to effectively

stabilize gaze (Peters & Bloomberg, 2005; Peters et al., 2013).

2.7 Oscillopsia and rehabilitation

Rehabilitation for individuals with BVH historically focused on sensory

substitution training for balance (Herdman, 1998; Brown et al., 2001). The subjective

problem of oscillopsia would only be addressed through exercises targeting gaze

stabilization, but those are often omitted from treatment when there is a diagnosis of

BVH (Bittar et al., 2006). As technology improves, newer options for treatment are

emerging that may prove beneficial when targeted toward the mechanisms that cause

of oscillopsia.

2.7.1 Traditional rehabilitation

As the primary cause of BVH has been attributed to gentamycin, the first step in

minimizing BVH symptoms is to discontinue the gentamycin (Hain et al., 2013).   Once

the damage is done, traditional rehabilitation suggests emphasizing sensory substitution

strategies through vestibular rehabilitation as the primary recourse for individuals with

BVH (Han et al., 2011; Herdman, 1998; Brown et al., 2001). In the case of BVH,

recovery of balance ability is primarily thought to occur due to sensory substitution

(McCall & Yates, 2011). Sensory augmentation/substitution strategies that enhance

postural control may not work as well for improving the VOR (Ward et al., 2013), and

may have little impact on oscillopsia. Thus, individuals with BVH are taught

compensatory strategies to minimize the effect of oscillopsia, like blinking or generating

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a saccade during head motion. These are imperfect compensatory strategies to minimize the disturbing sensation of oscillopsia. Despite not being perfect strategies, for some individuals with BVH this may improve but not ameliorate their symptoms.

2.7.2 Novel rehabilitation strategies

Currently, individuals with BVH are limited in their treatment options and the symptom improvement that they experience is typically incomplete. Advances in medical treatment options like an electrical vestibular prosthesis (Ward et al., 2013; Perez Fornos et al., 2014) and gene therapy to regenerate vestibular hair cells (Albu & Muresanu, 2012; Staecker et al., 2011) hold promise for individuals with BVH, but they are not currently available to most individuals. Vestibular rehabilitation techniques are also advancing with technology, and multi-sensory training in virtual reality may facilitate sensory adaptation in ways previously not available.

2.8 Summary

The ability to maintain stable vision while moving is an important issue for individuals with vestibular loss. Oscillopsia contributes to poor quality of life and is related to reduced activity participation (Ward et al., 2013). Current rehabilitation for gaze stability consists of active head rotations while attempting to fixate on a target (Han et al., 2011). Due to the postural impairments that are also associated with BVH these are often performed when sitting and occasionally when standing (Han et al., 2011; Keim et al., 1992). Evidence for locomotion specific efference copy contributions to gaze stability has recently been demonstrated in animal models (Combes et al.,

2008; Lambert et al., 2012; Arshian et al., 2014), which could suggest a paradigm shift

in the rehabilitation approach for individuals with BVH. If a walking specific neural

signal for gaze stability does exist then it follows that plastic adaptation of this

mechanism can only take place if task specific training is performed while walking

(Fleming et al., 2014). Demonstrating that gaze stability during active walking is better

than would be predicted by passive simulation of walking would provide supporting

evidence for future clinical trials to investigate walking specific visual acuity training.

Chapter 3 Experiment 1
Visual Control of Trunk Translation and Orientation During Locomotion

This Chapter has been published as:

3.1 Abstract

Previous studies have suggested distinct control of gait characteristics in the anterior-posterior (AP) and medial-lateral (ML) directions in response to visual input. Responses were larger to a ML visual stimulus, suggesting that vision plays a larger role in stabilizing gait in the ML direction. Here we investigated responses of the trunk during locomotion to determine if a similar direction dependence is observed. We hypothesized that translation of the trunk would show a similar ML dependence on vision, but that angular deviations of the trunk would show equivalent responses in all directions. Subjects stood or walked on a treadmill at 5 km/hr while viewing a virtual wall of white triangles that moved in either the AP or ML direction according to a broadband input stimulus. Frequency response functions between the visual scene motion and trunk kinematics revealed that trunk translation gain was larger across all frequencies during walking compared to standing. Trunk orientation responses were not different from standing at very low frequencies; however, at high frequencies trunk orientation gain was much higher during walking. Larger gains in response to ML visual scene motion were found for all trunk movements. Higher gains in the ML direction while walking suggest that visual feedback may contribute more to the stability of trunk movements in the ML direction. Vision modified trunk movement behavior on both a slow (translation) and fast (orientation) time-scale suggesting a priority for minimizing

angular deviations of the trunk. Overall, trunk responses to visual input were consistent

with the theme that control of locomotion requires higher-level sensory input to maintain

stability in the medial-lateral direction.

3.2 Introduction

Vision has long been known to provide important information for humans to walk through and interact with their environment (Gibson 1958; Patla 1998). Previous evidence suggests that the visual system decomposes information into a forward motion signal used for navigation and a postural cue to stabilize upright equilibrium (Woolacott et al. 1986). Investigations have demonstrated that optic flow contributes to multiple aspects of human walking including modulation of: gait parameters such as walking velocity and stride length (Varraine et al. 2002; Prokop et al. 1997; Konczak 1994; Lamontagne et al. 2007); foot placement variability (Patla & Vickers 2003; Reynolds & Day 2005; O'Connor & Kuo 2009; McAndrew et al. 2010); steering and obstacle avoidance (Warren et al. 2001; Marigold 2008; Bruggeman et al. 2007; Patla 1998); and postural stability (Warren et al. 1996; Bardy et al. 1999; Logan et al. 2010; McAndrew et al. 2010).

In the current study, we investigate the use of vision to stabilize trunk motion in different planes of movement. Previous studies have shown that kinematic responses to a visual stimulus are larger in magnitude in the medial-lateral (ML) direction than in the anterior-posterior (AP) direction (Bauby & Kuo 2000; Warren et al. 1996; O'Connor & Kuo 2009; McAndrew et al. 2010). Models of passive walkers without active control have been used to interpret such results. Kuo (1999) showed that a three-dimensional passive walker is stable in the AP direction but unstable in the ML direction. Stability means that small perturbations to the limit cycle are dissipated, insuring return to a cyclical gait pattern. Thus, differences in passive stability would predict larger responses to a limit cycle perturbation in the ML than the AP direction.

To translate this result from passive walkers to human walkers, Bauby and Kuo (2000) hypothesized that with somatosensory feedback mediated by the spinal cord, the multi-segment legs of humans behave like the single-segment legs of a passive walker. Somatosensory feedback provides AP stability, but high-level neural feedback provided by vision and the vestibular system is necessary for ML stability. As a consequence of noise due to high-level neural feedback, they predicted that lateral foot placement would show greater variability than fore-aft foot placement. They further predicted that removing vision would increase lateral variability more than fore-aft variability. Their experimental results supported these predictions. Human subjects walking over ground with eyes open displayed 79% more variability in lateral step width than in the fore-aft step length, and closing the eyes produced a greater increase in lateral variability than in fore-aft variability. In a related study, O'Connor & Kuo (2009) showed that subjects walking on a treadmill were 10 times more sensitive to visual-scene movement in the ML than AP direction (O'Connor & Kuo 2009). These modeling and experimental results suggest that vision plays a greater role in stabilizing the gait cycle in the ML direction than in the AP direction.

The studies cited above are based on gait parameters such as step width and length variability. To gain a better understanding of the locomotor control system, it is important to consider control of the trunk as well. Logan et al. (2010) recently emphasized that trunk motion in response to visual scene motion while walking can be decomposed into two simultaneously occurring components: absolute trunk position in space (translation) and trunk orientation with respect to vertical. Despite a strong mechanical coupling between trunk translation and orientation the response to visual

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scene motion was different. They showed that gain relative to visual stimulation in the fore-aft direction was smaller for trunk orientation than trunk translation, which was interpreted as vision simultaneously contributing to different sub-tasks (upright stability vs. navigation) of walking. The larger gain for trunk translation reflected visual scene motion "pushing" the trunk (body) in space to a greater extent than causing the trunk to lean. Moreover, ML and AP visual scene motion has directional effects on ML and AP trunk translation variability during walking, with greater effects compared to control conditions (McAndrew et al. 2010). Their results suggest a directionally specific increase in trunk displacement variability in response to visual scene motion (i.e. ML variability increased more with ML visual scene motion). Such results suggest that vision may play a greater role in stabilizing trunk displacement in the ML direction than in the AP direction, similar to findings with foot placement (O'Connor & Kuo 2009). Most of the studies referenced above focused on low frequency visual scene motion corresponding low frequency (longer time scale) responses (McAndrew et al. 2010; O'Connor & Kuo 2009). It is unclear if directionally specific behavior of trunk motion holds at higher frequencies that would require a much faster response.

However, control of trunk orientation during walking has not been studied extensively. Being the most massive segment of the body, the trunk must be balanced as the legs propel the body forward, and any deviation from vertical must be actively counteracted to resist gravitational forces that drive further deviation. This aspect of trunk control has no passively stable direction, meaning that all deviations from vertical must be actively controlled to maintain upright equilibrium. We hypothesized that such active control depends on high level neural control provided by proprioceptive, visual

and vestibular feedback. Based on this hypothesis, we predicted that visual-scene motion in both the AP and ML directions would have similar effects on trunk *orientation*, whereas trunk *translation* will be more strongly affected by visual-scene motion in the ML direction.

3.3 Methods

3.31 Subjects

Fourteen healthy subjects voluntarily participated in this study, 6 males and 8 females (mean age 22.1 ± 4.8, range 18-36). All subjects were by self report free from any neurological disorder, balance disorder, vertigo, or recent musculoskeletal injury. This study was approved by the Institutional Review board at the University of Maryland. All subjects provided written informed consent prior to participation in this experiment.

3.32 Experimental Set Up

Apparatus

Virtual reality environment

Subjects walked or stood on a treadmill (Cybex Trotter 900T, Cybex International, Inc., USA) approximately 12 inches in front of a 52" wide screen TV (Samsung LN52A550, Samsung, USA) while wearing goggles to limit vertical peripheral vision, as shown in Figure 3-1. The resultant field of view was 124° horizontally and 94° vertically. The visual scene consisted of 401 randomly spaced and oriented white triangles measuring 1.2 cm (height) x 1.2 cm (base) on a black background. The virtual display was created using CAVELib software (Mechdyne, USA), synched to a desktop

computer (Dell WORKSTATION PWS650Dell, USA). Visual signals were created

offline (MATLAB, The Mathworks, USA) and generated using Labview (National

Instruments, USA) on a desktop computer (Optiplex GX620 Dell, USA).
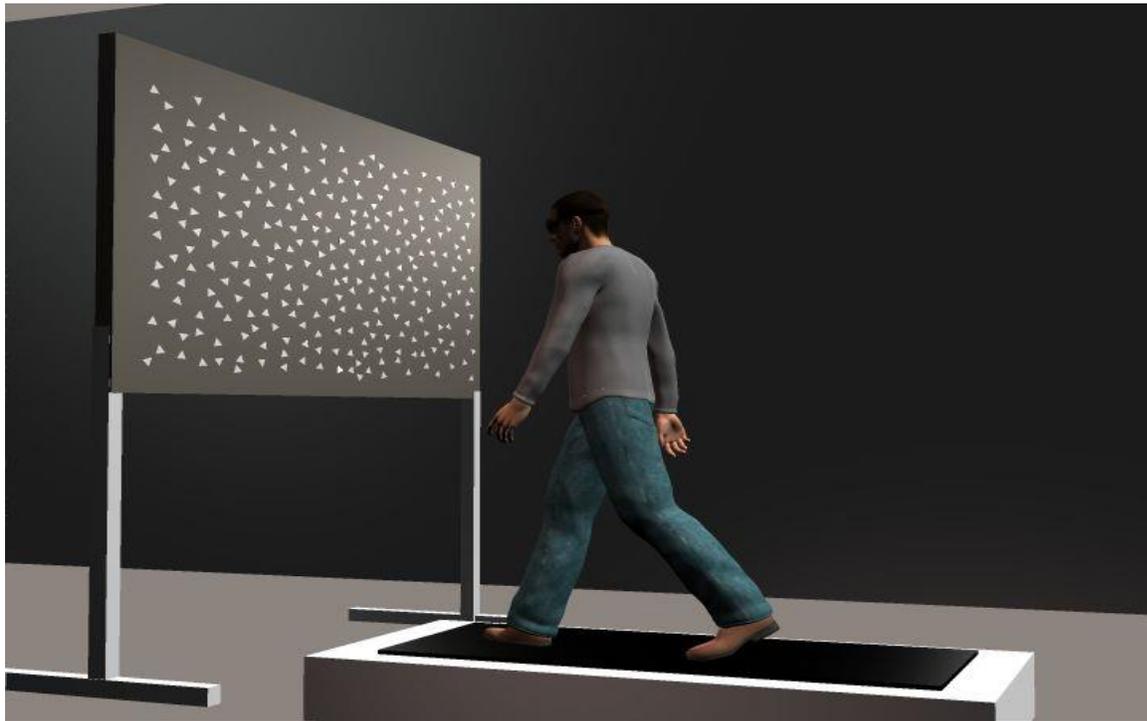
Figure 3-1. Illustration of the experimental set-up. Subjects stood or walked on the treadmill in front of a virtual display of randomly oriented white triangles on a black background. Subjects wore goggles which prevented them from seeing the borders of the TV.

Visual Signals

The visual display consisted of translational oscillations of the virtual wall of

triangles in the sagittal or frontal planes. A random number generator was used to

create white noise signals with a mean of zero that corresponded to the position of the

visual display in the static condition, as shown in Figure 3-2. Positive (negative) values

corresponded to reduction (increase) in triangle size to indicate motion of the scene

away from (toward) the subject in the sagittal plane and positive (negative) values

corresponded to rightward (leftward) motion of the visual scene in the frontal plane. A

different seed was used to initialize the random number generator for each trial for each

subject. The white noise signals were filtered using a first order low pass Butterworth
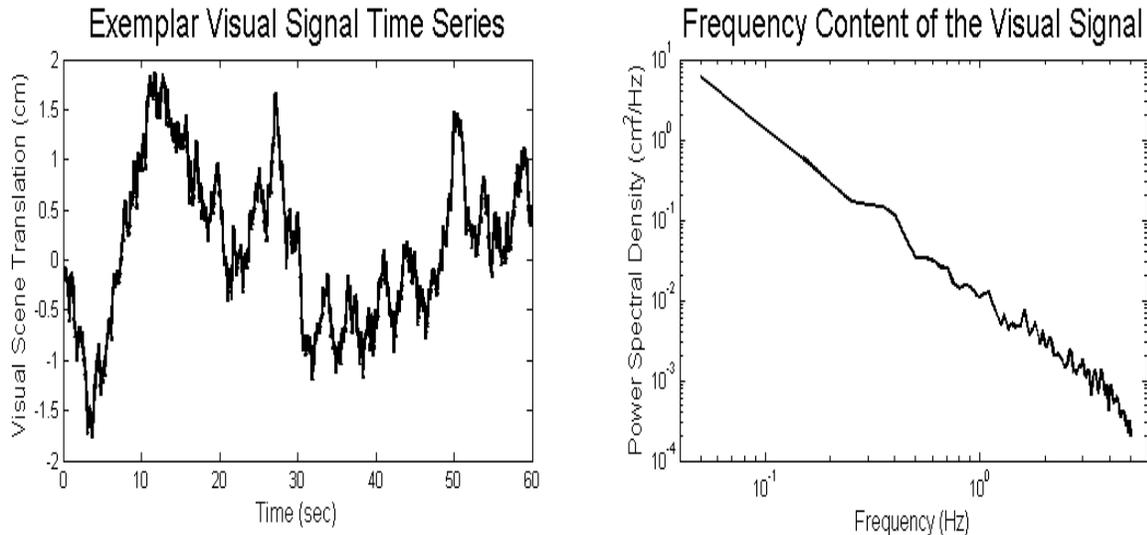
Figure 3-2. Exemplar time and frequency content of visual scene motion shown for 60 seconds
from a single trial. The position of the visual scene in the static condition corresponded to the
zero value during trials with visual scene motion. Positive (negative) values indicate that the
virtual wall of triangles was "moving away" (toward) from the subject during the AP stimulus
conditions. During ML stimulus conditions positive (negative) values indicate movement of the
virtual wall of triangles to the right (left).

filter with a cut-off frequency of .02 Hz, and an 8th order low pass Butterworth filter with

a 5 Hz cut-off frequency (Logan et al., 2010). This served to smooth the motion of the

visual scene and limit motion frequencies to the low frequency range of postural sway.

An external trigger synchronized display motion with the data acquisition computer.

Across subjects and directions the average root mean square error of the visual signal

was .94 cm and 1.52 cm/s. Across subjects and directions the average apparent

translation of the visual scene was ±2.6 cm with maximum values of ±4.2 cm. The

visual angle of the triangles for the static condition was 2.4°, and the angular change for

the AP motion condition was ±.525°, which corresponded to the maximum apparent linear AP displacement of ±4.2 cm. In the ML motion condition, there was no change in visual angle for the triangles.

Kinematics

Kinematics was recorded from the right side of the body and the trunk with respect to a global coordinate system using a single camera bank, three lenses, Optotrak (Northern Digital, Canada) camera system at a sampling frequency of 120 Hz. Anatomical locations that were used for the placement of infra-red diodes included fifth metatarsal, heel, lateral malleolus, lateral femoral condyle, greater trochanter, 3rd lumbar spinous process, 7th cervical spinous process, acromion, and mediolateral center of the back of the head (Logan et al. 2010). The addition of midline markers at the lumbar and cervical spine served to reduce the effect of axial rotation of the trunk during walking on the 3D measurements. Lumbar position was defined as the AP or ML displacement of the marker on the lumbar vertebrae. Neck position was defined as the AP or ML displacement of the marker on the cervical vertebrae. Trunk angle was defined as the AP or ML difference in position of the cervical and lumbar markers (Logan et al. 2010; Anson et al., 2013b). The difference between cervical and lumbar translations in the AP or ML direction approximates the trunk angle relative to vertical in the sagittal or frontal plane, respectively, when this angle is small. Foot markers were used for calculation of gait parameters.

3.33 Procedures

All subjects verified that they were able to walk comfortably at the required speed of 5 km/hr while viewing a static image of the visual scene prior to beginning any perturbation trials. Height of the TV was adjusted for each subject to ensure the focus of expansion corresponded to the subject's approximate eye height. Subjects were instructed to look straight ahead, but to not focus on any single triangle. Subjects were also instructed not to look for the edges of the TV screen for spatial orientation. Subjects were advised if a trial would be a standing or walking trial, but they were blinded to the condition of visual stimulus motion. All subjects were given approximately 30 seconds to reach a steady state walking pattern prior to initiation of the trial. After reaching steady state, subjects were asked if they were ready prior to beginning each 250 second trial. The experimental design included five conditions: (1) standing with an AP visual stimulus, (2) standing with an ML visual stimulus, (3) walking (5 km/h) with an AP visual stimulus, (4) walking (5 km/h) with an ML visual stimulus, (5) walking (5 km/h) with a static visual stimulus, as a control condition. Each condition was presented in random order as a block of trials, and this process was repeated for a total of three blocks. Standing rest breaks of one minute were given between each trial and a seated rest for 3-5 minutes was provided between blocks or as needed to prevent fatigue.

3.34 Analysis

A phase dependent response of the legs, but not the trunk, to moving visual stimuli during walking has been reported which violates the linear assumptions of our analysis methods (Logan et al. 2010). Therefore our kinematic analysis is confined to responses of the trunk which remained essentially linear throughout the gait cycle.

Spectral Analysis

Fourier transforms of the AP or ML visual scene (translation) and kinematics (lumbar and neck translation, and trunk angle) were calculated. One-sided power spectral densities (PSDs) and cross spectral densities (CSDs) using Welch's method (Bendat & Piersol 2000) with a 20 second Hanning window and one half overlap were then calculated with these transforms. The PSDs and CSDs are averaged across trials for each subject. For each subject the PSDs and CSDs were binned on a linear logarithmic scale up to 3.7Hz, resulting in 10 frequency bins. The frequencies included in each of the ten bins are as follows: .05, .1, .15, .2-.3, .35-.45, .5-.7, .75-1.1, 1.15-1.65, 1.7-2.5, and 2.55-3.7 Hz. The frequencies are averaged in each bin for plotting purposes resulting in the following ten frequencies: .05, .1, .15, .25, .4, .6, .925, 1.4, 2.1, and 3.125 Hz.

Gain and phase were computed to characterize the magnitude and timing of the kinematic response to the visual perturbations at each of the ten frequency bins of the frequency response functions (FRF). Gain is computed as the absolute value of the FRF, $\bar{H}_{xy}(f)$ and phase is the argument of the FRF, $\bar{H}_{xy}(f)$ converted to degrees.

Complex coherence was computed using the binned PSD and CSD values as $C_{xy}(f) = P_{xy}(f)/\sqrt{P_{xx}(f)P_{yy}(f)}$, where $P_{xy}(f)$ is the CSD of the stimulus (x) and the kinematic response variable (y). The FRF averaged across subjects was defined as $\bar{H}_{xy}(f) = \bar{C}_{xy}(f)\sqrt{\bar{P}_{yy}(f)/\bar{P}_{xx}(f)}$ where $\bar{C}_{xy}(f)$ is the mean complex coherence and $\bar{P}_{yy}(f)$ and $\bar{P}_{xx}(f)$ are the geometric means of the PSD's (Kiemel et al. 2008). This method weights subjects according to the coherence relative to the visual stimulus in

each bin, similar to methods employed in similar studies (Warren et al. 1996; Kiemel et al. 2008; Logan et al. 2010).

Due to our probe consisting of a wide range of frequencies, statistical tests were performed on each frequency bin of the FRF in the complex plane. These first statistics on the FRF, at each frequency bin, were performed to ensure coherence between the visual stimulus and the kinematic response variables over the full range of frequencies for which we are reporting gain and phase. First, 95% confidence intervals were computed using the percentile-t method with 4000 bootstrap re-samples and 400 nested re-samples for variance estimation (Zoubir & Boashash 1998). The bootstrapping method allows for an improved estimate of the average behavior (and variance) of a theoretical population based on a smaller set of existing subject data. The average FRF value for each frequency bin is calculated from 4000 virtual data sets that pulled 14 samples (allowing for re-sampling) from the existing 14 subject data set. This results in an improved population based estimate of the average behavior. The variance estimation is calculated with 400 virtual data sets for each of the 4000 virtual data sets that are used to estimate the mean FRF. The variance estimation is used to calculate 95% CI using the percentile-t method, which indicates whether a response is different from a reference value. We first compare all responses to zero, and then subsequent comparisons across conditions (i.e. standing vs. walking, AP vs. ML) only include "real" responses. The FRF was considered to have a "real" coherent response when the confidence region did not include zero in the complex plane ($\alpha = .05$). Log gain and phase of coherent FRF's are plotted with error bars representing ± the standard deviation of 10,000 bootstrap re-samples using the percentile-t method (Zoubir &

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Boashash 1998). To determine if posture and locomotion responses are different for each stimulus direction gain ratios and phase differences were computed using 4000 bootstrap re-samples and 400 nested re-samples and a 95% confidence interval was computed using the percentile-t method described above (Zoubir & Boashash 1998). This procedure was repeated to determine if the ML response was different from the AP response for both posture and locomotion. To determine speed (standing vs. walking) by frequency bin effects gain ratios and phase differences were first computed for neighboring frequency bins and then computed again across speed (standing vs. walking) using 4000 bootstrap re-samples and 400 nested re-samples and a 95% confidence interval was computed using the percentile-t method described above (Zoubir & Boashash 1998). These 95% CI represent the estimated population variability based on the sample variability from our subject pool.

Position Variance

Position variance for AP or ML trunk kinematics was computed as the integral of the PSDs using the trapezoid method, after averaging PSDs across trials for each subject. Variance linearly related to the visual scene motion was computed as the product of the kinematic PSD and the magnitude squared coherence ($|\bar{C}_{xy}(f)|^2$, $\bar{C}_{xy}(f)$ defined above) between the kinematic and the visual signal. Incoherent variance was the difference between total variance and coherent variance. The independent variables included in the analysis were speed (standing vs. walking), response direction (AP vs. ML), and kinematic segment (neck translation, lumbar translation, and trunk orientation). Three-way (2 speeds, 2 response directions, 3 kinematic segments) repeated measures ANOVA with Greenhouse-Geisser adjustment were computed on

geometric means for coherent and incoherent position variance (α = .05). To determine

if visual scene motion influenced trunk motion in a way not linearly related to the visual

stimuli, we compared the total variance for trials without visual scene motion (control)

with incoherent variance for conditions when the visual scene translated in the AP or ML

directions. Three-way (3 stimuli directions, 2 response directions, 3 kinematic

segments) repeated measures ANOVA with Greenhouse-Geisser adjustment were

computed on geometric means of both total (static stimulus condition) and incoherent

position variance (α = .05).

Gait Kinematics

Using kinematics from the right leg, general gait parameters and their coefficients

of variation were calculated. Heel-strike was defined as the local minima of the heel

marker in the vertical plane and toe-off was identified from limb axis minima (Borghese

et al. 1996; Ivanenko et al. 2004; Logan et al. 2010). The limb axis minimum was

defined as the local minimum of the angle formed by the fifth metatarsal-hip axis in the

sagittal plane, with the hip being the origin. Gait period for each trial was the average

time between successive toe-off events. Stance time for each trial was the average

time from heel-strike to toe-off. Stride length was computed as the average AP

movement of the heel marker between successive heel-strikes. Stance percentage was

computed as the stance time normalized to the gait cycle. Coefficients of variation were

computed using means and standard deviation for these measures within each trial.

The coefficient of variation was also calculated for swing time, computed as the duration

of time between toe off and heel strike. The standard deviation of the difference in ML

foot position from stride to stride was computed. One way (3 stimuli directions)

repeated measures ANOVA with unstructured covariance the Kenward-Roger method and Tukey-Kramer post-hoc adjustment were applied separately to each gait parameter and their coefficient of variation, alpha was adjusted for 12 comparisons (corrected α = 0.004).

3.4 Results

Gain and Phase

Gain. Figure 3-3 illustrates three main results from the frequency response analysis. First, Figures 3-3a and 3-3c show how gain of the neck and lumbar markers are consistently higher across all frequencies during locomotion compared to standing posture for both visual stimulus directions, AP and ML. The gain of these individual markers represents the translation of the trunk in the sagittal and frontal planes in response to the visual stimulus. In both the AP and ML directions, neck and lumbar translation gain was significantly greater ($p < .05$) during walking than standing posture in the majority of frequency bins (AP neck: 1-2, 4-8; AP lumbar: 1-2, 4-8, 10; ML neck: 1-5, 8-10; ML lumbar: 1-5, 7-9). The pattern of results clearly indicates higher overall gain during walking for translation of the upper body.
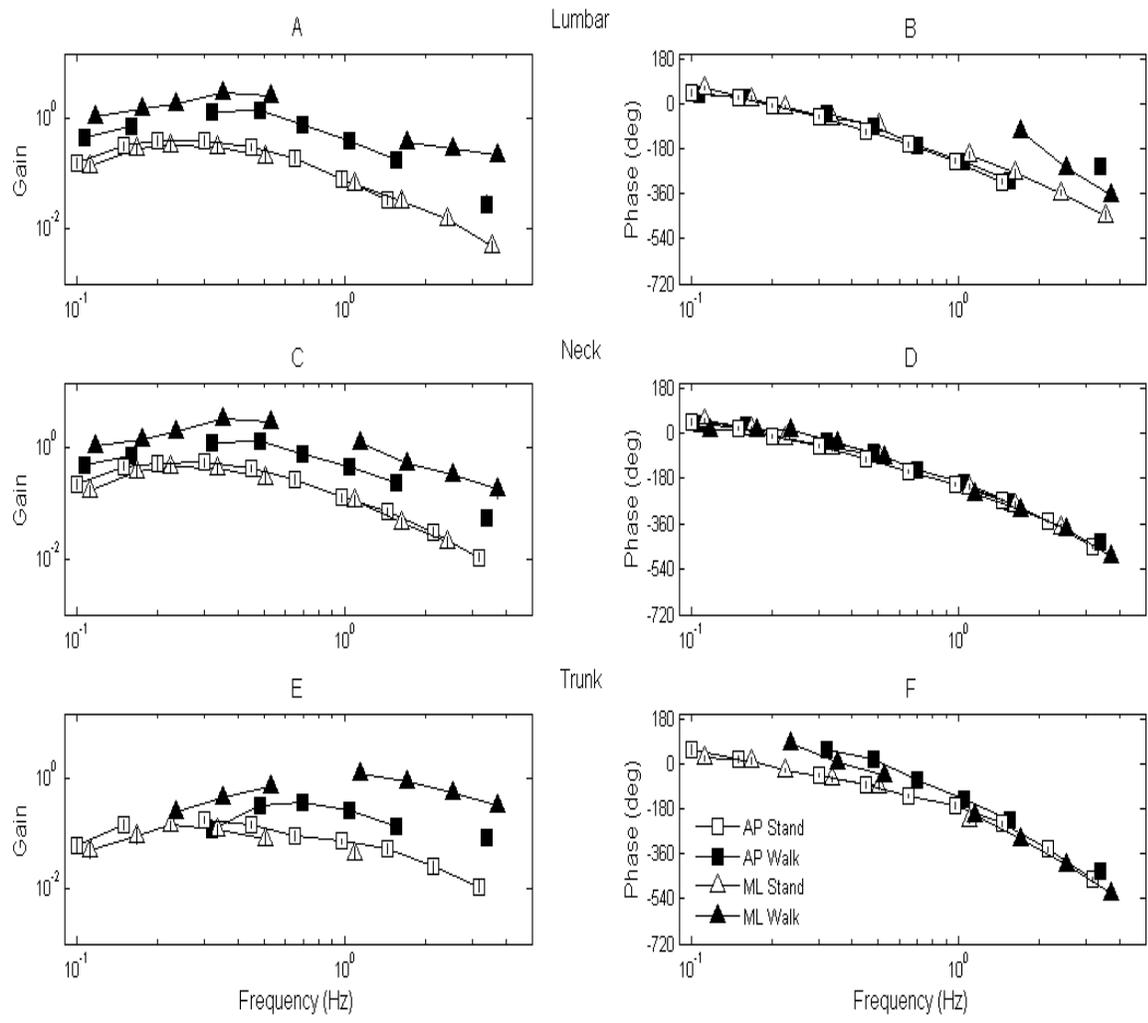
Figure 3-3. Gain and phase plots for condition comparison, only frequency bins significantly different from zero have been plotted. Frequency response functions (gain and phase) for *translation*: figure A) lumbar gain, figure B) lumbar phase, figure C) neck gain, figure D) neck phase; and *orientation*: figure E) trunk gain, figure F) trunk phase in response to visual scene motion. Error bars represent bootstrapped standard error.

The second major result involves gain of the trunk angle, which represents how the visual stimulus influences orientation of the trunk with respect to vertical in the sagittal and frontal planes, and which showed a different gain pattern than translation. Trunk angle gain was not different between standing and walking at low frequencies,

but was significantly greater during walking compared to standing at higher frequencies (α = .05), shown in Figure 3-3e. In the AP and ML directions, the middle and higher frequencies (AP trunk: bins 5-8, 10; ML trunk: bins 4-5, 7) show consistently higher trunk angle gain during walking (p < .05).

Third, both translation (lumbar and neck) and orientation (trunk angle) gain is higher in response to a visual stimulus in the ML direction than the AP direction during walking, but not during standing posture (p < .05). For neck and lumbar translation, ML gain was higher than AP gain across a broad range of frequencies (neck: 1, 2, 4, 5, 7, 8, and 10; lumbar: 1, 2, 4, 5, 8, 10).   For trunk orientation, ML gain was higher than AP gain at middle and higher frequencies (4, 5, 7, 8, 10).   Differences in AP and ML standing posture gain was only observed for a single frequency bin (5) for both translation and orientation (p < .05). Overall, these results indicate a kinematic (translation vs. orientation) by speed (standing vs. walking) by direction (AP vs. ML) interaction.

Phase. Regardless of direction, or kinematic variable, phase started at positive values at the lowest frequencies, indicating a visual lead relative to a kinematic variable (neck, lumbar, trunk angle), and decreased with increasing frequency to negative values, indicating a visual lag. For neck and lumbar translation, phase values were very similar across frequency. At high frequencies, lumbar phase values were more negative for locomotion than standing posture (p < .05). For trunk angle, phase values tended to be higher for locomotion than standing posture in the middle frequency range.

Kinematic Variance

To investigate the visual influence on overall variability, variance was partitioned into variance coherent with the visual signal and incoherent with the visual signal, shown in Figure 3-4. Coherent variance reflects variance in the response that is directly caused by motion of the visual scene. Incoherent variance is the difference between total variance and the coherent variance, i.e. that not caused by the visual scene motion. Control variance refers to total variance during the static visual scene condition. Although there are numerous effects which are expected, such as overall higher variance for walking than standing, there are two findings that are particularly revealing about trunk control. First, similar to previous findings on foot placement (O'Connor & Kuo 2009), directional effects for trunk angle variance in response to visual stimulation are observed not with standing but only with walking, with the ML direction displaying higher coherent variance than the AP direction (p < .001). Second, trunk translation shows consistently higher variance for the ML direction than the AP direction during walking but not standing (p < 0001), for all walking conditions. However, trunk angle shows a directional effect, with larger ML variance *only* for the coherent portion of variance (p < .0001). Trunk angle variance not caused by visual scene motion was equivalent in the AP and ML directions.
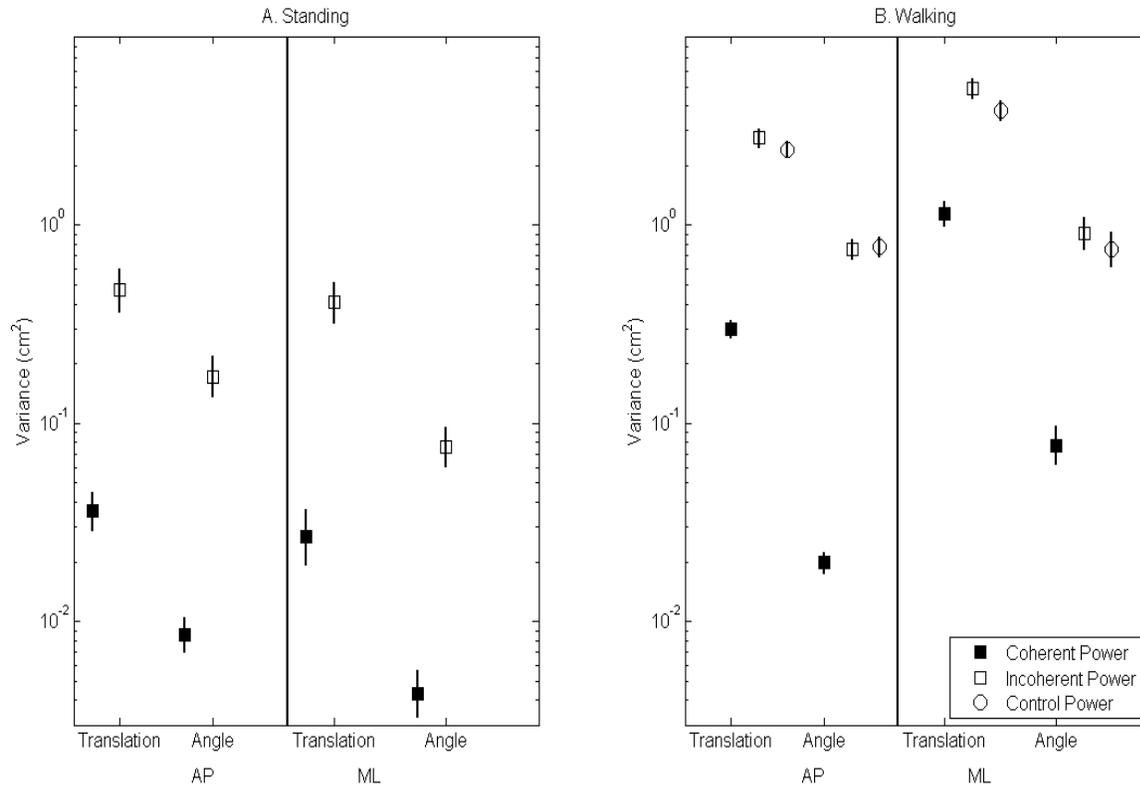
Figure 3-4. Coherent and incoherent position (subplots A and B) variance. Open squares represent variance incoherent with dynamic visual scene motion and filled squares represent variance coherent with dynamic visual scene motion. Circles represent total variance with stationary visual scene. AP and ML references on the x-axis correspond to both kinematic direction and visual stimuli direction. Comparisons between incoherent variance for dynamic visual scene conditions and total variance for the static visual scene condition are shown in subplot B. Lumbar refers to translation, while trunk refers to trunk angle. Errorbars represent standard error of the mean.

During walking variance not caused by visual scene motion was significantly higher than variance in the control condition for translation in all directions (p < .05), but not for orientation. Translation variance not caused by visual scene motion and translation variance in the control condition both display directional effects which were greater in

the ML direction (p < .0001). The implications of these results for control of the trunk are discussed below.

Gait Parameters

The ensemble averages for each gait parameter are presented in Table 1. Across condition comparisons made with Tukey-Kramer adjustments demonstrate that the coefficient of variation for right leg stance time during the ML visual scene motion was significantly greater than during the AP visual scene motion condition (p < .004). The standard deviation of the difference in ML foot placement from stride to stride also demonstrated a significant condition effect with ML visual scene motion resulting in greater variability in ML foot placement compared to either the AP visual scene or the static visual scene conditions (p < .004).

Table 3-1. General gait parameters for all locomotion conditions. C_V is the coefficient of variation for the corresponding gait parameter. * indicates ML stimulus condition significantly different from Static condition (p < .004). † indicates ML stimulus condition significantly different from AP condition (p < .004).

General Gait Parameters	Stimulus Motion		
Parameter	AP	Static	ML
Gait Period	1.03	1.04	1.02
C_V	.02	.01	.02
Gait Frequency/sec	0.97	0.97	0.99
Stride Length (cm)	147.2	148.08	146.45
C_V	.02	.02	.02
Single Leg Stance (sec)	.64	.65	.63
C_V	.02	.02	.03
Single Leg Stance (%)	62.46	62.51	62.43
C_V	.02	.02	.02
SD of ML difference in foot placement (cm)	2.47	2.47	3.82 *†
Swing time C_V	.04	.04	.06

3.5 Discussion

The purpose of this study was to gain a more complete understanding of trunk control during locomotion. A moving visual scene was used to probe the use of vision in stabilizing trunk translation and orientation. Our results were consistent with our hypothesis that vision plays a greater role in stabilizing trunk translation in the ML

direction than in the AP direction. The results did not support our hypothesis that the use of visual information to stabilize trunk orientation during walking would be similar in the AP and ML directions.

Gain Responses to Visual Scene Motion

Gain of the trunk relative to visual scene motion was larger during walking than standing, as previous studies have found (Logan et al. 2010). More striking was that trunk gain showed a directional dependence during walking: across all frequencies ML gains were larger compared to the AP direction for trunk translation and at higher frequencies for trunk orientation (see Figure 3-3). Such directional dependence in response to visual scene motion was not observed during standing. This is similar to the finding of greater sensitivity to ML visual scene motion reported by O'Connor and Kuo (2009). Their sensitivity measure was based on a comparison of center of pressure (COP) variability between a static visual scene and a moving visual scene. Here, we compared gain of the trunk between AP and ML visual scene motion conditions. Others have reported a directional effect during standing in response to platform tilt based on integrated proprioceptive and vestibular feedback demonstrating that postural control during stance is not always symmetrical in the AP and ML directions (Allum et al., 2008).

These results for trunk translation are similar to previous findings cited above showing a directional dependence to kinematic responses during walking. Bauby & Kuo (2000) and O'Connor and Kuo (2009) interpreted such results as evidence of the importance of high-level visual and vestibular feedback to stabilize walking in the side-

to-side direction, somatosensory feedback being thought sufficient to stabilize walking in the fore-aft direction. Our translation results are also consistent with McAndrew et al. (2010) who suggested a similar conclusion for control of trunk translation: the ML direction seems inherently less mechanically stable, requiring more neural control that depends on sensory feedback. It may not be surprising that trunk translation shows a similar directional dependence as step variability (O'Connor and Kuo, 2009); any translation of the legs will passively carry the trunk along or vice versa (Hurt et al., 2010), an effect that is clearly a function of the mechanical linkage between the trunk and legs. Supporting this argument is the higher variability of the ML foot placement from stride to stride in the condition with ML visual scene motion (see Table 1). A direction dependent interaction of trunk displacement and leg displacement during perturbed standing on a moving platform has previously been interpreted as a function of the biomechanical linkage of the legs and trunk (Preuss & Fung, 2008). However, there is no such simple relationship between leg/step translation and trunk orientation relative to vertical. Alternatively, the larger responses in the ML direction for translation reflect a response to a perceived change in navigational direction. Subjects were instructed not to fixate a point indicating path direction, nor was there a circular component to the visual display (Buccello-Stout et al., 2013), but the ML translation may have been perceived as a change in heading.

Unlike trunk translation gain, which displayed higher ML gains across the frequency spectrum, trunk orientation gain showed a directional dependence only at mid-to-high frequencies, with peak gain responses in the ML direction (see Figure 3-3e). Trunk orientation is not more mechanically stable or resistant to mechanical

perturbations in either the AP or ML direction (Gardner-Morse & Stokes, 2001). Unlike

experiments that impose ML treadmill translations which mechanically displace the

subject (McAndrew et al., 2010; Sinitski et al., 2012), trunk orientation responses driven

by sensory feedback from visual scene motion in this experiment can not be explained

as a direct mechanical response to the perturbation. The mid-to-high frequency

directional dependence suggests a visual feedback mechanism as a more likely

candidate to explain the observed responses (Warren et al., 1996). In response to

visual roll perturbation individuals either leaned their trunk or deviated their path, which

was interpreted as visuo-vestibular integration for trunk control (Keshner & Kenyon,

2000). Unlike previous work that described coordinated head and body motion during

walking or turning (Imai et al., 2001), the present analysis reports only on the kinematic

behavior directly related to the visual scene motion in the FRFs and the coherent

variance. It is possible that the trunk orientation motion included a visuo-vestibular

interaction to facilitate head stabilization that could not be identified (Pozzo et al., 1991).

The direction dependent trunk orientation responses to visual perturbations during

walking would not be predicted by standing postural responses that depend on

mechanical stability (Ivanenko et al., 2000), or the directional interaction of leg

segments and trunk (Preuss & Fung, 2008). The trunk orientation gains observed in

this study further demonstrate differences in upright trunk orientation control between

standing and walking. Future studies providing treadmill perturbations and mechanical

perturbations to the trunk in addition to sensory perturbations should explore the

relationship between mechanical coupling of the trunk and legs as well as the

interaction of mechanical and neural control for upright orientation of the trunk during walking.

At low frequencies, trunk orientation displayed either no detectable response or gains similar to those observed during standing. These low frequencies, from .05 – .15 Hz, are only about one tenth the frequency of the gait cycle (≈ 1 Hz). Considering the larger overall variance observed with walking compared to standing, trunk responses to visual-scene motion at these low frequencies may be too small to be detectable.

We observed a time difference between trunk translation and orientation in response to visual stimulation. Peak gains for trunk orientation occurred at frequencies above 1 Hz while maximal gains for translation (both lumbar and neck) occurred between .25 and .6 Hz (see Figure 3). This suggests that trunk orientation movements respond on a shorter time scale than trunk translation movements (Kiemel et al. 2010). This time scale difference suggests different cost functions associated with translation and orientation, which may reflect the consequences of a disturbance while walking. A deviation from the intended path (translation) temporarily speeds up or slows down forward progression, which may be less deleterious compared to deviations in trunk orientation that threaten upright equilibrium. Corrections for lateral path deviations caused by lateral translation of the body could easily be corrected by appropriate placement of the foot at the next step (O'Connor and Kuo, 2009). The more rapid orientation response may serve as a mechanism to prevent the head and trunk from exceeding a safe range of angular displacement from vertical, reducing fall-risk. This is consistent with the concept that corrections in whole body angular momentum occur during double support (Robert et al., 2009), rather than waiting for the next step. Future

studies could explore the flexibility of this orientation over translation prioritization to determine if the observed relationship is fixed or adaptive.

Variance

While gain indicates the response to the visual-scene motion, decomposing total variance into coherent and incoherent components illustrates trunk behavior that is and is not directly caused by the visual stimulation. Coherent variance depends on the gain at each frequency and the PSD of the visual-scene motion. Since the PSD of the visual-scene motion was the same in all conditions, one expects similar effects for gain and coherent variance. This was observed: coherent variance was higher in the ML direction for both trunk translation and orientation during walking (filled squares in Figure 3-4B), and there was no directional dependence during standing (filled squares in Figure 3-4A). For incoherent variance and variance in the control condition (open squares and circles in Figure 3-4B), directional dependence was observed for trunk translation but not trunk orientation, effects that are consistent with our original hypotheses. This is exemplified by incoherent variance (open squares) representing greater variance than in the control condition (open circles) for translation in Figure 3-4B. The addition of visual scene motion may have led to reduced reliability of visual input for position control while walking on the treadmill, resulting in less resistance to visual perturbation (Logan et al 2010). This helps to explain the larger incoherent variability for translation with visual scene movement compared to the static visual condition, since proprioceptive and vestibular input provide limited information regarding absolute position in space to compensate for less reliable visual input.

In contrast, proprioception and vestibular inputs could provide adequate sensory input to stabilize trunk orientation when visual scene motion becomes less reliable. The increase in variance from standing to walking reflects a decrease in stability with a moving base of support (walking) compared to a stationary base of support (standing) as has been suggested by Logan et al (2010). However, during walking there was no increase in incoherent variance compared to the control condition for the trunk angle. Persistent upright stability from redundant sensory input could facilitate an increase in coupling of the trunk angle to motion of the visual scene. Alternatively, the consistency of trunk angle variance regardless of visual scene motion, may suggest an emphasis on a stable platform for the head during walking (Pozzo et al., 1991). This may explain the lack of directional effect as well as the lack of difference for the trunk angle variance between the control condition and incoherent variance from conditions with visual scene motion.

3.6 Conclusion

A number of studies have suggested that visual control of leg characteristics during locomotion is different in the AP and ML directions. The current results add to this perspective, illustrating that trunk translation *and* orientation show a directional dependence during walking. This may not be surprising for translation of the body, as trunk translation is mechanically tied to translation of the legs. A mechanical explanation, however, is less straightforward for orientation of the body to upright during walking. Our results show stronger responses of trunk orientation to visual scene

motion in the side-to-side direction, indicating that visually mediated control of upright

orientation demonstrates directional dependence that operates on a faster time scale

than trunk translation.

Chapter 4: Experiment 2
Age differences in use of visual feedback training during treadmill walking to improve postural control

This Chapter has been published as:

4.1 Abstract

Background: Most current applications of visual feedback to improve postural control are limited to a fixed base of support and produce mixed results regarding improved postural control and transfer to functional tasks. Currently there are few options available to provide visual feedback regarding trunk motion while walking. We have developed a low cost platform to provide visual feedback of trunk motion during walking. Here we investigated whether augmented visual position feedback would reduce trunk movement variability in both young and older healthy adults.

Methods: The subjects who participated were 10 young and 10 older adults. Subjects walked on a treadmill under conditions of visual position feedback and no feedback. The visual feedback consisted of anterior-posterior (AP) and medial-lateral (ML) position of the subject's trunk during treadmill walking. Fourier transforms of the AP and ML trunk kinematics were used to calculate power spectral densities which were integrated as frequency bins "below the gait cycle" and "gait cycle and above" for analysis purposes.

Results: Visual feedback reduced movement power at very low frequencies for lumbar and neck translation but not trunk angle in both age groups. At very low frequencies of body movement, older adults had equivalent levels of movement variability with

feedback as young adults without feedback. Lower variability was specific to translational (not angular) trunk movement. Visual feedback did not affect any of the measured lower extremity gait pattern characteristics of either group, suggesting that changes were not invoked by a different gait pattern.

Conclusions: Reduced translational variability while walking on the treadmill reflects more precise control maintaining a central position on the treadmill. Such feedback may provide an important technique to augment rehabilitation to minimize body translation while walking. Individuals with poor balance during walking may benefit from this type of training to enhance path consistency during over-ground locomotion.

4.2 Introduction

Older adults and some patient populations are at increased risk of falling, with a high probability of those falls resulting in injuries (Kannus et al., 1999; Lord et al., 1993). Falls and fall-related injuries negatively impact the ability of older individuals to perform daily tasks (Fuller, 2000), and substantially impact health care costs. Less easily quantified, but arguably more important, is the reduced quality of life from fall related injuries: disability, dependence on others, lost time from work or household duties (Zijlstra et al., 2007), and self-restricted social interactions due to fear of falling (Arfken et al., 1994). It is essential to identify *affordable* solutions to this growing medical, social, and economic problem that are easily accessible to a *large segment of the aging population*. Most falls occur during dynamic activities like walking or transitions from sitting/standing to walking (Lord et al., 1993; Gabell et al., 1985; Winter, 1995), yet most visual biofeedback for postural control is provided during standing (Van Peppen et al., 2006; Cheng et al., 2004; Waterston et al., 1993; Sihvonen et al., 2004; Winstein et al., 1989; Zijlstra et al., 2010). Here we propose a device that has the potential to improve balance through visual feedback of self-motion during walking.

During walking, excessive body/trunk motion has been related to instability in older individuals and individuals with balance disorders (Simoneau et al., 1999; Allum et al., 2001; Gill et al., 2001). Measures of trunk movement during locomotion have been used to identify older individuals with balance problems from individuals without balance problems (Yack & Berger, 1993; Chou et al., 2003). ML center of mass (COM) displacement during walking increased with age, even when adjusted for stride velocity

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(Schrager et al., 2008). Individuals with unilateral and bilateral vestibular loss have demonstrated impaired path consistency for goal directed walking (Borel et al., 2004; Glasaurer et al., 1994). It has recently been suggested that responses of trunk translation through space versus orientation of the trunk to vertical in response to visual stimulation reflect different roles (i.e., navigation versus upright stability) of vision during walking (Logan et al., 2010). Such findings suggest that the application of position feedback could reduce COM path deviations in older adults.

Several studies have examined the benefit of visual feedback, usually center of pressure (COP) position feedback during standing, with mixed results regarding improved standing postural control and limited transfer to walking (Van Peppen et al., 2006; Cheng et al., 2004; Waterston et al., 1993; Sihvonen et al., 2004; Winstein et al., 1989; Zijlstra et al., 2010). Visual feedback reduced sway in both healthy controls and individuals with Parkinson's disease (Waterston et al., 1993). COP visual biofeedback training combined with traditional physical therapy did not enhance the effects of traditional physical therapy for individuals recovering from an acute stroke (Walker et al., 2000). Stance symmetry feedback improved standing symmetry, but did not enhance recovery of a symmetrical walking pattern (Winstein et al., 1989). Visual feedback paradigms emphasizing weight shifting demonstrated more consistent carryover from standing to walking, possibly related to the shared dynamic weight shifting component required for both obstacle avoidance and walking (Hatzitaki et al., 2009). Balance strategies during walking are not the same as standing (Shkuratova et al., 2004); therefore, providing visual feedback during walking (compared to standing)

may be more effective for improving balance during walking (Darter & Wilken, 2011; Wollacott, 1986).

The use of treadmills in rehabilitation, to normalize a walking pattern is supported by only minor differences in electromyographic, kinematic, and force between over-ground and treadmill walking (Goldberg et al., 2008; Lee & Hidler, 2008; Riley et al., 2007; Watt et al., 2010). Despite this, there are only a few reports on the use of augmented visual feedback during treadmill walking; most have not provided visual feedback to improve control of trunk motion, rather the goal was to improve foot placement or improve use of a robotic assistive device for walking (Banz et al., 2008; Dingwell & Davis, 1996). Verhoeff et al (2009) provided multisensory (visual, vibratory, and auditory) cues signaling excessive trunk tilt during over-ground walking; however, no directionally specific trunk sway information was provided by the visual cues. Due to the multisensory nature of the feedback in that study, it is unclear what specific role visual feedback played in reducing trunk motion during walking. A case report described improvement in frontal plane gait mechanics after three weeks of training using real time visual feedback, verbal cues, and virtual reality for an individual with a transfemoral amputation (Darter & Wilken, 2011). The expense of the virtual reality systems such as that used in this case study would be prohibitive for most clinics and hospitals, a limitation to its broad application. Moreover, the improvement in frontal plane gait mechanics may not be solely attributable to the visual feedback.

Here we implemented a novel *affordable* approach to determine 1) whether augmented visual position feedback provided during treadmill walking would reduce AP and ML trunk motion variability during walking and 2) age related differences in ability to

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use feedback. Understanding how visual feedback influences body motion will provide insight regarding rehabilitation options for visual feedback to improve control of body movements during walking.

4.3 Methods

4.31 Subjects

Twenty healthy adults, 8 males and 12 females participated in this study. The participants were grouped by age as younger (mean ± SD 22.6 ± 4.9), and older adults, (mean ± SD 72.6 ± 5.8), participants over age 65 were considered older in this study. All subjects were by self report free from any neurological or recent (prior 12 months) musculoskeletal injury, balance disorder, or vertigo. Young adults were recruited by fliers and word of mouth. Older adults were recruited through an advertisement in a newspaper with a readership age greater than 55 years old. Respondents to the advertisement were screened by phone to verify age and health eligibility before scheduling a participation session. This study was approved by the University of Maryland Institutional Review Board. All subjects provided written informed consent prior to participation.

4.32 Experimental Set Up

Virtual reality environment

Subjects walked or stood on a treadmill with belt dimensions 0.51 x 1.52 meters (Cybex Trotter 900T, Cybex International, Inc., USA) approximately 0.6 meters in front of a 1.27 meter wide screen TV (Samsung LN52A550, Samsung, USA) aligned with the front edge of the treadmill belt, shown in Figure 4-1. The visual display consisted of a

grey background textured to look like a treadmill belt with a red and white bull's-eye target superimposed. This image was presented from a top down (bird's eye) camera perspective. The diameter of the ten rings of the bull's-eye increased successively by one inch (total target diameter - 10 inches). The visual display was created using custom scripts in Vizard (WorldViz, USA), on a desktop computer (Dell PWS650 Dell, USA). The position of a colored marker, worn at the height of the navel, was tracked using two webcams (Logitech Orbit AF, Logitech International S.A., USA). Stereoscopic calibration was accomplished using open source code in MATLAB (Mathworks, USA) (Bouguet, 2009). The position of the marker was displayed as a cursor on the TV screen. Cursor movement in the vertical direction corresponded to anterior-posterior (AP) movement of the subject on the treadmill, while right-left movement of the cursor corresponded to medio-lateral (ML) movement of the subject on the treadmill. This two dimensional representation of the cursor movement was similar to descriptions of COP feedback displays in previous literature (Waterston et al., 1993; Sihvonen et al., 2004; Winstein et al., 1989). Cursor motion on the screen was scaled relative to the display resulting in a 1:1 ratio of subject motion to cursor motion.
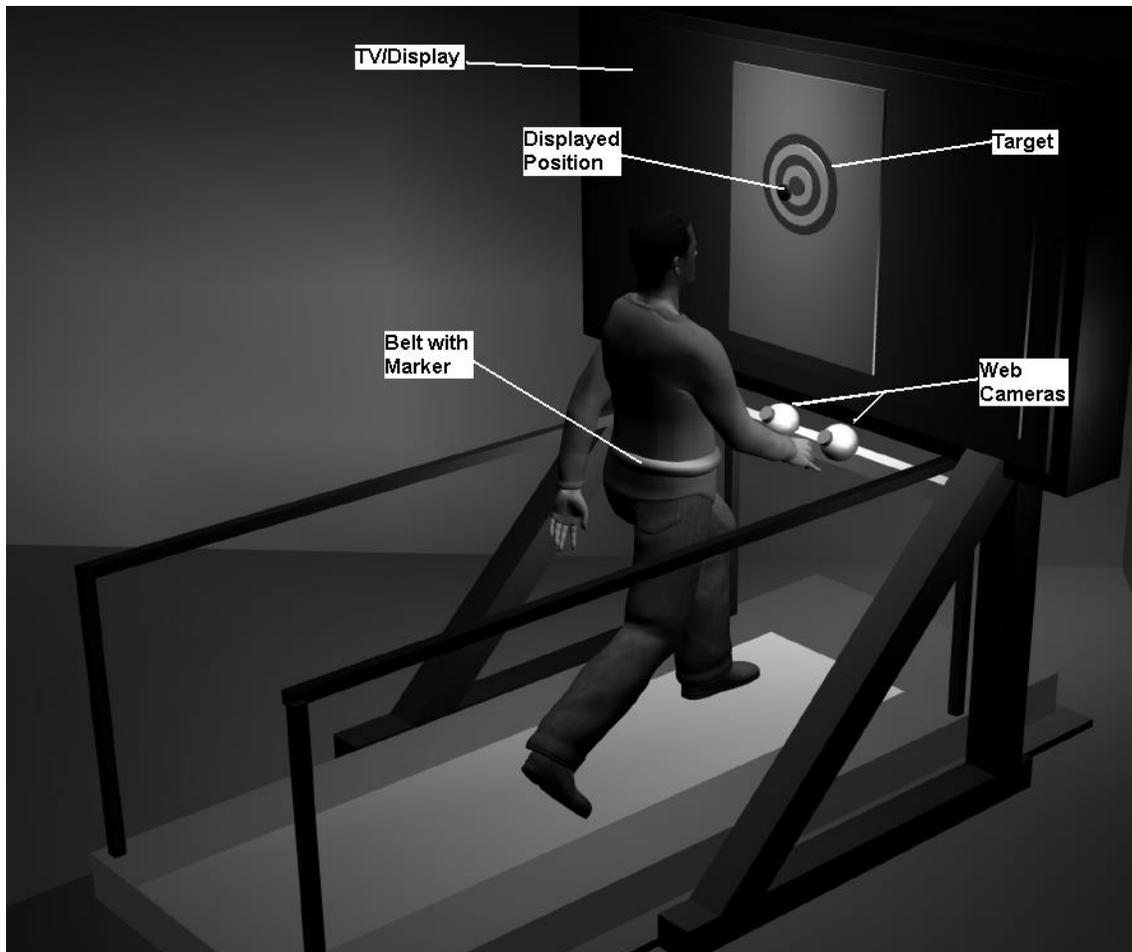
Figure 4-1. Illustration of the experimental set-up. Subjects stood or walked on the treadmill in front of a wide screen TV. A display of their position on the treadmill was indicated by a cursor over a bulls-eye target as a goal area. Depicted is the feedback condition. The TV was turned off and covered with a cloth for the no-feedback condition.

Kinematics

Kinematics for the young adults were recorded using an Optotrak camera system (Northern Digital Inc., Canada) connected to a desktop computer (Intel Xeon CPU, Dell, USA). Kinematics for the older adults were recorded using a Vicon MX40 (Vicon Motion Systems Inc., USA) camera system connected to a desktop computer (Intel Xeon CPU, Vicon Motion Systems Inc., USA). All kinematics were recorded from the trunk and the

right side of the body at a sampling frequency of 120 Hz. Markers were placed at the

following anatomical locations: fifth metatarsal, heel, lateral maleolus, lateral femoral

condyle, greater trochanter, third lumbar vertebrae, seventh cervical vertebrae,

acromion, and head (occiput, left/right temple). Lumbar translation was defined as the

AP or ML displacement of the marker on the lumbar vertebrae. Neck translation was

defined as the AP or ML displacement of the marker on the cervical vertebrae. Trunk

angle (orientation) was defined as the AP or ML difference in position of the cervical and

lumbar markers. The difference between cervical and lumbar position in the AP or ML

direction is approximately proportional to the trunk angle relative to vertical in the

sagittal or frontal plane, respectively, when this angle is small. This allows a direct

comparison between measures of trunk orientation and trunk translation using the same

units (Logan et al., 2010). Trunk translation and orientation are illustrated in Figure 4-2.
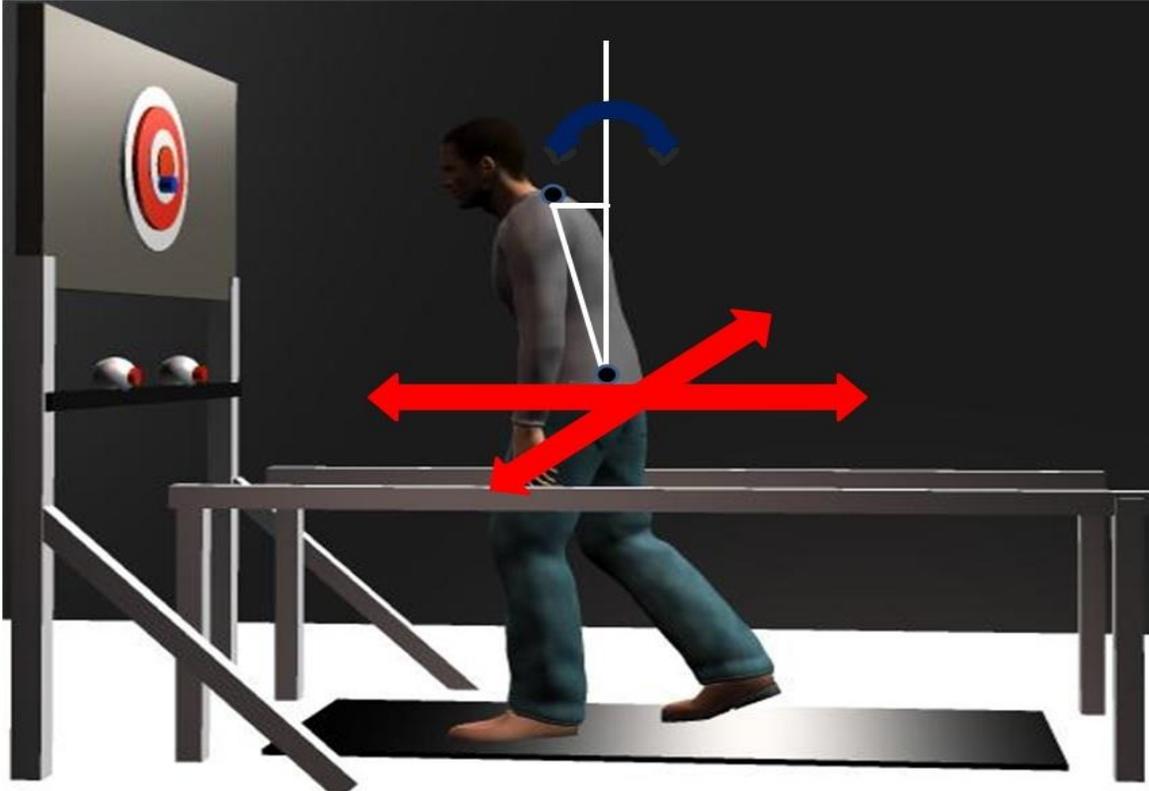
Figure 4-2. Illustration of the difference between trunk translation and trunk orientation. The red arrows depict trunk translation as defined by displacement of the markers on the lumbar vertebrae in AP or ML (neck translation was defined in a similar way). Curved blue arrows represent trunk orientation defined as the AP or ML difference in position of the cervical and lumbar markers, depicted by the horizontal white line.

4.33 Procedures

All subjects demonstrated that they were able to walk comfortably at 1.39 m/s (approximately 3.1 miles per hour) without hand rails under conditions of no-feedback and feedback prior to data collection (Browning et al., 2006; Malatesta et al., 2003). Television height was adjusted for each subject to center the screen at the subject's approximate eye height. All subjects were able to use their body movement to control cursor movement to the desired location of the bull's-eye, as the task during feedback

conditions was to center the cursor on the bull's-eye. Subjects were instructed to look

straight ahead at the covered TV screen during no-feedback trials. All subjects were

given approximately 30 seconds to reach a steady state walking pattern prior to starting

each 240 second trial. The experimental design consisted of two different visual

feedback conditions: 1) no feedback (NFB) with the TV off and covered; 2) a ten inch

diameter bulls-eye target with a cursor to indicate current position (FB). Each condition

was presented randomly in five blocks of two trials. Between trials subjects were asked

to perform 5 mini-squats to reduce motor memory and were given a standing rest break

lasting 1 minute. Between blocks (or as needed to prevent fatigue) all subjects received

a seated rest for 3-5 minutes to reduce fatigue.

4.34 Analysis

Power Spectral Density (PSD)

Fourier transforms of the AP and ML kinematics (lumbar position, neck position,

and trunk angle) were calculated. One-sided power spectral densities (PSDs) using

Welch's method with a 20 second Hanning window and one half overlap were then

calculated with these transforms (Bendat & Piersol, 2000). Geometric means of the

PSDs were averaged across trials for each subject. For each subject, PSDs were

divided into two frequency categories: 1) "below the gait cycle" which included

frequencies in the range .05 - .7 Hz; and 2) "gait cycle and above" which included

frequencies .75 – 5 Hz. The cut-off frequency of .7 Hz was selected as the upper bound

to define "below the gait cycle" as this frequency was below the range of cycle-by-cycle

values of gait frequency for all subjects. Frequencies below the gait cycle represent

very slow translational or angular oscillations of the body while walking on the treadmill.

Motion Variability

To evaluate motion variability with visual feedback compared to no feedback, position variance below (.05 - .7 Hz) and above (.75 – 5 Hz) the gait cycle was calculated. Variance for AP and ML trunk kinematics was computed as the integral of the position PSDs using the trapezoid function (trapz.m) in MATLAB (Mathworks, USA). Variance modulated by visual feedback was the difference between variance for no-feedback trials and variance for visual feedback trials.

Gait Kinematics

Using right leg kinematics, stride time, gait frequency, stride length stance time, stance percentage and their coefficients of variation were calculated. Heel-strike was defined as the local minima of the heel marker in the vertical direction and toe-off was identified from the limb axis minima (Logan et al., 2010; Borghese et al., 1996; Ivanenko et al., 2004). This kinematic method was previously validated against force plate measurements with less than 2% error for detection of heel strike and toe off events (Borghese et al., 1996; Ivanenko et al., 2004). The limb axis minima was defined as the local minima of the angle formed by the fifth metatarsal-hip axis in the sagittal plane, with the hip being the origin. Stride time was the average time between successive toe-off events. Stance time was the average time from heel-strike to toe-off. Stride length was computed as the average AP displacement of the heel marker between successive heel-strikes. Coefficients of variation were computed using means and standard deviations for these measures within each trial.

Statistical Analyses

Statistical analyses were completed using SAS version 9.2 (SAS Institute Inc., Cary, NC). Separately for each group, we analyzed log transformed position variance using a four-way Feedback (FB , NFB) x Direction (AP, ML) x Kinematics (lumbar, neck, trunk) x Frequency ($\leq$ .7 Hz, > .7 Hz) mixed model with all factors repeated, a Kenward-Roger adjustment, and a Tukey-Kramer adjustment for post-hoc within factor comparisons (α = .05). For older adults, this analysis showed a minor increase in variance for only one kinematic variable (trunk angle) in only the ML direction for both feedback conditions in the frequency range including/above the gait cycle (i.e., > 0.7 Hz). For young adults, no significant differences were found between feedback conditions for the high frequency range. Therefore, to better characterize the effects of visual feedback, subsequent analyses were restricted to the low frequency range, below the gait cycle. To determine the effect of age, we analyzed log-transformed position variance using a four-way Age (young, older) x Feedback (FB , NFB) x Direction (AP, ML) x Kinematics (lumbar, neck, trunk) mixed model with Feedback, Direction and Kinematics as repeated factors, an unstructured covariance matrix, a Kenward-Roger adjustment, and a Tukey-Kramer adjustment for post-hoc within factor comparisons (α = .05). Similarly, we analyzed each gait parameter and coefficient of variation using a two way Age (young, older) x Feedback (FB, NFB) mixed model with Feedback as a repeated factor, a Kenward-Roger adjustment, and a Tukey-Kramer post-hoc adjustment (α = .05).

4.4 Results

Figure 4-3 shows an exemplar PSD function of the lumbar marker in the FB and NFB conditions for one trial of a single older adult subject. The first peak at approximately 1 Hz represents the average gait cycle frequency and the width of the peak at the base indicates the stride to stride variability of the gait cycle frequency. Subsequent peaks are harmonics of the gait cycle frequency. Differences in spectral power were observed between FB and NFB conditions below the gait cycle frequency (≤ 0.7 Hz), described in detail below. In contrast, spectral power was not significantly different at or above the gait cycle frequency, emphasizing that FB influenced body position only for very slow body movements.

Exemplar PSD Lumbar
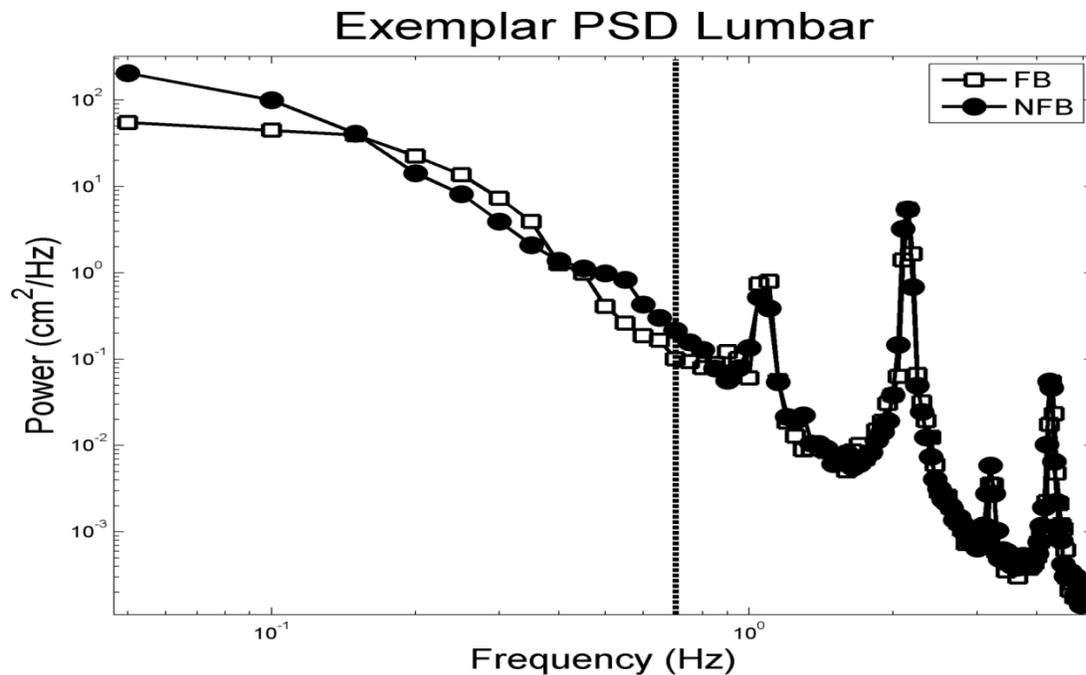
Figure 4-3. Exemplar PSD for the AP position of the lumbar marker during a walking trial on the treadmill for one trial for a single subject. The peak at approximately 1 Hz is the frequency of the gait cycle and the peaks at approximately 2, 3, and 4 Hz are subsequent harmonics. The dashed line marks the frequency (0.7 Hz) separating the frequency bands designated as below the gait cycle and including/above the gait cycle.

Kinematic Variance

Figure 4-4 displays position variance up to .7 Hz. The main findings for low frequency position variance were: 1) There was a significant age difference for translation but not orientation responses regardless of visual FB condition, supported by an interaction between age and kinematics ($p < .0001$); 2) The older adults had significantly greater variance in both the AP and ML directions regardless of FB condition, supported by an interaction between age and response direction ($p < .05$);

3) Visual feedback significantly reduced movement variance regardless of age for translation, but not orientation, supported by a significant interaction between Kinematics and FB (p < .0001), with no significant three- or four-way interactions including age; 4) Visual FB reduced AP position variance significantly more than ML position variance regardless of age, supported by an interaction between Direction and Feedback (p < .01).
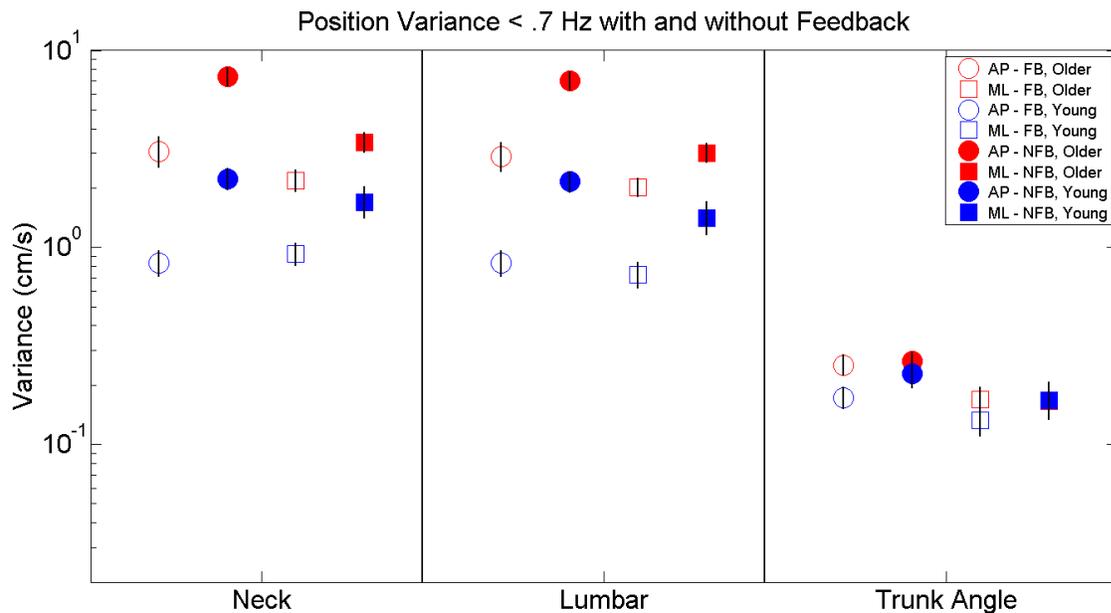
Figure 4-4. Open symbols represent the feedback condition and filled symbols represent the no-feedback condition. Red represents older adult and blue represents younger adults. Comparisons between AP (circles) and ML (squares) movement directions for each kinematic segment are presented. Lumbar and neck labels represent translation, while trunk angle represents orientation to vertical. Error bars represent standard error of the mean.

Overall, responses of young adults to visual FB differed from that of older adults in the following ways: 1) Visual FB reduced trunk angle variance from NFB to FB for young adults ($p < .05$), only in the AP direction.

General Gait Measures

Neither older nor younger adults displayed within age group differences across FB conditions for any gait parameters after post-hoc Bonferoni corrections for multiple tests. Older adults demonstrated significantly higher gait frequency ($p < .05$) compared to the young adults. Older adults also demonstrated significantly higher variability in stride time, stance time, and percentage of time in stance than younger adults ($p < .05$). Average gait parameters are presented by age and FB condition in Table 4-1.

Table 4-1. General gait parameters for feedback and no-feedback conditions. C_V is the coefficient of variation for the corresponding gait parameter. Significant differences between age groups are indicated by an * ($p < .05$).

Gait Parameter	Older Adults		Young Adults	
	FB	NFB	NFB	FB
Stride Time (sec) *	0.96	0.98	1.05	1.03
C_V*	.02	.01	.01	.01
Gait Frequency/sec *	1.05	1.02	.956	.973
Stride Length (cm)	134.9	138.8	142.1	138.7
C_V	.02	.02	.01	.01
Stance Time (sec)	0.62	0.63	.654	.642
C_V *	.02	.02	.01	.01
Stance (%)	64.3	64.4	62.3	62.2
C_V *	.02	.01	.01	.01

4.5 Discussion

The novel approach in this experiment demonstrated that concurrent augmented visual position FB provided during treadmill walking minimized trunk translation. Reduced trunk translation was specific to low frequencies of trunk movement, with translational (not angular) movements, but without changing the characteristics of gait.

Our results have implications as a potential rehabilitation method for those with impaired control of trunk movement during locomotion.

The primary reduction in trunk movement variance was observed at low frequencies of body movement, well below the frequency of the gait cycle ($\approx$ 1 Hz). A number of factors favor such low frequency adjustments. First, frequencies of body movement up to .7 Hz contain significant power during standing posture and locomotion (during locomotion the percentage of total power was 38% for trunk angle and 77% for trunk translation). These relatively large, slow movements of the body are amenable to visual control: they are easier to detect visually than smaller movements, vision is known to have slower processing loops than modalities like proprioception (Fitzpatrick & McCloskey, 1994), and vision is known to influence low frequency movement during standing (Diener et al., 1986). Furthermore, the visual feedback presented here required voluntary adjustments, which necessitates slower processing than reflexive adjustments.

Reduction in very low frequency translational movements while walking on the treadmill minimized trunk translation while walking on the treadmill. The functional correlate of reduced body translation during walking is enhanced path consistency. Clinical tests for dynamic walking balance include assessments of path deviation, a difficult task for individuals with impaired balance (Shumway-Cook & Woollacott, 2001). The older adults were able to reduce their low frequency trunk translation variability during walking with visual FB, displaying similar or lower variability than young adults without visual FB. The lack of significant change in the ML direction for the young adults with respect to neck translation is likely due to the lower variance for neck ML

translation compared to that of older adults. This is consistent with previous reports that older adults present with increased COM displacement in the ML direction while walking (Yack & Berger, 1993; Chou et al., 2003; Schrager et al., 2008). The reduction in ML COM translation variability suggests a specific rehabilitation avenue for older individuals and individuals with balance disorders to improve control of body movement during walking. The reduction in ML COM translation variability may be interpreted as an increase in path consistency.

There was a significant reduction in low frequency AP translation variability of the lumbar and neck regardless of age. This corresponds to less drift in the AP direction while walking on a treadmill. The functional relevance of this is unclear as the implicit task for treadmill walking is to not "walk off" (Dingwell et al., 2010), which can be accomplished in multiple locations on the treadmill. This illustrates a primary difference between using AP COM translation during treadmill and over-ground walking. AP COM translation during over-ground walking defines the forward path, but on a treadmill is only task relevant at the extreme edges. Reduction in movement variance from visual FB was found for trunk translation in both young and older adults. In contrast, the young adults showed a small but significant reduction in low frequency AP trunk orientation movements, with no effect observed for trunk angle in older adults (as shown in Figure 4-4). The response specificity observed for older adults to position visual FB during walking may have implications for rehabilitation. In response to multi-modal biofeedback of their trunk angle sway older adults were able to reduce ML trunk angle sway during walking (Davis et al., 2010). Providing visual feedback specifically related

to the rehabilitation movement goals (i.e. trunk translation versus trunk orientation) may result in greater benefit and functional carryover.

Visual FB presented in this way may be able to reduce age or pathology associated increases in translation of the COM during walking (Chou et al., 2003; Schrager et al., 2008; Swinnen et al., 2013). The translation-specific response to augmented visual FB seen in older adults in this study may provide some insight regarding the mixed effects to visual feedback previously reported (Van Peppen et al., 2006; Cheng et al., 2004; Waterston et al., 1993; Sihvonen et al., 2004; Dault et al., 2003). During walking, translation and orientation of the trunk serve the roles of navigation and upright stability, respectively. Since navigation is not relevant for standing, such separation of function does not apply to standing sway (Logan et al., 2010). Thus, it may be inappropriate to provide COM translation FB if the goal is to reduce trunk deviations from vertical while walking. Visual feedback training for path consistency during walking may be more amenable to COM translation FB training.

Finally, an argument could be made that the presence of visual feedback induced a change in control of walking as there is significant literature reporting the influence of vision on gait (Konczak, 1994; Lamontagne et al., 2007). The lack of difference in the measured gait parameters between feedback conditions demonstrates that average spatial/temporal aspects of walking were unchanged, despite reduced AP and ML trunk translation in space. This is consistent with the idea that cyclic behavior of the legs, path consistency and upright orientation are separate tasks during walking (Winter, 1995; Woollacott, 1986; Liang & Brown, 2013), and demonstrates that path consistency can be modified independent of changes to the average walking pattern. The

implication for rehabilitation is that isolated functional impairments in COM translation control may be effectively improved during walking using concurrent visual FB.

This study demonstrated that healthy young and older adults were able to effectively use visual feedback to reduce low frequency trunk translation while walking on a treadmill. A potential advantage of visual feedback provided during treadmill walking versus standing is the more dynamic component of the walking activity. The current results provide proof of concept for a low cost device that provides visual position feedback during walking to minimize excessive body movements. Whether this method of training will improve over-ground walking remains to be seen and is currently under investigation. Such low frequencies of body sway contain the majority of spectral power for standing posture, suggesting that the changes observed may be related to the control of balance during walking. The response-specific nature of this visual feedback may also enable greater carryover to functional mobility. Further research in this area is needed to determine whether other aspects of body movement during walking can be influenced with different types of feedback and to determine whether beneficial carry over effects exist for over-ground walking.

4.6 Conclusion

Visual position feedback provided during treadmill walking minimized trunk motion specific to the nature of the feedback. The response specific effect of the visual feedback indicates that for healthy adults the different aspects of body control during walking (trunk translation vs. trunk orientation) (Logan et al., 2010), do not respond similarly to the same visual feedback. This suggests that just as different mechanisms

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are responsible for control of standing and walking balance (Winter et al., 1995),

different mechanisms also underlie control of the upright orientation versus translation

of the body during walking. Rehabilitation of balance during locomotion may benefit

from provision of specific sensory feedback tailored to these mechanisms.

Chapter 5 Experiment 3

Visual Feedback Improves Trunk Control While Walking in Adults with Vestibular Loss

This chapter will be submitted to the J Vestib Res

5.1 Abstract

Background: Individuals with bilateral vestibular loss/hypofunction (BVH) have poor visual acuity and excessive trunk motion while walking. They also demonstrate path deviations and have excessive trunk motion. Previous investigations with visual feedback for whole body translation indicated an improvement in path consistency when visual feedback was present. Here we investigated whether individuals with BVH could modify trunk (body) orientation (translation) movement while walking in response to trunk motion visual feedback.

Methods: The subjects who participated were 4 healthy adults and 4 adults with BVH. Subjects walked on a treadmill under conditions of translation visual feedback (T-FB), orientation visual feedback (O-FB) and no feedback (NFB). The visual feedback consisted of anterior-posterior (AP) and medial-lateral (ML) translation (orientation) of the subject's body (trunk) during treadmill walking. Fourier transforms of the AP and ML trunk kinematics were used to calculate power spectral densities which were integrated as frequency bins "below the gait cycle" and "gait cycle and above" for analysis purposes.

Results: T-FB reduced body translation variance at frequencies below the gait cycle for both groups. O-FB increased trunk angle variance below the gait cycle in both groups.

Individuals with BVH displayed lower variability for ML translational trunk movement in response to O-FB, a response not observed in the healthy group.

Conclusions: Individuals with BVH reduced ML translation variability using both forms of visual feedback while walking on the treadmill, reflecting more precise control of their body in space while walking. Both forms of visual feedback were beneficial for reducing lateral body translation while walking on a treadmill for individuals with BVH. As individuals with BVH were able to extract useful visual feedback information while walking, despite reported gaze instability during walking, this type of training may improve trunk motion during over-ground walking for this population.

5.2 Introduction

Individuals with vestibular dysfunction have balance impairments that frequently result in falls (Agrawal et al., 2013; Jáuregui-Renaud et al., 2013). Falls are known to occur most frequently during walking or transitions from sitting/standing to walking (Robinovitch et al., 2014). Individuals with vestibular loss are known to move differently than healthy individuals when walking. They veer laterally more with eyes closed while walking to a remembered target (Glasauer et al., 1994; Glasauer et al., 2002; Cohen et al., 2000) and demonstrate greater lateral translation of the head and trunk when walking on a treadmill (Mamoto et al., 2002). Individuals with unilateral vestibular loss demonstrate impaired path integration, due to altered perception of self motion (Arthur et al., 2012). Individuals with bilateral vestibular loss/hypofunction (BVH) initiate walking with shorter steps and a smaller step angle compared to healthy individuals (Sasaki et al., 2001). Impaired coordination of head and trunk motion during walking is often observed with BVH and on return from space-flight (Pozzo et al., 1991; Bloomberg et al., 1997). Rats with BVH demonstrate a profound path integration impairment that persists long after the lesion (Zheng et al., 2009). The altered trunk/body movement during walking may contribute to the increased frequency of falling for individuals with vestibular loss.

Current rehabilitation approaches for individuals with vestibular loss fall into one of two broad categories: vestibular adaptation or substitution (Han et al., 2011; Herdman, 1998). In the case of BVH, recovery of balance ability is primarily due to the latter (McCall & Yates, 2011). Augmented sensory feedback to stabilize body motion has received considerable attention as a substitution strategy, with mixed results that

were context dependent (i.e. standing vs. walking) for individuals with BVH (Hegeman et al., 2005; Wall et al., 2009; Sienko et al., 2013; Honegger et al., 2013; Barros et al., 2010). Auditory biofeedback reduced trunk sway during standing, with no significant effects during walking for individuals with vestibular loss (Hegeman et al., 2005). Small vibro-tactile devices imbedded in a torso vest or worn on the head reduced trunk motion during specific walking tasks (Wall et al., 2009; Sienko et al., 2013; Honegger et al., 2013).

Another method of augmented biofeedback is use of visual feedback, which until recently has been restricted to training standing balance. Visual feedback during treadmill walking has been reported as beneficial for individuals with balance difficulties. Walking balance improved after training in a virtual reality environment that included visual feedback as a component of the training (Gottshall et al., 2013). Augmented visual feedback of trunk motion while walking on a treadmill improved standing and walking balance for a group of older adults with elevated fall risk (Anson et al., 2013a). Individuals with vestibular dysfunction reported symptom reduction and improved walking balance after training which consisted of walking in an immersive virtual reality environment (Alahmari et al., 2014).

Unlike auditory or vibro-tactile feedback, visual feedback could be designed with qualities of both substitution and adaptation when employed during walking. The gravity sensitive otolith organs provide an internal measurement of vertical. Increased medio-lateral (ML) sway was associated with loss of otolith function (Serrador et al., 2009). Error signals from visual feedback can serve as a sensory substitution for absent otolith signals regarding verticality. The sensory substitution from visual feedback may serve

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to stabilize ML sway. A bulls-eye visual feedback representation of verticality would augment the estimate of gravitational vertical (center of the bulls-eye) and an individual's deviation from vertical (the radial deviation from the center). Visually substituted information may be integrated in a similar way as otolith input for egocentric alignment tasks (Tarnutzer et al., 2012). It has been suggested that the vestibulo-ocular reflex (VOR) developed specifically for the purpose of facilitating stable vision during locomotion (Walls, 1962; Leigh & Brandt, 1993). Head motion during walking, despite having rhythmic properties, also is unpredictable and for individuals with BVH results in gaze instability due to a poor compensatory VOR (Grossman & Leigh, 1990). Gaze instability may prevent individuals from extracting meaningful information from visual feedback during walking due to reduced dynamic visual acuity (Badaracco et al., 2010). Specifically, gaze instability may impair the ability to continuously identify the position of a cursor relative to a target (an error signal used to drive corrective movement). However, ~60% of individuals with BVH may not actually have complete loss of vestibular function, with sparing of the otolith organs (Agrawal et al., 2013). Therefore, for those individuals a visual feedback mechanism may facilitate gaze stability adaptation. Providing visual feedback that requires target fixation while walking may enhance gaze stability from either neck afferents or spinal efference copy allowing individuals with BVH to modify body motion during walking (Fukushima et al., 2010; Lambert et al., 2012; Arshian et al., 2014).

Here we implemented a novel approach to investigate whether individuals with vestibular loss could use augmented visual feedback to modify trunk motion during treadmill walking. Demonstrating that individuals with BVH are able to extract

meaningful information from visual feedback to modify trunk motion behavior during walking would suggest new avenues for rehabilitation for vestibular loss.

5.3 Methods

5.31 Subjects

Eight subjects participated in this study. Four healthy individuals (mean age 24.8 ± 8.9, range 19-38) and four individuals with BVH (mean age 44.3 ± 12.2, range 26-52). Healthy subjects reported that they were free from any neurological or recent musculoskeletal injury, balance disorder, or vertigo. Diagnostic information for the individuals with BVH is listed in Table 1. All subjects provided written informed consent prior to participation, and the study protocol was approved by the University of Maryland IRB.

Table 5-1. Diagnostic information for individuals with BVH.

Subject	Age	Gender	VNG	Head Impulse	Rotary Chair
1	49	F	No response to ice water	+	NT
2	49	M	No response to ice water	+	Reduced Gain (.01-.32Hz)
3	26	F	No response Bi-thermal calorics	+	τ = 0.2 Gain < 0.08 (.01-1 Hz)
4	52	M	No response Bi-thermal calorics	+	NT

5.32 Experimental Set Up

Virtual reality environment

Subjects walked on a treadmill with belt dimensions 51cm x 152cm (Cybex

Trotter 900T, Cybex International, Inc., USA) approximately 24 inches in front of a wide

screen TV (Samsung LN52A550, Samsung, USA), shown in Figure 1. The visual

feedback system has been described in detail previously and is only briefly described

here (Anson et al., 2013b). The visual display was created using custom scripts in

Vizard (WorldViz, USA), on a desktop computer (Dell PWS650 Dell, USA). Two

webcams (Logitech Orbit AF, Logitech International S.A., USA) tracked 3 green markers

(one at the naval and one at each shoulder) worn on suspenders attached at the waist

(see inset Figure 1).
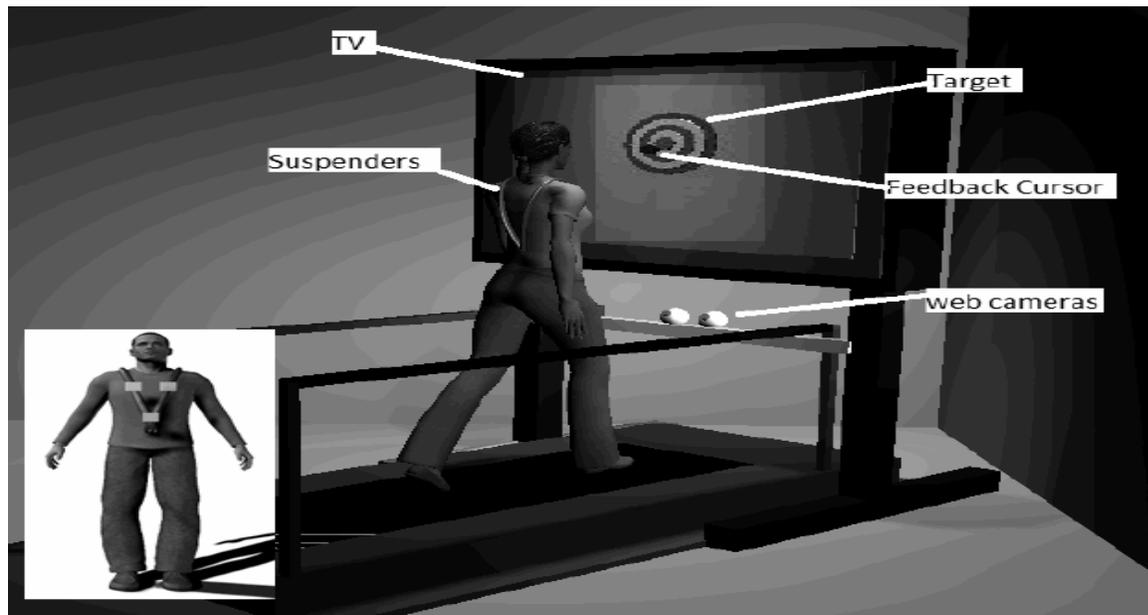
Figure 5-1. Illustration of the experimental set-up. Subjects walked on the treadmill in front of a

wide screen TV. Center of mass displacement or trunk orientation was indicated by cursor

motion over a bulls-eye target. Depicted is the feedback condition. The TV was turned off and

covered with a cloth for the no-feedback condition.

Stereoscopic calibration was accomplished using modified open source code in

(Bouguet, 2009). Displacement of the subject's approximate center of mass (anterior-

posterior (AP) and ML displacement of the marker at the naval) or their trunk orientation

relative to vertical (AP and ML angular displacement of the segment defined by the

naval marker and the midpoint of the shoulder markers) was presented as a cursor

superimposed on a bulls-eye. Each 1 inch ring represented 1 inch (translation) or 1

degree (orientation) of deviation from the center. Cursor motion on the screen was

scaled to a 1:1 ratio of subject motion to cursor motion. During translation trials the

target center was the average position of the lower marker over .4 seconds after ~20

seconds of walking. The target center for orientation feedback was the average trunk

orientation with respect to vertical while standing. Vertical cursor movement for

translation (orientation) feedback corresponded to AP trunk translation (trunk angle),

while right-left cursor movement corresponded to ML trunk translation (trunk angle) of

the subject on the treadmill.

Kinematics

Kinematics were recorded using a Vicon MX40 (Vicon Motion Systems Inc.,

USA) camera system at a sampling frequency of 120 Hz connected to a desktop

computer (Intel Xeon CPU, Vicon Motion Systems Inc., USA). Infrared reflective

markers were placed at the third lumbar vertebrae and seventh cervical vertebrae.

Lumbar translation was defined as the displacement of the marker on the lumbar

vertebrae (Anson et al., 2013b). AP and ML trunk angles were defined as the angular

deviation of the segment defined by the cervical and lumbar markers in the sagittal and

frontal planes.

5.33 Procedure

The experimental design included three conditions: translation visual feedback (T-FB), orientation visual feedback (O-FB), and no-feedback (NFB). Each condition was presented in random order in each of five blocks of three trials each. Seven subjects walked at 5 km/hr and one subject with BVH walked at 4 km/hr without using hand rails under all conditions. All subjects practiced (~5 minutes) both feedback conditions prior to data collection and were able to use their body movement to control cursor motion for both translation and orientation feedback conditions. The television screen was centered to each subject's eye height. For all trials, subjects were instructed to look straight ahead; and for feedback trials subjects were informed of the type of feedback (translation vs. orientation), reminded what body motions controlled the cursor, and instructed to keep the cursor in the center of the bull's-eye. All subjects were given approximately 20 seconds to reach steady state walking prior to initiating each trial. Trials were 240 seconds for healthy adults and 120 seconds for individuals with BVH. Between trials subjects were asked to perform 5 mini-squats to reduce motor memory and were given a standing rest break of 1 minute. A seated rest was provided between blocks (or as needed to prevent fatigue) for all subjects to reduce fatigue. Individuals with BVH were asked if the display appeared to be stable such that they could focus on it.

5.34 Analysis

Power Spectral Density (PSD)

Fourier transforms were calculated for the AP and ML kinematics (lumbar position, and trunk angles) recorded using the Vicon system. One-sided power spectral

densities using Welch's method with a 20 second Hanning window and one half overlap were then calculated with these transforms (Bendat & Piersol, 2000). For each subject, PSDs were divided into two frequency categories: 1) "below the gait cycle" which included frequencies in the range .05 - .7 Hz; and 2) "gait cycle and above" which included frequencies .75 – 5 Hz (Anson et al., 2013b). Frequencies below the gait cycle represent the very slow movements of the body while walking on the treadmill.

Motion Variance

To evaluate change in body and trunk motion from NFB to visual feedback conditions, variance was calculated for frequency bins .05-.7 Hz and .75-5 Hz (defined above). Variance for AP and ML trunk kinematics was computed as the integral of the PSDs using the trapezoid method.

Statistical Analyses

Three-way (3 feedback conditions [T-FB, O-FB, NFB], 2 response directions [AP, ML], 2 kinematics [lumbar, trunk angle]) repeated measures ANOVA with a Greenhouse-Geiser adjustment were computed separately on log-transformed position variance for frequency bins .05-.7 Hz and .75-5Hz (α = .05), resulting in tests of whether the geometric mean of position variance depended on the three factors.

5.4 Results

Position Variance

There were no significant main effects or interactions for condition, direction, or group for variance including the gait cycle and above. Overall, the individuals with BVH demonstrated greater low frequency variance than healthy individuals ($p < 0.05$).

As shown in Figure 5-2, for both groups (healthy individuals or individuals with BVH) T-FB reduced low frequency whole body displacement compared to the NFB condition and individuals with BVH showed a greater reduction indicated by an interaction between group and feedback (p > 0.05).
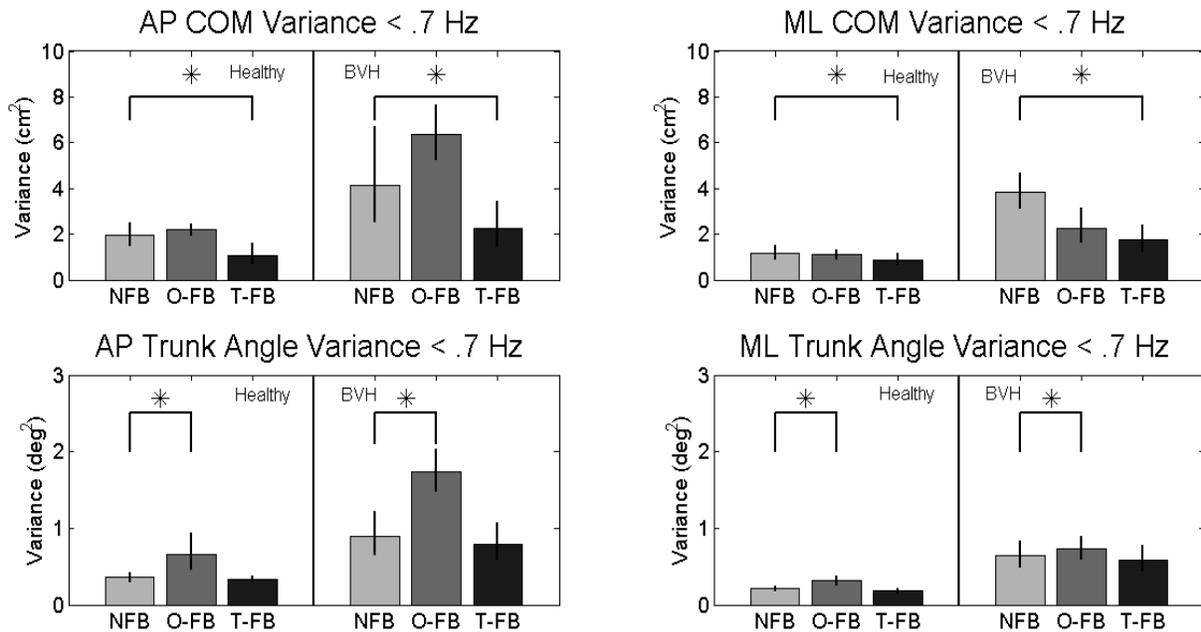
Figure 5-2. Position Variance. Light gray is the NFB condition, dark gray is the O-FB condition, and black is the T-FB. Upper figures (A & B) represent trunk displacement responses in the AP and ML directions, lower figures (C & D) represent trunk angle responses in the AP and ML directions. Comparisons between AP and ML movement directions for each kinematic segment are presented. COM labels represent whole body translation, while trunk angle represents orientation to vertical. Error bars represent standard error of the mean. Asterisks indicate significant condition differences.

O-FB increased low frequency trunk angle variance but not lumbar translation compared to NFB (p = 0.036) for both groups as indicated by a kinematic by feedback type interaction.

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There was not a significant crossed effect (i.e. change in translation variance with O-FB, or visa-versa) for the healthy group; however, both O-FB and T-FB resulted in a reduction of whole body ML translation variance ($p < 0.05$) for the BVH group as indicated by an interaction between group and type of feedback as shown in Figure 5-2.

5.5 Discussion

We previously reported that providing T-FB reduced low frequency whole body translation variance for both young and older healthy adults (Anson et al., 2013b). Reduction in low frequency ML translation was interpreted as improved path consistency. The current results are consistent with previous results that T-FB resulted in a reduction in low frequency translation for healthy individuals and extends that to individuals with BVH. In addition, for both healthy and individuals with BVH there was an increase in low frequency trunk angle variance with O-FB evidenced by a significant interaction between kinematic response and type of feedback, see Figure 2. This increase in trunk angle variance with O-FB is likely due to attempting to maintain a more upright trunk orientation while walking. The center of the bulls-eye represents their trunk orientation during *standing* and as such requires a different trunk/legs segmental orientation during O-FB (i.e. less forward lean) than typical walking (Thorstensson et al., 1984). Voluntary correction is needed to reduce natural forward trunk inclination during walking (Anson et al., 2013b). Unlike treadmill drift, trunk orientation may have a biomechanically defined point of attraction. Deviation from this attraction point i.e. walk "more upright" using O-FB may result in increased low frequency trunk motion variance above that seen when walking without O-FB. It remains to be seen whether this

increase in variance in response to O-FB is a transient process that would decrease with repeated practice. It is not clear from this experiment whether this attraction point could be modified with repeated training.

Previously we reported a response specific to the type of visual feedback (Anson et al., 2013b). That was also the case here for healthy adults. O-FB resulted in a significant increase in low frequency trunk angle variance and no change for COM translation. However, individuals with BVH demonstrated an increase in AP COM translation variance during the O-FB condition. This may suggest that individuals with BVH may have greater difficulty with spatial location during treadmill walking while changing their typical walking trunk motion in response to O-FB. This is consistent with recent work on spatial navigation in UVL with impaired AP distance estimation (Arthur et al., 2012). This is consistent with the idea that an individual's AP treadmill location is only relevant to the treadmill walking task at the extremes (Dingwell et al., 2010). As long as the participants avoided the edges of the treadmill they could still perform the walking task while attending to the feedback task. The ML borders of the treadmill present a greater potential threat to the task of walking on the treadmill compared to the AP borders for the same absolute displacement. This could also explain the reduction in ML translation variance in response to O-FB. For the individuals with BVH, both forms of visual feedback reduced low frequency ML whole body translation which suggests visual feedback during walking may be appropriate as a rehabilitation training method for this population. It remains to be seen whether repeated training with this type of visual feedback will result in transfer to over-ground walking or long term improvement for individuals with BVH.

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The adults with BVH in this study were able to use the visual feedback in a manner similar to healthy adults to modify their trunk motion. The reduction in ML translation of the COM is consistent with improved path consistency. The small sample size in this study limits generalization, but rather suggests a proof of concept that will be developed by future investigations. Future studies of this kind should also employ eye/gaze tracking to aid in the interpretation of how the individuals with impaired gaze stability were able to extract meaningful body/trunk position information from a visual image that they were not able to see clearly. Continuous online monitoring of visual feedback error signals may not be required to use that type of error signal to modify trunk motion. Discrete sampling of the visual feedback at specific points in the gait cycle may be all that is needed, and this should be investigated in future studies.

5.6 Conclusion

For individuals with vestibular loss, using visual feedback to modify excessive trunk motion during walking appears feasible, despite gaze instability. Individuals with vestibular loss were able to modify their trunk motion in response to both types of visual feedback (translation or orientation) in a manner similar to healthy individuals. Whether repeated training with visual feedback during treadmill walking has any carry over benefit for individuals with vestibular loss remains to be seen, but it appears to be a viable treatment method for these individuals.

Chapter 6: Experiment 4
Mechanisms of gaze stability during walking: physiological measures of gaze stability and oscillopsia

6.1 Abstract

Background: Individuals with bilateral vestibular hypofunction (BVH) often report symptoms of oscillopsia during walking. Subjective complaints of oscillopsia are inconsistently associated with measures of gaze stability. It is not known whether gaze stability during walking is better than would be predicted by passive testing in humans. Animal models have demonstrated that efference copy/proprioception contribute to gaze stability during locomotion, sometimes inhibiting the vestibulo-ocular reflex (VOR). The VOR is enhanced in humans with active head motion compared to passive head motion. Comparing gaze stability during treadmill walking and "seated walking" will enhance our understanding of the mechanisms that contribute to gaze stability during walking following loss of vestibular function. Characterizing the association between walking gaze stability and oscillopsia related activity limitations will bridge the gap between subjective quality of life and diagnostic testing for individuals with vestibular loss.

Methods: Gaze stability was measured for eight individuals with BVH and eight healthy controls matched for age and gender while walking on a treadmill and sitting on a six degree of freedom platform that replicated their walking head motion. Frequency response functions (FRF) were calculated from pitch eye and head velocity during active walking and seated walking conditions to enable group and condition comparisons. A one way ANOVA adjusted for false discovery rate and family-wise error was conducted to determine group and condition differences for each frequency bin of

the FRF. Pearson correlation coefficients were calculated to determine the relationship between Oscillopsia Functional Index (OFI) scores and the real and imaginary parts of the FRF.

Results: Individuals with BVH demonstrated lower gains than healthy controls at higher frequencies when walking, but their phase was compensatory for frequencies below 3 Hz. During seated walking, individuals with BVH actually had higher gains than during walking but also had greater phase lags at frequencies between 1 and 3 Hz. OFI scores were positively correlated with the real part of the FRF from active walking, corresponding to higher OFI scores at lower gain values. During passive walking OFI scores were positively correlated with the imaginary part of the FRF, corresponding to higher OFI scores at greater phase lags.

Conclusions: Gaze stability was enhanced during active walking compared to seated walking for individuals with BVH. Oscillopsia scores were associated with gain during active walking and with phase during seated walking which paralleled the aspects of gaze stability that were deficient for individuals with BVH. Gaze stability testing during walking is not the same for individuals with BVH as gaze stability testing during seated passive motion. Walking gaze stability should be tested for individuals with BVH to more accurately determine impairments in functional gaze stability.

6.2 Introduction

During locomotion, the ability to fixate gaze on objects (to avoid or interact with them) or to facilitate use of optic flow for heading is essential (Patla & Vickers, 2003). Individuals with bilateral vestibular loss (BVH) have impaired gaze stability (Whitney & France, 1996). Impaired gaze stabilization makes navigation and obstacle avoidance during walking more challenging, which may contribute to gait variability in individuals with BVH (Schniepp et al., 2011). Gaze instability from loss of vestibular function results in retinal slip that exceeds the tolerable limit of 2-4°/s (Demer et al., 1994; Crane & Demer, 1997). Retinal slip refers to motion of an image across the retina (Crane & Demer, 1997). Retinal slip in healthy individuals during locomotion on a treadmill has been reported as less than 4°/s, but increases for close targets (Crane & Demer, 1997).

It has been suggested that the primary purpose of the vestibulo-ocular reflex (VOR) is to stabilize gaze during locomotion, when frequencies of head movement far exceed the compensatory capabilities of pursuit or optokinetic systems (Grossman et al. 1989; Leigh & Brandt, 1993). Gaze instability during walking has been directly attributed to loss of function of the VOR (Crawford, 1952; Badaracco et al., 2010; Fetter, 2007; Leigh & Brandt, 1993). After VOR failure, a commonly reported complaint was that stationary environmental objects appear to "jump" during walking (Crawford, 1952). However, complaints of oscillopsia are not consistent across all individuals with a diagnosis of BVH (Bhansali et al., 1993). Oscillopsia has also been reported in individuals with intact saccular function suggesting that it may be related to angular VOR capabilities (Brandtberg & Lofqvist, 2007).

Current physiological vestibular function tests do not adequately characterize oscillopsia or the daily life impairments experienced by individuals with BVH. Oscillopsia has been studied using visual analogue scales of symptom severity (Herdman et al., 2007; Badaracco et al., 2010) or symptom frequency (Guinand et al., 2012; Grunfeld et al., 2000). However, oscillopsia severity and frequency do not consistently relate to physiological (i.e. VOR) or perceptual assessments of vestibular function like Dynamic Visual Acuity (DVA) (Bhansali et al., 1993; McGath et al., 1989; Schubert et al., 2002; Guinand et al., 2012; Badaracco et al., 2010). This disconnect between diagnostic testing and subjective quality of life may represent a limitation in the ability of existing questionnaires to adequately capture the functional impact of oscillopsia symptoms on daily life. Moreover, comparing oscillopsia severity in the vertical plane during walking with perceptual gaze stability tests (i.e. DVA) in the yaw plane (Herdman et al., 2007), using passive head motion DVA (Badaracco et al., 2010), or self-generated predictable pitch head movements during DVA testing (Schubert et al., 2002) may also contribute to the disconnect. Some individuals with BVH display elevated object motion detection thresholds during head motion (Wist et al., 1983). Therefore, during walking larger retinal slip magnitudes may be imperceptible for some individuals with BVH, resulting in minimal complaints of oscillopsia. There is no activity participation scale that characterizes the impact of oscillopsia symptoms on daily life activities. This suggests that improved functional methods for physiological testing and subjective measures that are functionally relevant are needed to completely describe the relationship between vestibular pathology and oscillopsia.

In a pilot experiment aimed at characterizing gaze stability during locomotion, head kinematics and eye movement were recorded during walking while subjects viewed a stationary visual image (virtual wall of randomly oriented triangles). Subjects were instructed to look through the virtual wall of triangles and not to fixate on any particular triangle. Six healthy individuals and five individuals diagnosed with BVH participated. Gain and phase relationships were calculated using head angular velocity as the input signal and eye angular velocity as the output signal. Surprisingly, compared to normal individuals, individuals with BVH demonstrated similarly compensatory relationships between the magnitude and timing of eye and head movements for frequencies up to ~1 Hz, as seen in Figure 6-1.
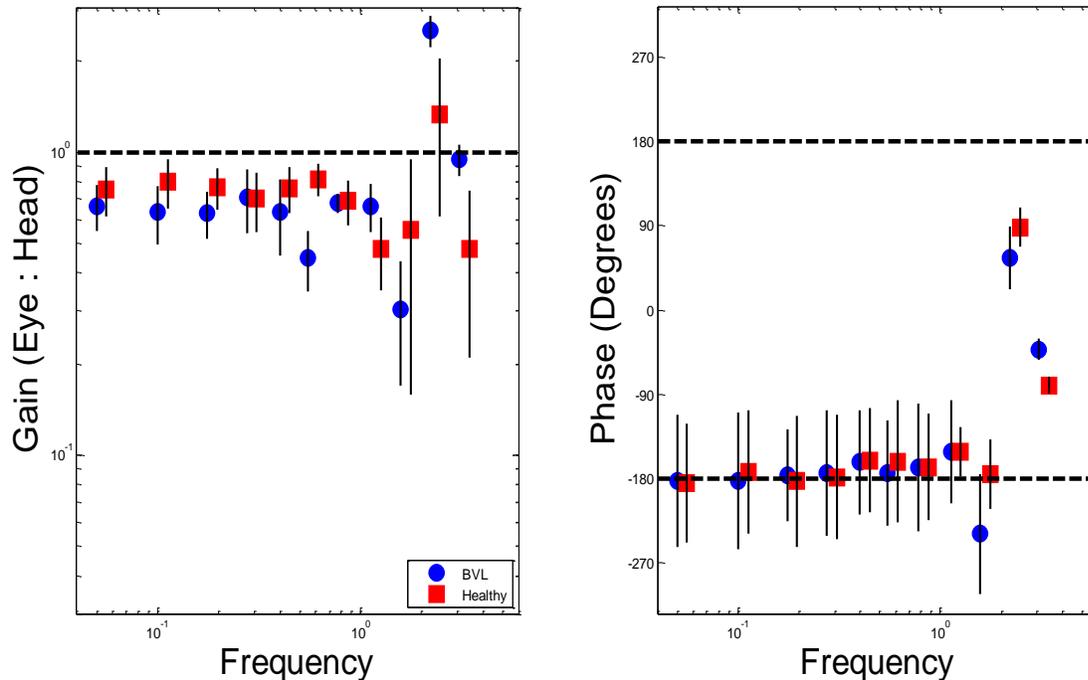
Figure 6-1. Gain and phase from pilot subjects including 5 individuals with BVH and 6 unmatched healthy subjects. Lower than unity gain is expected as the subjects were instructed to "stare through" a field of triangles without fixating on any single one. Lower gain for BVHs (blue circles) is expected given the impairment of the VOR, but the BVHs demonstrated compensatory eye velocity below ~1Hz.

The difficulty in interpreting these results is that there are several possible mechanistic explanations for the observed gain and phase behavior: 1) individuals identified with BVH may in fact have residual vestibular function (Schubert et al., 2002; Brantberg & Löfqvist, 2007; Agrawal et al., 2012); 2) gaze stability during locomotion may be mediated by an efference copy from the spinal central pattern generator (CPG) only found during walking (Solomon & Cohen, 1992; Combes et al., 2008; Sadeghi et al., 2012); 3) central pre-programming may enhance gaze stability via covert saccades or cerebellar gain adaptation for self-generated head movements during active walking

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(Herdman et al., 2001; Della Santina et al., 2002; Schubert et al., 2006; Schubert & Zee, 2010; Sadeghi et al., 2012); and 4) proprioceptive input from the neck and legs may contribute to gaze stability during walking (Arshian et al., 2014; McCall et al., 2013). Recent evidence also supports layered CNS contributions to human locomotion including descending cortical input (Capaday et al., 1999), presence of muscle synergies (Ivanenko et al., 2004; Dominici et al., 2011), and coherence between EEG and leg EMG activity (Petersen et al., 2012). All of these observations suggest multiple potential ways in which gaze stability might be augmented during walking for individuals with vestibular loss that would not be captured by passive testing.

Traditional methods of probing vestibular function remain artificial in nature, and the relevance of these assessments to natural functional behavior has been questioned (Demer et al., 2001; Badaracco et al 2010). Using standard assessments may limit the ability of existing vestibular diagnostic tests to detect residual vestibular function (Honrubia et al., 1985). It has been suggested that vestibular assessments should include higher frequency ranges (up to 8 Hz) that are unpredictable and more natural (Grossman & Leigh 1990; King et al., 1992). Angular pitch head rotation and vertical head translation during walking include frequency content up to 5 Hz (King et al., 1992), as shown in Figure 6-2.
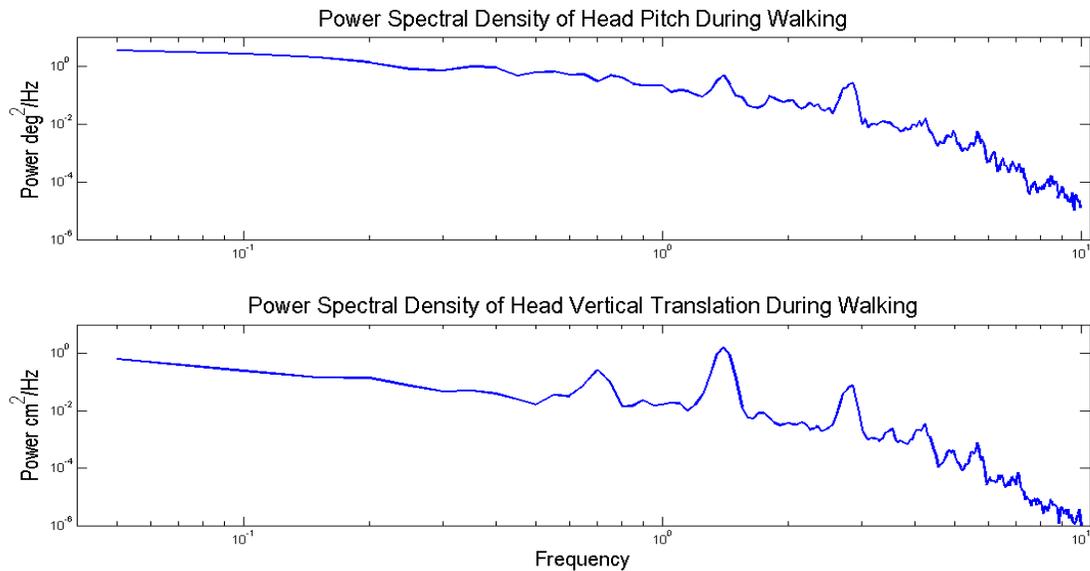
Figure 6-2. Exemplar PSD of head angular (pitch, top pane) and linear (vertical, lower pane) movement during treadmill walking at 0.55 m/s for a healthy subject. The first peak in the lower pane at ~.7Hz represents the gait cycle frequency. Note that harmonic peaks of the gait cycle exist above 5 Hz.

The ability to measure eye movements and characterize the capabilities of the gaze stabilization system during more functional tasks, such as locomotion, would add to current clinical assessments, particularly due to the tenuous link between clinical vestibular testing and daily functional gaze stability and postural/locomotive control abilities (Demer et al., 2001).

Since oscillopsia is a major complaint during walking, it seems only natural to explore oscillopsia and gaze stability in a mechanistic way when the functional impairments from oscillopsia are the greatest. Preliminary data (as shown in Figure 6-1) suggest that the relationship between eye and head movements during treadmill walking may provide a window for assessing gaze stability in a functionally meaningful way using a more natural input stimulus (Grossman & Leigh 1990). A better

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understanding of the relationship between gaze stability mechanisms and subjective

complaints could lead to more specific intervention strategies that improve quality of life.

A new questionnaire, the Oscillopsia Functional Impact (OFI) scale (see appendix A),

was developed to more completely characterize the impact of oscillopsia on daily life.

The OFI was modeled after a scale designed to characterize symptoms of autophony

for individuals with superior canal dehiscence (Crane et al., 2009), and is scored out of

a total of 215 points.

The challenge in assessing vestibular function during natural head movements is

that the resultant eye movements could also be generated from other sources including

voluntary eye movements, cervico-ocular reflexes, or eye movements driven by

efference copy/locomotor CPG commands. Thus, measuring gaze stability during

walking and suggesting that the results are *only* a measure of vestibular function in a

more "natural" context is probably misleading. On the other hand, a measurement of

overall gaze stability in individuals with BVH under natural walking conditions might

provide more insight into which individuals with BVH suffer from oscillopsia. Such a

measure might also provide a tool for ultimately exploring the means by which some

individuals with BVH compensate better than others.

Here we compare the gain and phase relationship of eye:head velocity during

walking on a treadmill to head movements during "seated walking" in a group of

individuals with BVH and a group of age matched healthy individuals. "Seated walking"

refers to passive motion of a chair based on walking head motion such that the evoked

head motion while sitting in the chair is similar to that during treadmill walking.

Comparing gaze stability during treadmill walking and "seated walking" will facilitate

better understanding of symptom severity following loss of vestibular function and provide mechanistic insight on potentially enhanced gaze stability during walking.

6.3 Method

6.31 Subjects

Interested participants were screened by phone to ensure eligibility to participate: 1) the ability to walk unsupported on a treadmill for at least six minutes, 2) have a diagnosis of vestibular loss. Twelve individuals with BVH were recruited to participate in the study. Three individuals with BVH cancelled multiple appointments due to transportation/weather problems. Nine age and gender matched individuals were recruited to serve as a control group. One control subject was removed due to abnormally low head impulse gains and one individual with BVH withdrew during the experiment resulting in matched samples with eight individuals per group. Demographic information on the 16 individuals who completed the experiment is provided in Table 6-1.

Table 6-1. Subject demographics and diagnostic criteria

	Age	Gender	Matches	Bithermal Caloric Response	Ice Calorics	vHIT	O-VEMP absent	C-VEMP absent	Etiology
Individuals with BVH									
BVH_1	43	M	A	NR	NR	Abn	Yes	Yes	Unknown
BVH_2	53	F	B	NR	NR	Abn	Yes	Yes	Unknown
BVH_3	50	F	G	(L) weakness	n/t	Abn	Yes	Yes	Unknown
BVH_4	69	F	C	(L) weakness	n/t	Abn	Yes	Yes	Ménière's
BVH_5	35	M	D	(L) weakness	n/t	Abn	Yes	Yes	Ménière's
BVH_6	73	M	E	NR	NR	Abn	Yes	Yes	Unknown
BVH_7	48	M	F	NR	NR	Abn	Yes	Yes	Labrynthectomy/ neuritis
BVH_8	74	M	H	NR	n/t	Abn	Yes	Yes	Unknown
Healthy controls									
HC_1	62	F	C	n/t	n/t	Nor	n/t	n/t	n/a
HC_2	66	M	E	n/t	n/t	Nor	n/t	n/t	n/a
HC_3	52	M	F	n/t	n/t	Nor	n/t	n/t	n/a
HC_4	59	F	B	n/t	n/t	Nor	n/t	n/t	n/a
HC_5	33	M	D	n/t	n/t	Nor	n/t	n/t	n/a
HC_6	49	F	G	n/t	n/t	Nor	n/t	n/t	n/a
HC_7	45	M	A	n/t	n/t	Nor	n/t	n/t	n/a
HC_8	75	M	H	n/t	n/t	Nor	n/t	n/t	n/a

Abreviations
NR – no response
Abn – abnormal response
Nor – normal response
n/t – not tested
n/a – not applicable
M – male

vHIT – video head impulse test
F – female

All enrolled participants provided informed consent prior to participating in any aspect of the experiment. This experiment was approved by the Institutional Review Boards at the University of Maryland College Park and The Johns Hopkins Medical Institutes.

6.32 Experimental Set Up

Apparatus: The walking portion of this experiment was conducted on a treadmill (Woodway USA, Inc) in the motion analysis laboratory at Kennedy Kreiger Institute. Head and body kinematics were recorded at 120 Hz using two banks of three Optotrak camera systems (Northern Digital, Inc). Eye and head velocity was recorded with an EyeSeeCam (Interacoustics, Eden Prairie, MN) video oculography system at 220 Hz. The EyeSeeCam consists of an integrated 6 degree of freedom inertial sensor to record head movements and an infrared video camera to record 3-D eye movements (Schneider et al., 2009). The seated walking portion of this experiment was conducted using a six degree of freedom motion platform (MOOG, Inc; hereafter referred to as the MOOG) in the vestibular research laboratory at The Johns Hopkins Medical Institutes, as shown in Figure 6-3.

6.33 Experimental Protocol

Each subject completed several questionnaires including: 1) an oscillopsia VAS (Herdman et al., 2007); 2) the OSQ (Guinand et al., 2012); and 3) the Oscillopsia Functional Impact scale.
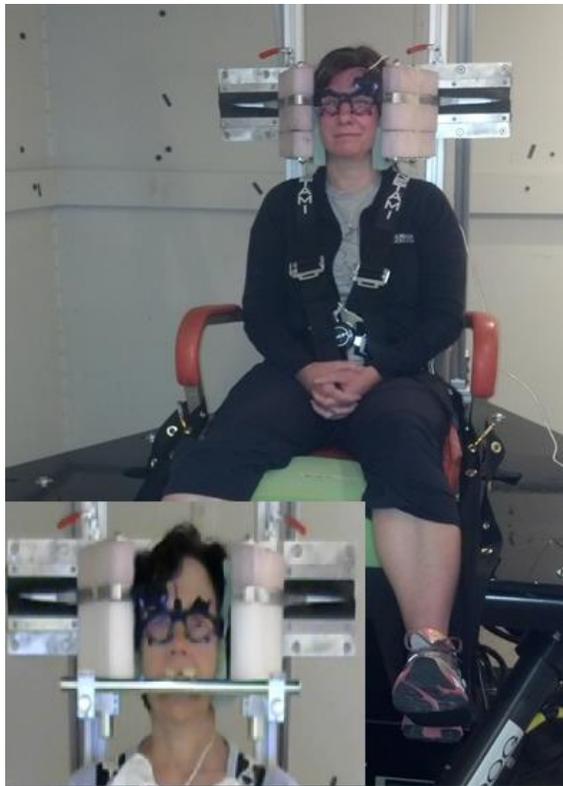
Figure 6-3. Picture of the experimental set-up for the "seated walking" portion on the MOOG. The bite bar and head restraint are shown in the inset.

All subjects wore the EyeSeeCam for the walking and "seated walking" fixation tasks (see Figure 6-3) to measure head and eye motion (Schneider et al., 2009). The monitor was centered approximately 5° below the subject's eye height at a distance of 2.2 meters. All subjects walked on the treadmill at 0.55 m/s (2 km/hr). This speed was selected as individuals with BVH: 1) demonstrated gaze instability while walking at 2km/hr (Guinand et al., 2012); and 2) were able to walk on the treadmill at 2km/hr without holding handrails (see Chapter 5). A fixation point ("+" displayed in the center of the screen at a logMAR size of 1.00) was used for the three fixation walking trials (2 minutes each). LogMAR is defined as $\log_{10}x$ where x is the minimum angle resolved in arcmin, with 1 arcmin equal to 1/60° (Ferris et al., 1982). All subjects were instructed to

"stare at the center of the plus sign" and to minimize the frequency and duration of blinks during walking trials. Blinks and saccades were identified using a Kalman filter which compared actual eye velocity to predicted eye velocity (McGibbon et al., 2001). Large differences occur during blinks and saccades which were used to identify gaps which were then filled using a cubic spline interpolation (McGibbon et al., 2001). A 1-2 minute standing rest was provided between every trial to minimize fatigue.

An overhead harness which only provided support if upright equilibrium was lost was worn by all subjects. Light touch stabilizes walking center of mass sway (Dickstein & Laufer, 2004); therefore, subjects were instructed to walk without "holding on" to the rails unless a loss of balance occurred. One individual with BVH touched the hand rail for stability in one trial and that trial was terminated and repeated. Following the treadmill walking portion of the experiment all subjects were provided a rest period lasting at least 45-90 minutes while offline data processing was completed.

Translational and angular head motion recorded from the Optotrak camera system was processed offline and saved to subsequently control motion of the MOOG. Translation in the AP and vertical directions as well as head pitch angle were used to specify MOOG motion which led to sagittal plane head movement during "seated walking" that was based on that experienced during treadmill locomotion. Subjects sat in a custom chair on the MOOG equipped with 4-point seatbelts, a head restraint, and a bite bar, as shown in Figure 6-3. The EyeSeeCam was used to record head and eye movements while on the MOOG. Each subject completed three repetitions of composite motion (combination of pitch, vertical and fore-aft motions) and three repetitions of isolated pitch, isolated vertical, and isolated fore-aft motion. This chapter

will only consider the composite motion trials on the MOOG to facilitate direct

comparison with the walking results. The order of MOOG motion signals was

randomized for each of three blocks which correspond to the original walking trials.

Each MOOG trial lasted ~2.5 minutes. All MOOG conditions were performed with

available light and used the same visual fixation point as the walking conditions

centered approximately 5° below seated eye height. All participants received $50

compensation upon completion of the study.

Clinical Vestibular Testing

All individuals were tested with semicircular canal specific video head impulse tests

(Halmagyi et al., 2001) using the EyeSeeCam (Interacoustics, Eden Prairie, MN) to

record head and eye velocities according to published specifications (Schneider et al.,

2009; MacDougal et al 2013). Individuals with vestibular loss were also tested with both

cervical and ocular VEMPS (Colebatch et al., 1994) and caloric testing (Barber &

Stockwell, 1980) unless those tests had been completed in the previous 12 months.

The procedures for cervical and ocular VEMPS have been described elsewhere

(Agrawal et al., 2012) in detail and are presented in brief here. Subjects were

positioned in supine with their head elevated ~30° from horizontal as 500-Hz, 125-dB

SPL tone bursts were delivered at a rate of 5 Hz monaurally via headphones. Cervical

VEMPS were recorded from ipsilateral sternocleidomastoid muscles with the head

rotated and flexed to ensure sternocleidomastoid muscle activation. Midline head tap

ocular VEMPS were recorded from contralateral inferior oblique muscles while subjects

maintained maximum vertical gaze. Taps were delivered manually at the midline of the

hairline ~30% of the distance between the inion and the nasion with an Aesculap model AC012C reflex hammer fitted with an inertial microswitch trigger. EMG signals were recorded with disposable, self-adhesive, pregelled, Ag/AgCl electrodes (Schaumburg, IL, USA).

6.34 Analysis

Spectral Analysis

Fourier transforms of vertical eye rotation velocity and head pitch velocity were calculated. One-sided power spectral densities (PSDs) and cross spectral densities (CSDs) using Welch's method (Bendat & Piersol, 2000) with a 20 second Hanning window and one half overlap were then calculated with these transforms. The PSDs and CSDs are averaged across trials for each subject. For each subject the PSDs and CSDs were binned on a linear logarithmic scale up to 5 Hz, resulting in 12 frequency bins. The frequencies included in each of the ten bins are as follows: .05, .1, .15-.2, .25-.3, .35-.45, .5-.6, .65-.9, .95-1.3, 1.35-1.8, 1.85-2.55, 2.6-3.55 and 3.6-5 Hz. The frequencies are averaged in each bin for plotting purposes resulting in the following twelve frequencies: .05, .1, .175, .275, .4, .55, .775, 1.125, 1.575, 2.2, 3.075, and 4.3 Hz.

Gain and phase were computed to characterize the magnitude and timing of the eye velocity response to head velocity at each of the twelve frequency bins of the frequency response functions (FRF). Gain is computed as the absolute value of the FRF, $\bar{H}_{xy}(f)$ and phase is the argument of the FRF, $\bar{H}_{xy}(f)$ in degrees. The FRF averaged across subjects was defined as $\bar{H}_{xy}(f) = \bar{P}_{xy}(f)/\bar{P}_{yy}(f)$ where $\bar{P}_{xy}(f)$ is the

mean CSD between head pitch (x) and eye velocities (y) and $\bar{P}_{yy}(f)$ is the PSD of head

pitch velocity (Kiemel et al. 2008).

As a first pass analysis due to the multiple frequency bins, FRFs were averaged

across repetitions for each subject and then a one way ANOVA was used to compare

the complex valued response for each frequency bin and zero. To control for family-

wise error (FWE) due to multiple comparisons alpha levels were corrected using the

Holm-Bonferoni method (Holm, 1979). Only frequency bins with responses significantly

different from zero after correcting for multiple tests were used for subsequent between

group and within group comparisons. To compare gain and phase responses between

groups (BVD vs. Healthy) or conditions (FRF$_{WALK}$ vs. FRF$_{MOOG}$), the difference between

the complex valued FRF was compared to zero. Both gain and phase are transforms of

the same complex valued FRF and separate testing is not appropriate. 95% confidence

intervals were computed based on the complex valued FRFs for gain and phase for

each frequency bin. Differences in gain and/or phase between groups and across

conditions were identified when the confidence intervals did not overlap and when

differences between complex valued FRFs were significantly different from zero

correcting for FWE. PSDs for head pitch velocity were compared across conditions to

verify similarity of head motion during active walking and seated walking. To control for

multiple comparisons for all 12 frequency bins, FWE criteria were applied to the *P*

values as indicated above (Holm, 1979).

Clinical Analysis

A one-way ANOVA was performed to identify significant group differences in video head impulse testing, and in all oscillopsia measures. To determine the relationship between gaze stability and oscillopsia Pearson correlation coefficients were computed between OFI scores and both the real and imaginary parts of the FRFs. The OFI was correlated with the FRFs rather than gain and phase because gain and phase are both calculated from the same FRF value and thus cannot be analyzed separately. The real and imaginary parts of the FRF can be analyzed separately and can be related back to gain (real part) and phase (imaginary part). Significance was tested at $\alpha = 0.05$ for all statistical tests.

6.4 Results

Condition equivalence

The frequency content of head pitch during walking was similar to that during the composite seated walking condition on the moog, see Figure 6-4. Overall the frequency content was similar between treadmill walking and seated walking conditions. After controlling for FWE and FDR, the 2.2 Hz frequency bin had significantly less power during the seated walking condition for the healthy group.
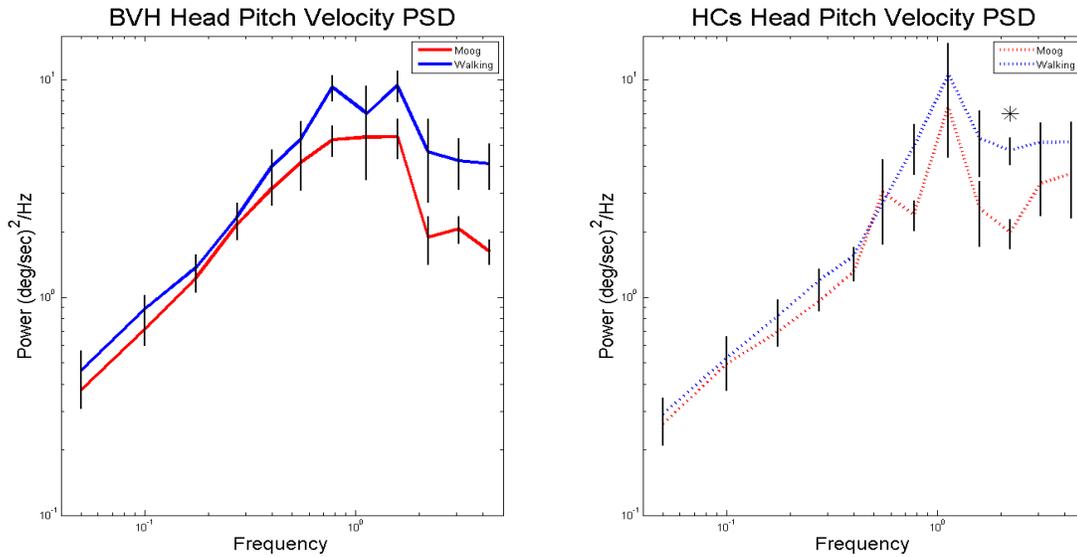
Figure 6-4. Average Power Spectral Densities for head pitch velocity for the seated walking (red) and treadmill walking conditions (blue). Solid lines represent the individuals with BVH and dashed lines represent healthy matched control subjects. Error bars represent standard error. Significant condition differences are indicated by *.

Group Comparisons

Canal specific video HIT results are presented in Table 6-2. Individuals with BVH present with significantly lower video HIT gains for all semi-circular canals (*p's* < .001), as shown in Figure 6-5 for group average gains. Individuals with BVH reported more severe oscillopsia that interfered with daily activities compared to healthy controls (*p's* < .001), as shown in Table 6-3.

Table 6-2. Canal specific video head impulse test

Subjects	(R) Lat	(R) Ant	(R) Post	(L) Lat	(L) Ant	(L) Post
BVH_1	0.22	0	0.69	0.13	0.34	0
BVH_2	0	0.16	0	0	0	1.09
BVH_3	0.58	0.48	0.45	0.53	0.54	0.52
BVH_4	0.55	0.97	0.7	0.32	0.47	0.82
BVH_5	0.2	0.36	0.1	0.21	0.42	0
BVH_6	0.12	0.23	0.31	0.12	0	0.38
BVH_7	0.05	0.65	0.03	0.08	0	0.17
BVH_8	0	0.1	0	0	0	0.27
HC_1	0.93	1.47	0.78	1.24	0.92	0.88
HC_2	0.99	1.84	0.69	1.21	0.58	1.05
HC_3	0.93	1.35	1.14	0.94	1.52	1.36
HC_4	0.84	1.54	0.77	1.06	0.85	0.95
HC_5	0.96	1.23	0.51	1.03	0.89	0.95
HC_6	1.01	1.27	0.89	1.32	0.92	1.23
HC_7	0.87	1.39	0.95	1.12	0.77	1.24
HC_8	1.09	0.84	0.82	1	0.41	0.86

Abbreviations

Lat – Lateral Semi-Circular Canal

Ant – Anterior Semi-Circular Canal

Post – Posterior Semi-Circular Canal

(R) – Right

(L) – Left
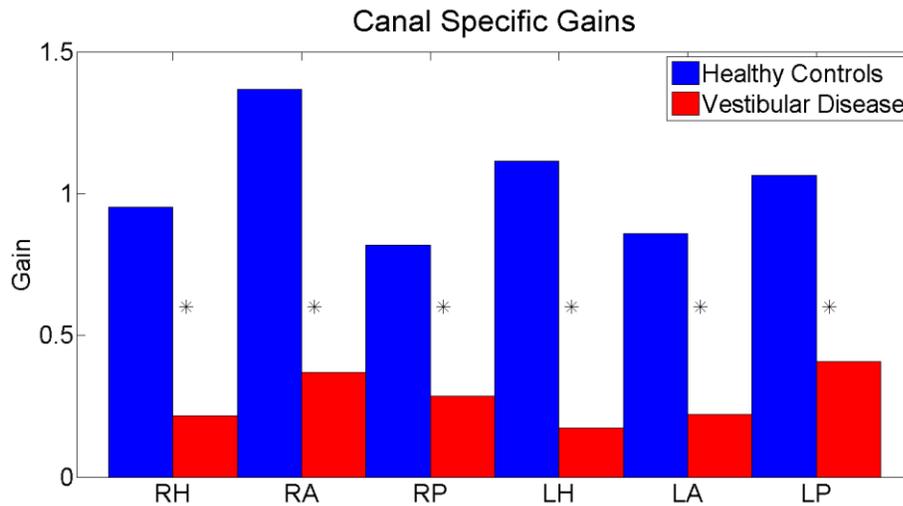
Figure 6-5. Average canal specific VOR gain for individuals with BVH (red) and healthy controls (blue). Significant group differences indicated by *. R – Right, L – Left, H – Horizontal, A – Anterior, P - Posterior

Table 6-3 Between group differences on subjective measures of oscillopsia. Average (SEM) [95% CI] are presented and significant group differences are indicated by an *, p's < .002.

Group	OFI total *	OFI average *	OSC *	OS VAS *
BVH	64 (8.9) [42.8-85.1]	1.68 (.21) [1.2-2.2]	3.01 (.28) [2.4-3.7]	4.2 (.79) [2.3-6.1]
Healthy	7.4 (2.1) [2.5-12.2]	0.18 (.05) [.06-.31]	1.08 (.05) [.98-1.2]	0.19 (.10) [-.05-.43]

Abbreviations
OFI – Oscillopsia Functional Impact scale
OSC – Oscillopsia Severity scale
OS VAS – Oscillopsia Visual Analogue Scale

Frequency Response Functions

Walking. Eye velocity responses to head velocity for all frequency bins were significantly different from zero; therefore group and condition analyses were conducted on all frequency bins. Individuals with BVH had significantly lower gains while walking compared to healthy individuals for frequency bins: .275, .55, .775, 1.125, 1.575, 2.2, 3.075, and 4.3 Hz. ($p's$ < .004), as shown in Figure 6-6. Despite lower gains, individuals with BVH demonstrated a stable and compensatory phase response that did not differ from healthy controls below 3 Hz.
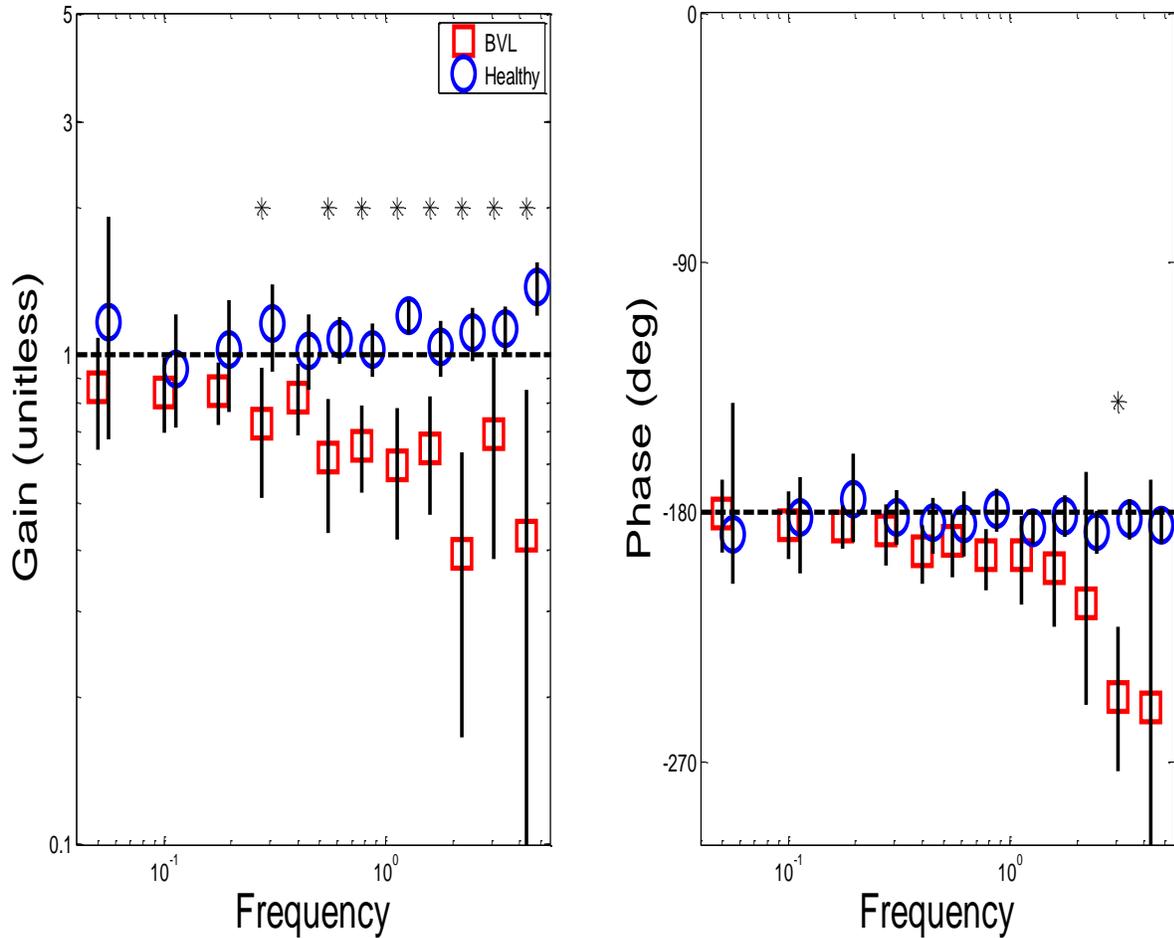
Figure 6-6. Gaze stability during walking. Blue circles represent the healthy controls and red squares represent individuals with BVH. Error bars represent 95% confidence intervals. * indicate significant group differences in gain and phase.

At 3 Hz, the individuals with BVH displayed a significant phase lag compared to healthy controls (p < .004).

Seated Walking. During seated walking conditions, individuals with BVH had significantly lower gain only at .4 Hz compared to healthy controls (p < .05). Individuals with BVH demonstrated a phase lag compared to healthy controls for frequencies .775, 1.125, 1.575 Hz, as shown in Figure 6-7.
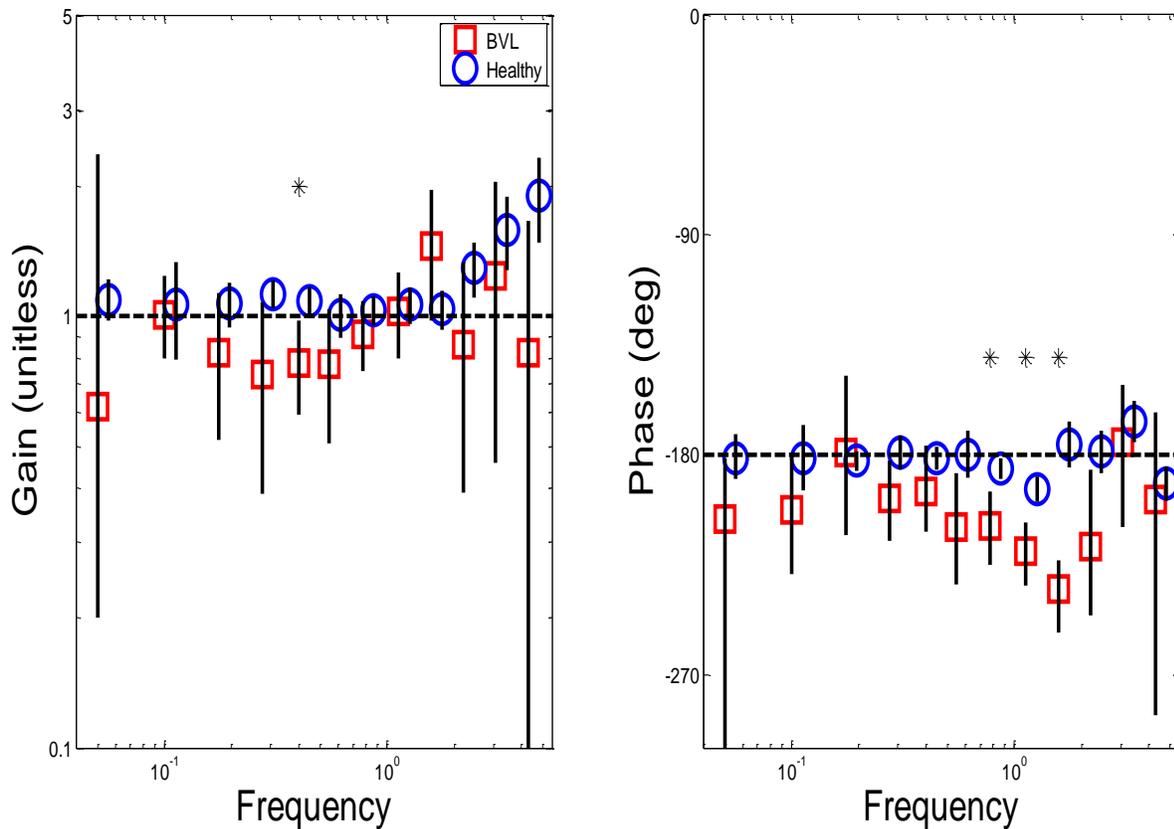
Figure 6-7. Gaze stability during the seated walking condition. Blue circles represent the healthy controls and red squares represent individuals with BVH. Error bars represent 95% confidence intervals. * indicates significant group differences.

<u>*Condition Comparisons*</u>

Frequency Response Functions

Healthy individuals phase responses were not different for any frequency between treadmill walking and seated walking. Healthy individuals displayed higher gain responses in the seated walking condition compared to treadmill walking only at the highest frequencies (3.075 Hz and 4.3 Hz). Individuals with BVH however, displayed some significant condition differences. Specifically, individuals with BVH had

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higher gain at 1.125, 1.575 Hz during the seated walking condition compared to treadmill walking. Individuals with BVH also had greater phase lag at 1.575 and 3.075 Hz (p's < .05) during the seated walking condition compared to treadmill walking.

There were significant correlations between OFI scores and both the real and imaginary parts of the frequency response functions from both the walking and seated walking conditions, as shown in Table 6-4. During the seated walking condition the majority of significant correlations with OFI scores were with the imaginary part of the FRF (frequency bins .05, .55-1.575, 4.3 Hz). The real part of the seated walking FRF was only significantly correlated with OFI scores for two frequency bins (.175 and .4 Hz). In contrast, the majority of significant correlations during the walking condition were between the OFI and the real part of the FRF (frequency bins .175-4.3 Hz). The only exception was frequency bin .775 Hz which was also correlated with the imaginary part of the FRF.

Table 6-4. Correlation coefficients between oscillopsia scores on the OFI and the real and imaginary parts of gaze stability frequency response functions during walking and on the MOOG. Significant correlations are indicated by an *.

	.05 Hz	.1 Hz	.175 Hz	.275 Hz	.4 Hz	.55 Hz	.775 Hz	1.125 Hz	1.575 Hz	2.2 Hz	3.075 Hz	4.3 Hz
Real FRF_moog	r = .00 p = .99	r = .31 p = .25	r = .53* p = .04	r = .40 p = .17	r = .53* p = .04	r = .28 p = .30	r = .47 p = .07	r = .42 p = .10	r = .07 p = .80	r = .22 p = .42	r = .17 p = .54	r = .17 p = .53
Real FRF_walk	r = .44 p = .09	r = .35 p = .18	r = .58* p = .02	r = .63* p = .009	r = .51* p = .04	r = .67* p =.005	r = .62* p = .01	r = .54* p = .03	r = .49* p = .05	r = .73* p = .002	r = .59* p = .02	r = .75* p = .001
Imag FRF_moog	r = .56* p = .03	r = .36 p = .17	r = .20 p = .46	r = .44 p = .09	r = .46 p = .07	r = .66* p = .006	r = .73* p = .001	r = .64* p = .008	r = .78* p = .00	r = .03 p = .93	r = .10 p = .70	r = -.52* p = .04
Imag FRF_walk	r = -.18 p = .51	r = -.01 p = .97	r = .12 p = .67	r = .06 p = .82	r = .23 p = .39	r = .21 p = .44	r = .57* p = .02	r = -.07 p = .81	r = .12 p = .67	r = .15 p = .58	r = .43 p = .10	r = .41 p = .12

Abbreviations
FRF – Frequency Response Function
OFI – Oscillopsia Functional Index

6.5 Discussion

In this experiment, gaze stability during treadmill walking was compared to gaze stability during "seated walking" in a group of individuals with severe BVH and a group of age matched healthy individuals. Overall, individuals with BVH demonstrate different mechanisms for gaze stability depending on whether they actively walked on a treadmill or sat in a chair and passively experienced sagittal plane walking head movements.

Overall, individuals with BVH reported more severe oscillopsia and had lower VOR gains on clinical head impulse testing. During walking individuals with BVH displayed lower gains as frequency increased compared to healthy controls. Lower eye:head velocity gain during walking for individuals with BVH was also consistent with low VOR gains measured with video head impulses. This suggests that the gain component of the FRF may be directly attributable to vestibular function. Individuals with BVH did not differ from healthy controls with respect to phase for frequencies below 3 Hz. When walking, individuals with BVH have lower velocity eye movements that were appropriately timed. These results suggest that the timing for eye movements in response to head motion during walking was not dependent on a fully functioning vestibular system. Animal investigations have identified proprioception and spinal efference copy signals as mechanisms that contribute to control of eye movements during locomotion (McCall et al., 2013; Solomon & Cohen, 1992; Combes et al., 2008; Sadeghi et al., 2012; Shanidze et al., 2013). The compensatory phase at frequencies below 3 Hz for individuals with BVH while walking suggests that

timing information is available for feed forward control of gaze stability. This is

consistent with prior research describing efference copy enhanced gaze stability

for self-generated head movements (Herdman et al., 2001; Della Santina et al.,

2002; Schubert et al., 2006). Cognitive intent has been shown to mediate

somatosensory contributions to horizontal eye velocity during constant velocity

circular walking (Weber et al., 2000). Eye movement control during constant

velocity circular walking may differ from typical treadmill walking that allows bi-

directional pitch head motion. It is not known to what extent the intent to walk in

a specific direction contributed to the results in the present experiment as the

current experiment did not involve circular walking.

Healthy controls only differ between active walking and seated walking

with higher gain in the two highest frequency bins during the seated walking

condition. This finding is consistent with previous work demonstrating that VOR

gain increases at higher frequencies (Tabak & Collewijn, 1995). Phase was

compensatory for the healthy controls indicating that the vestibular system

generated eye movements that were compensatory during the seated walking

condition. In contrast to the healthy controls, individuals with BVH demonstrated

higher gain and a larger phase lag for frequencies between 1 and 3 Hz.

The increased gain response for individuals with BVH was surprising, but

oculomotor tracking may explain both the increased gain and phase lag we

observed. A previous study showed that tracking eye movements that stop just

prior to onset of head motion enhanced early components of the VOR (Das et al.,

1999). Both pursuit and saccadic eye movements enhanced the VOR as long as

they were in the plane of subsequent head rotation. Eye velocity may have

primed the neural integrator, which receives input from oculomotor gaze shifts

and also vestibular signals (Das et al., 1999). Goldreich and colleagues (1992)

demonstrated higher than expected gains to high frequency pursuit when high

frequency target motion was superimposed on constant target velocity. The

target in the present experiment was stationary; therefore, the pursuit system

would not be necessary if the VOR was intact as retinal slip would be minimal

(Leigh et al., 1994). However, individuals with BVH would experience retinal slip

which could serve as an error signal to initiate pursuit eye movements (Das et al.,

1995; Leigh et al., 1994). Changing head pitch direction would also provide a

position error signal consistent with changing pursuit target direction which

results in eye movements in the direction to correct for the position error

(Tarnutzer et al., 2007). This is consistent with the individuals with BVH using a

pursuit style mechanism during the seated walking which results in higher gain

and a greater phase lag as found in this experiment, see Figure 6-6. Pursuit

onset latencies of ~100 ms are much longer than the typical VOR latency of 7-13

ms and would contribute to the phase lag during seated walking (Lencer &

Trillenberg, 2008). The phase lag during seated walking further suggests that

timing information for stable gaze was missing, relative to the walking condition.

The lack of timing information necessitated a transition to a feedback

driven system like oculomotor pursuit. Whether the timing information came from

an efference copy/CPG or somatosensory contributions to the central vestibular

system, the overall effect during walking was enhanced gaze stability. The

specific mechanism contributing this timing information cannot be elucidated based on this experiment, but future experiments will probe the effects of external versus internal pacing and the role of bilateral spatio-temporal synchrony to better understand what gait mechanisms contribute to the observed phase response for the individuals with BVH.

Previous attempts to relate subjective reports of oscillopsia to measures of vestibular function have been inconsistent (Bhansali et al., 1993; McGath et al., 1989; Grunfeld et al., 2000; Schubert et al., 2002; Herdman et al., 2007; Guinand et al., 2012; Badaracco et al., 2010). In this experiment there were significant correlations between OFI scores and aspects of the FRFs that were condition specific, see Table 6-4. The real part of the FRF was positively correlated with OFI scores during walking. This corresponds to higher OFI scores being associated with lower gain during walking. In contrast, during the seated walking condition the OFI scores were positively associated with the imaginary part of the FRF. This relationship corresponds to higher OFI scores at greater phase lags from ideally compensatory. Gaze instability could be caused by inadequate gain or non-compensatory phase (Wist et al, 1983). In this experiment, individuals with BVH demonstrate inadequate gain during walking, and non-compensatory phase during seated walking. OFI scores were correlated to the specific aspects of gaze instability that were impaired for individuals with BVH in each condition. Oscillopsia was not related to gain during the passive part of this experiment which may explain why associations were not found between VOR gain and oscillopsia in some previous reports (Bhansali et al., 1993; McGath et al., 1989).

Oscillopsia was negatively related to VOR gain during walking, unlike a previous report in which gaze stability was measured by DVA (Guinand et al., 2012). This discrepancy may actually be due to differences in how gaze stability was measured. In the present experiment gaze stability was the relationship between eye and head velocity, while in the other experiments DVA was the measure of gaze stability (Schubert et al., 2002; Herdman et al., 2007; Guinand et al., 2012). While DVA scores are related to VOR gain (Schubert et al., 2006), DVA scores only accounted for 45% of the variance in VOR gain abnormalities for individuals with vestibular disease. In fact, our own results demonstrate that for this same group of subjects oscillopsia was not related to DVA scores (see chapter 7) regardless of whether the walking was active or passive. Activity restriction due to oscillopsia symptoms was captured by OFI scores. The exact mechanism for the activity restriction remains to be elucidated and how pathology impacting the linear and angular VOR systems contributes to activity restriction remains to be determined.

The results from this experiment demonstrated that gaze stability was enhanced during walking for individuals with vestibular loss in ways not predicted by passive testing. It is not clear whether this enhancement can be leveraged to facilitate better rehabilitation outcomes for individuals with vestibular loss and future studies are needed.

6.6 Conclusion

Individuals with BVH demonstrate different mechanistic contributions to gaze stability depending on whether they are actively or passively walking. Active walking results in better gaze stability than would be predicted by passive testing. Intrinsic knowledge of timing during walking via a locomotion efference copy may contribute to improved gaze stability during walking for individuals with BVH. Oscillopsia scores were related to the specific components of gaze stability that were impaired during both active and passive movement. During active walking, oscillopsia was related to gain; however during passive (seated) walking oscillopsia was related to phase. The results from this experiment suggest that gaze stability should be measured during walking to most accurately determine the degree of functional impact from vestibular loss. Individuals with BVH may benefit from gaze stabilization activities performed while walking in order to take advantage of the walking specific phase enhancement in gaze stability.

Chapter 7: Experiment 5
Mechanisms of gaze stability during walking: perceptual measures relating gaze stability to oscillopsia

7.1 Abstract

Background: Visual acuity degrades during walking compared to stranding, especially for individuals with bilateral vestibular hypofunction (BVH). Dynamic visual acuity (DVA) scores provide a measure of functional gaze stability, and improve with active head motion compared to passive head motion. It is not known whether DVA scores during treadmill walking are enhanced in a similar way compared to DVA scores during passive sagittal plane head motion based on walking head motion. DVA scores are not consistently related to oscillopsia complaints. The Oscillopsia Functional Impact scale (OFI) was designed to describe the impact of oscillopsia on activity participation in an effort to better link impairments in gaze stability to oscillopsia complaints.

Methods: Eight individuals with BVH and eight healthy controls matched for age and gender were tested for visual acuity while standing, walking on a treadmill and sitting in a chair on a six degree of freedom platform that moved to passively replicate sagittal plane walking head motion (seated walking). DVA scores were calculated as the change in visual acuity between standing and both active walking and seated walking conditions. Group and condition comparisons were performed using a repeated measures ANOVA. Spearman correlation coefficients were calculated to determine the relationship between the OFI and other questionnaires that characterize oscillopsia, dizziness, and balance

perception to demonstrate face validity. A one way ANOVA was conducted for group differences on all questionnaires.

Results: A trend toward better DVA scores during active walking compared to seated walking was observed (p = .059), but no group difference was found for DVA scores. The Oscillopsia Functional Index (OFI) was highly correlated with measures of oscillopsia severity (r = .88) and frequency (r = .88) and also with the Dizziness Handicap Inventory (r = .89) and the Activities Specific Balance Confidence scale (r = -.85). Individuals with BVH scored worse on all measures of oscillopsia, dizziness handicap and balance confidence compared to healthy individuals (p's < .002).

Conclusions: Gaze stability trended toward significant enhancement during active walking compared to seated walking, suggesting an option for rehabilitation. The OFI demonstrated internal and face validity and also discriminated healthy individuals from individuals with BVH. Activity restriction due to oscillopsia was not correlated with DVA scores suggesting that other factors mediate oscillopsia induced changes in activity participation.

7.2 Introduction

The ability to see clearly while the body is in motion is referred to as gaze stability. Unstable gaze during walking has been attributed to loss of function of the vestibulo-ocular reflex (VOR) (Crawford, 1952; Badaracco et al., 2010; Fetter, 2007; Leigh & Brandt, 1993). When the VOR fails, the eyes no longer move in a way that compensates for head motion which results in bouncing or jumping vision during walking, known as oscillopsia (Brickner, 1936; Crawford, 1952).

Dynamic visual acuity (DVA) testing is a perceptual measure of how well the VOR stabilizes an image on the retina. DVA is defined as the change in visual acuity between conditions when the head is stationary and when the head is moving. Visual acuity is measured by correctly identifying the orientation (i.e. right/left/up/down) of optotypes (i.e. letter "E") that get progressively smaller (Herdman et al., 1998; Herdman et al., 2001). The difference in the smallest accurately identified optotype sizes between head still and head moving conditions is the DVA score. DVA testing can be performed while sitting, standing, or walking, in the transverse and sagittal planes, and with active or passive head motion (Herdman et al., 1998; Schubert et al., 2002; Vital et al., 2010; Kao et al., 2010; Demer et al., 1994).

The two most common subjective measures of oscillopsia are the oscillopsia visual analogue scale (OS VAS, Herdman et al., 2007) and an oscillopsia severity questionnaire (OSQ, Guinand et al., 2012). The OS VAS describes symptom severity (Herdman et al., 2007) and the OSQ describes symptom frequency but is not specific to head motion induced oscillopsia.

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Symptom severity and frequency may not adequately characterize activity

participation resulting in an inconsistent relationship between DVA and

oscillopsia. The existing scales do not adequately characterize how oscillopsia

impacts daily function from an activity participation perspective (World Health

Organization, 2007).

The relationship between subjective oscillopsia complaints and DVA score

is inconsistent; some studies report no relationship and others report a significant

correlation (Bhansali et al., 1993; Badaracco et al 2010; Grunfeld et al., 2000;

Guinand et al., 2012; Herdman et al., 2007; Schubert et al,. 2002). Individuals

with poor DVA scores report oscillopsia severity that ranges from mild to severe

(Guinand et al., 2012). Increased tolerance for retinal slip despite poor DVA

scores may contribute to the inconsistent relationship between DVA scores and

oscillopsia complaints (Grunfeld et al., 2000; Schubert et al., 2002). Efference

copy enhances gaze stability during active head motion (Vital et al., 2010), which

could also reduce the relationship between DVA and oscillopsia. DVA in the

transverse plane or performed while sitting may not accurately reflect gaze

stability during walking, an activity commonly associated with oscillopsia

complaints (Crawford, 1952; Grossman & Leigh, 1990; Lambert et al., 2010).

DVA testing while walking provides a more functionally relevant estimation of

gaze stability.

DVA during active head motion is better than during passive head motion

(Vital et al., 2010; Tian et al., 2002) consistent with VOR enhancement during

active head rotation (Della Santina et al., 2002; Gielen et al., 2004). Although

walking is an active behavior, efference copy may not be able to perfectly

compensate for an impaired VOR (Grossman & Leigh, 1990; King et al., 1992).

Individuals with vestibular loss show a greater decrement in visual acuity while

walking than healthy controls when compared to standing visual acuity

(Badaracco et al., 2010; Lambert et al., 2010; Hillman et al., 1999). It is not clear

whether walking DVA is better than would be predicted from passive DVA. The

closest previous reports to passive walking head motion that measured DVA

involved sinusoidal pitch rotation (Demer et al., 1994) and sinusoidal vertical

translation with the head unrestrained (Peters et al., 2013). However, the

passive motions were not derived from walking patterns, and direct comparisons

with walking DVA were not made. Here we characterized functional gaze

stability measured by DVA during treadmill walking and seated walking derived

from sagittal plane walking head motion. We also developed a new scale to

characterize oscillopsia in an effort to better understand the functional impact of

oscillopsia and impaired gaze stability during walking for individuals with

vestibular loss.

7.3 Methods

7.31 Subjects

Sixteen individuals participated in this experiment, (10 male, 6 female)

which was approved by the institutional review boards at Johns Hopkins Medical

Institutes and the University of Maryland. Eight of the individuals who

participated in this experiment had severe bilateral vestibular hypofunction mean

age 55.6 (± 14.6) years and they were matched for age and gender by eight

healthy individuals mean age 55.1 (± 13.2) years. Subject demographic data is

presented in Table 6-1.

7.32 Experimental Set Up

Apparatus: The walking portion of this experiment was conducted in the

motion analysis laboratory at Kennedy Kreiger Institute on a treadmill (Woodway

USA, Inc). An overhead harness which only provides support upon loss of

equilibrium was worn by all subjects. Head and body kinematics were recorded

at 120 Hz using two Optotrak three camera systems (Northern Digital, Inc). The

"seated walking" portion of this experiment was conducted using a six degree of

freedom motion platform (MOOG, Inc; hereafter referred to as the MOOG) in the

vestibular research laboratory at The Johns Hopkins University. Subjects sat in a

custom chair on the MOOG equipped with a 4-point seatbelt, a head restraint,

foot support, and a bite bar.

7.33 Experimental Protocol

Vestibular function was characterized as described in Chapter 6, see

Tables 6-1 and 6-2 for vestibular function test information. Each subject

completed several questionnaires including: 1) the Activity Specific Balance

Confidence scale (Powell & Meyers, 1996); 2) the Dizziness Handicap Inventory

(Jacobson & Newman, 1990); 3) the OS VAS (Herdman et al., 2007); 4) the OSQ

(Guinand et al., 2012); and 5) the Oscillopsia Functional Impact (OFI) scale

developed for this experiment. The OFI scale (see Appendix 1) was designed to characterize the impact of oscillopsia on daily life activity participation. The OFI was modeled after an autophony scale for individuals with superior canal dehiscence (Crane et al., 2009), and is scored out of a total of 215 points. Questions were designed to identify the degree to which oscillopsia interferes with participation in daily activities.

All subjects walked on the treadmill at 0.55 m/s (2 km/hr). This speed was selected as individuals with vestibular loss were previously reported to be able to walk on a treadmill at 2km/hr (Guinand et al., 2012; Hillman et al., 1999), and head velocities during pilot studies at 2km/hr were within the mechanical limits of the MOOG. Individuals with bilateral vestibular loss have demonstrated gaze instability walking at 2km/hr compared to individuals with UVL and control subjects (Guinand et al., 2012). Subjects were instructed to walk without "holding on" to the rails unless a loss of balance occured as light touch stabilizes center of mass sway during walking (Dickstein & Laufer, 2004). One individual with vestibular loss touched the hand rail for stability during the DVA trial, which was stopped and repeated.

Visual acuity was characterized for all subjects while 1) standing, 2) walking on a treadmill, and 3) sitting on the MOOG. Visual acuity was tested with vision uncorrected for all but one subject to enable simultaneous eye movement recording (data not shown). Visual acuity was measured by asking subjects to identify the direction an optotype (i.e. "E") faced when displayed on a computer monitor (Schubert et al., 2008). The monitor was centered approximately 5^0

below the subject's eye height when standing on the treadmill and when sitting on the MOOG at a distance of 2.2 meters. Each optotype was presented for 400ms. Long optotype durations increase the gaze stability challenge for individuals with vestibular disease (Peters et al., 2013). Subjects viewed 5 optotypes per acuity level, with optotype size decreasing in steps equivalent to a visual acuity change of 0.1 logMAR. LogMAR is defined as $\log_{10}x$ where x is the minimum angle resolved in arcmin, with 1 arcmin equal to 1/60° (Ferris et al., 1982). One standing trial was completed to determine standing visual acuity (SVA) prior to the walking trial. The DVA score is the difference between the SVA and the walking (or seated) visual acuity. The DVA walking trial continued until the subject was not able to accurately identify the orientation of 100% of the optotypes presented at the current size or their logMAR score reached 0.00 (Schubert et al., 2008). The standing and walking trials lasted ~2.5 minutes. A 1-2 minute standing rest was provided between the standing and walking trials to minimize fatigue.

Following the treadmill walking portion of the experiment all subjects were provided a rest period lasting at least 45-90 minutes while offline kinematic data processing was completed. Head motion recorded from the Optotrak camera system was processed offline to control motion of the MOOG. Translation in the AP and vertical direction and head pitch angle were used to specify MOOG motion such that the subject's head experienced similar sagittal plane motion during "seated walking" as they did during treadmill walking. The frequency content of head pitch velocity was similar across both conditions; see Figure 6-4

for details. The MOOG DVA trial lasted ~2.5 minutes and consisted of composite motion (combination of pitch, vertical and fore-aft motions) to simulate the sagittal plane head motion from the walking trial. Performance of the DVA on the MOOG required the following modification due to the bite bar: subjects indicated the direction of the rotated "E" by pointing with their fingers. SVA from the standing trial was used as a comparison for both dynamic visual acuity conditions. Subjects were compensated $50 for participation in this study.

7.34 Analysis

Dynamic Visual Acuity

A two-way repeated measures ANOVA with two factors 1) group (healthy vs. BVH) and 2) DVA condition (active walking, seated walking) was performed to identify group and condition differences in DVA.

Oscillopsia

To determine internal consistency Chronbach's α was calculated for scores from the Oscillopsia Functional Impact (OFI) scale. To determine face validity, Spearman's Correlation coefficients were calculated to determine the relationships between OFI scores, walking DVA scores, seated DVA scores, OS VAS, OSC, ABC, VVAS, and DHI. One way ANOVA was performed to determine group differences on OFI scores, OS VAS, OSC, ABC, VVAS, and DHI.

7.4 Results

DVA Scores

There was not a significant group difference (*p* = .22) or group by condition interaction (*p* = .82) for DVA, as shown in Figure 7-1 for individual DVA values for each group and condition. There was a trend that approached a significant difference for DVA condition. Worse DVA scores were found in the seated walking MOOG condition compared to the active walking condition (p = .059).

Figure 7-1 DVA scores by group (Healthy and BVH) and condition (walking and seated walking) are presented as the difference between dynamic condition and standing condition. Each symbol represents an individual participant in their respective group.

Oscillopsia/Dizziness/Balance Measurements

Chronbach's α was calculated on 34 of the original 43 items due to missing data (coded as "n/a" by subjects) or due to lack of variance. Unstandardized Chronbach's α for the OFI scores was .84 and standardized Chronbach's α for OFI scores was .92 demonstrating high internal consistency. This is consistent with calculations from a larger data set (n = 30) that revealed Chronbach's α = .87 for all 43 items (complete data not shown here). The OFI scores were highly correlated with the other subjective measures of dizziness, oscillopsia, and balance confidence. Spearman correlation coefficients are presented in Table 7-1. DVA scores (active and passive) were highly correlated with each other, but were not significantly correlated with any subjective measure of dizziness, oscillopsia, or balance.

Table 7-1 Spearman correlation coefficients between subjective rating scales and DVA scores from walking and seated walking. Significant correlations are indicated with an *.

	OFI total	OFI average	wDVA	mDVA	ABC scale	OSC	OS VAS	DHI	VVAS
OFI total	1	.99 * p < .001	-.2 p = .45	-.18 p = .51	-.85 * p < .001	.88 * p < .001	.88 * p < .001	.89 * p < .001	.89 * p < .001
OFI average		1	-.17 p = .53	-.12 p = .66	-.89 * p < .001	.85 * p < .001	.89 * p <.001	.92* p <.001	.89 * p <.001
wDVA			1	.85 * p <.001	.08 p = .76	-.17 p = .53	-.33 p = .21	-.09 p = .74	-.17 p = .54
mDVA				1	.03 p = .90	-.12 p = .67	-.22 p = .42	.04 p = .88	-.07 p = .79
ABC scale					1	-.79 * p <.001	-.80 * p <.001	-.89 * p <.001	-.91 * p <.001
OSC						1	.86 * p <.001	.84 * p <.001	.87 * p <.001
OS VAS							1	.82 * p <.001	.88 * p <.001
DHI								1	.90 * p <.001

Abbreviations
OFI – Oscillopsia Functional Impact scale
wDVA – Walking Dynamic Visual Acuity
mDVA – MOOG Dynamic Visual Acuity
ABC scale – Activity Specific Balance Confidence scale
OSC – Oscillopsia Severity scale
OS VAS – Oscillopsia Visual Analogue Scale
DHI – Dizziness Handicap Inventory
VVAS – Visual Vertigo Analogue Scale

Individuals with BVH displayed greater oscillopsia impairment, perceived handicap from dizziness, and lower balance confidence than the healthy controls on all subjective measures (p's < .002). Group average scores with SEM and 95% confidence intervals are presented in Table 7-2.

Table 7-2 Between group differences on subjective measures of oscillopsia, dizziness, and balance. Average (SEM) [95% CI] are presented and significant group differences are indicated by an *, p's < .002.

Group	OFI total *	OFI average *	OSC *	OS VAS *	ABC scale *	DHI *	VVAS *
BVH	64 (8.9) [42.8-85.1]	1.68 (.21) [1.2-2.2]	3.01 (.28) [2.4-3.7]	4.2 (.79) [2.3-6.1]	73.1 (6.1) [58.6-87.6]	44.3 (9.1) [22.8-65.7]	25.9 (5.4) [13.1-38.7]
Healthy	7.4 (2.1) [2.5-12.2]	0.18 (.05) [.06-.31]	1.08 (.05) [.98-1.2]	0.19 (.10) [-.05-.43]	97.6 (.93) [95.4-99.8]	.75 (.53) [-.5-2.0]	0.70 (.22) [.18-1.2]

Abbreviations

OFI – Oscillopsia Functional Impact scale

wDVA – Walking Dynamic Visual Acuity

mDVA – MOOG Dynamic Visual Acuity

ABC scale – Activity Specific Balance Confidence scale

OSC – Oscillopsia Severity scale

OS VAS – Oscillopsia Visual Analogue Scale

DHI – Dizziness Handicap Inventory

VVAS – Visual Vertigo Analogue Scale

7.5 Discussion

Overall, there was a trend for DVA scores to be worse during seated walking compared to active walking on a treadmill. This is consistent with previous literature demonstrating that active head rotation DVA is better than passive head rotation DVA (Tian et al., 2002; Vital et al., 2010). While this experiment cannot identify mechanisms contributing to improved DVA during active walking, it highlights the limitations of seated clinical measurements for characterizing functional deficits for individuals with severe BVH.

DVA performance for individuals with severe vestibular loss was not distinguishable from healthy individuals matched for age and gender. Our results contrast with recent reports of walking DVA, which found that individuals with vestibular loss walking at 2km/hr had poorer DVA compared to healthy individuals (Guinand et al., 2012; Lambert et al., 2010). Methodological and sample size differences may help account for non-significant group differences. The total sample of 16 participants may have been under-powered to demonstrate group differences. A "tumbling E" optotype displayed for 400ms at a distance of 2.2 meters was used for this experiment, others have projected standard block letters on a screen at 6 meters (duration not specified) (Lambert et al., 2010) or used a chart with SLOAN letters constantly visible (Guinand et al., 2012). Our method also required 100% failure (Schubert et al., 2008; Kao et al., 2010) at each optotype size while others used 60% as the cut off (Guinand et al., 2012) or an adaptive step algorithm (Lambert et al., 2010).

Longer display times have recently been suggested to improve the discriminative capability of the DVA test compared to shorter display times for individuals with vestibular disease (Peters et al., 2013). Our display time of 400ms should have made the task more difficult by requiring fixation for a longer period of time; however, the longer display time was also sufficient to allow corrective oculomotor gaze shifts to the target if fixation was not adequate (Leigh et al., 1993; Goldring et al., 1996; Walker et al 1995). Corrective gaze shifts would have enhanced gaze stability despite an impaired VOR. VOR gain is rapidly suppressed during the onset of a gaze shift and then returns to normal by the end of the gaze shift (Cullen et al., 2004). Gaze shifts have been suggested as an oculomotor compensation for a pathologic VOR (Schubert & Zee, 2010). The error signal from retinal slip of the target image provides both position and velocity error signals that can drive a catch-up saccade (Daye et al., 2014). Compensatory gaze shifts would be more relevant during fixation tasks with a transiently visible target (i.e. DVA task) regardless of whether motion was actively or passively induced, as individuals with BVH demonstrated appropriate compensatory timing for vertical eye velocity during treadmill walking while viewing a constantly visible target (see chapter 6 results).

The OFI demonstrated high internal consistency as well as excellent face validity based on excellent correlations with other measures of oscillopsia and also the DHI and the ABC scale. Scores on the OFI and OS VAS and OSQ were all positively correlated which indicates that activity restriction, symptom severity, and symptom frequency all increase together. The OFI did capture activity

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limitations for the individuals with BVH; however OFI scores were not correlated with DVA scores. When retinal slip exceeds 2-3^0/s, functional gaze stability becomes impaired (Demer et al., 1994). Despite no group difference for DVA scores, all of the subjective measures discriminated healthy individuals from individuals with BVH. None of the subjective reports of oscillopsia correlated with measured DVA scores from active or passively induced head motion. Several of the individuals with BVH scored at or close to zero for their DVA (see Figure 1), yet their OFI scores ranged from 32 to 96. Oculomotor mechanisms may have compensated for the impaired VOR, yielding an artificially enhanced DVA score. This potential bias in DVA scores could explain the non-significant relationship between DVA and OFI scores. Another potential explanation for the discordance between oscillopsia impairments (whether severity, frequency, or participation based) and DVA or other measures of gaze stability is tolerance for perceived retinal image motion (Grunfeld et al., 2000). Lower oscillopsia ratings have been associated with larger magnitude retinal slip measurements which were interpreted as a compensatory mechanism (Grunfeld et al., 2000). This would suggest that individuals with worse DVA scores may have developed a tolerance for oscillopsia further confounding any possible relationship. Activity restriction, as measured by the OFI, may depend on multiple factors and thus cannot be explained by a single measure of gaze stability. Belief (or fear) that secondary symptoms (i.e. falls, dizziness, oscillopsia, anxiety/depression) will result in negative effects (injury, embarrassment) may contribute more to activity restriction than gaze instability itself (Yardley et al., 2001; Mira, 2008).

Walking may serve the function of movement based priming to enhance neuroplastic changes for gaze stability (Stoykov & Madhavan, 2014). The present results suggest that rehabilitation may be augmented by including gaze stabilization activities during walking for individuals with BVH. Compensatory timing for vertical eye movements while walking (see chapter 6) suggests that the central nervous system has timing information specific to the walking task that facilitates gaze stability. Leveraging this information into a gaze stability training visuo-motor adaptation paradigm may improve rehabilitation outcomes for this population. Future studies to examine the safety and efficacy of gaze stabilization exercises performed during walking are necessary.

7.6 Conclusion

A trend consistent with previous literature suggests that actively generated head motion during walking facilitates gaze stability to a greater extent than passive head motion. Adding walking gaze stabilization exercises to rehabilitation protocols may be beneficial for individuals with BVH. The OFI was able to discriminate between healthy individuals and individuals with BVH; however, OFI scores did not correlate with either active or passive DVA scores. Perceptions of oscillopsia severity and associated activity restrictions probably reflect complicated interactions that cannot be distilled down to a perceptual measure of gaze stability.

Appendix A

Oscillopsia Functional Impact Scale
For each of the following questions, select the answer that best describes how often or how severe the indicated symptom affects you in your daily life. Please use the following scale and answer each question.
0 = Not at all
1 = A little of the time
2 = Some of the time
3 = A good deal of the time
4 = Almost all the time
5 = I have given up this activity because of symptoms
n/a = Don't know, as I just don't do this activity

		Not at all	A little of the time	Some of the time	A good deal of the time	Almost all the time	I have given up this activity because of symptoms	Don't know, as I just don't do this activity
1.	How often does the world around you seem to move / bounce / jump when you are sitting still?	0	1	2	3	4	5	n/a
2.	How often does the world around you seem to move / bounce / jump when you are standing still?	0	1	2	3	4	5	n/a
3.	How often does the world around you seem to move / bounce / jump when you are walking?	0	1	2	3	4	5	n/a
4.	How often does the world around you seem to move / bounce / jump when you are running?	0	1	2	3	4	5	n/a
5.	How often does the world around you seem to move / bounce / jump	0	1	2	3	4	5	n/a

	when driving a car?							
6.	How often does the world around you seem to move / bounce / jump when riding in a car?	0	1	2	3	4	5	n/a
7.	How often do you have trouble finding food items you are looking for when grocery shopping?	0	1	2	3	4	5	n/a
8.	How often do you miss a turn when driving somewhere new because you could not read the sign?	0	1	2	3	4	5	n/a
9.	How often do you miss a turn when walking somewhere new because you could not read a sign?	0	1	2	3	4	5	n/a
10.	How often do you have difficulty recognizing familiar faces as you approach a group of people?	0	1	2	3	4	5	n/a
11.	How often do you let other people drive because you might miss a turn?	0	1	2	3	4	5	n/a
12.	How often are you able to use your mobile phone while walking to make a call?	0	1	2	3	4	5	n/a
13.	How often are you able to use your mobile phone while walking to **send** a text / email?	0	1	2	3	4	5	n/a
14.	How often are you able to use your mobile phone while walking to **read** a text / email?	0	1	2	3	4	5	n/a
15.	How often are you able to use your mobile phone while a passenger in a car to **send** a text / email?	0	1	2	3	4	5	n/a
16.	How often are you able to use your mobile phone while a passenger in a car to **read** a text / email?	0	1	2	3	4	5	n/a
17.	How often do you have to stop walking to use your mobile phone to make a call?	0	1	2	3	4	5	n/a
18.	How often do you have to take extra time when crossing a street / walking in a parking lot to check for cars because it is difficult to tell when the cars are moving?	0	1	2	3	4	5	n/a

19.	How often do you avoid spending time with family / friends because the world around you seems to move / bounce / jump?	0	1	2	3	4	5	n/a
20.	How often does it take you extra time to find a specific book / movie on a shelf at the store?	0	1	2	3	4	5	n/a
21.	How often are you able to read a shopping list while you are walking at your normal speed?	0	1	2	3	4	5	n/a
22.	How often are you able to read a shopping list while you are walking at a **slower** than normal speed?	0	1	2	3	4	5	n/a
23.	How often are you able to read a shopping list while you are walking at a **faster** than normal speed?	0	1	2	3	4	5	n/a
24.	How often are you able to read a shopping list while you push a cart and walking at normal speed?	0	1	2	3	4	5	n/a
25.	How often do you feel isolated because the world around you seems to move / bounce / jump?	0	1	2	3	4	5	n/a
26.	How often do you feel out of control because the world around you seems to move / bounce / jump?	0	1	2	3	4	5	n/a
27.	How often do you fall down because the world around you seems to move / bounce / jump?	0	1	2	3	4	5	n/a
28.	How often do you trip without falling down because the world around you seems to move / bounce / jump?	0	1	2	3	4	5	n/a
29.	How often do you avoid using stairs because the world around you seems to move / bounce / jump?	0	1	2	3	4	5	n/a
30.	How often do you have to stop walking to read your watch to find out what time it is?	0	1	2	3	4	5	n/a
31.	How often does the world around you seem to move / bounce / jump more when you walk on grass or sand?	0	1	2	3	4	5	n/a
32.	How often have you stopped participating in recreational activities because the world around you seems to move / bounce / jump?	0	1	2	3	4	5	n/a

33.	How often have you changed jobs / had difficulty maintaining a job because the world around you seems to move / bounce / jump?	0	1	2	3	4	5	n/a
34.	How often have you avoided driving because the world around you seems to move / bounce / jump?	0	1	2	3	4	5	n/a
35.	If you drop a ball (or other object) that starts to roll away from you, how often do you wait for it to stop moving before you move to pick it up?	0	1	2	3	4	5	n/a
36.	How often do you avoid attending live sporting events because you can not follow the movement of the players and balls?	0	1	2	3	4	5	n/a
37.	How often have you had to move to a different residence because the world around you seems to move / bounce / jump and you either fell or did not feel safe walking in your home?	0	1	2	3	4	5	n/a
38.	How often do you have trouble sitting and reading a stationary computer screen?	0	1	2	3	4	5	n/a
39.	How often do you have trouble sitting and reading a computer screen while scrolling the screen?	0	1	2	3	4	5	n/a
40.	How often do you have trouble recognizing which light is illuminated on a traffic signal when **driving** a car?	0	1	2	3	4	5	n/a
41.	How often do you have trouble seeing which light is illuminated on a traffic signal when **riding** in a car?	0	1	2	3	4	5	n/a
42.	How often do you have trouble reading something when riding as a passenger in a car?	0	1	2	3	4	5	n/a
43.	How often do you have trouble reading the "ticker" that scrolls on the bottom of the TV when sitting still?	0	1	2	3	4	5	n/a

Appendix B

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