Chapter 2
The Effect of Fear of Falling on Vestibular Feedback Control of Balance

Introduction: Vestibular sensation contributes to head stabilisation and fall prevention. To what extent fear of falling influences these different vestibular feedback processes is currently undetermined.
Method: We used galvanic vestibular stimulation (GVS) to induce vestibular reflexes while participants stood at ground level and also on a narrow walkway at 3.85 m height to induce fear of falling. Fear was confirmed by questionnaires and elevated skin conductance. Full-body kinematics was measured to differentiate the whole-body centre of mass response (CoM) into component parts (cervical, axial trunk, appendicular short-latency and medium-latency). We studied the effect of fear of falling on each component to discern their underlying mechanisms. Statistical parametric mapping analysis provided sensitive discrimination of early GVS and height effects.
Results: Kinematic analysis revealed responses at 1 mA stimulation previously believed marginal through EMG and force plate analysis. The GVS response comprised a rapid, anode-directed cervical-head acceleration, a short-latency cathode-directed acceleration of lower extremities and pelvis, an anode-directed upper thorax acceleration and subsequently a medium-latency anode-directed acceleration of all body parts. At height, head and upper thorax early acceleration were unaltered, however short-latency lower extremity acceleration was increased. The effect of height on balance was a decreased duration and increased rate of change of the CoM acceleration pattern.
Discussion: These results demonstrate that fear modifies vestibular control of balance, whereas cervical-head stabilisation is governed by different mechanisms unaffected by fear of falling. These results also show that the short- and medium-latency appendicular reflexes contribute to whole body balance and function biomechanically as a coordinated response.

2.1 Introduction

Fear of falling is known to influence human balance (Stins et al., 2011; Tersteeg, 2012; Osler et al., 2013). When fearful, movements become more cautious and joint stiffness tends to increase (Adkin et al., 2002; Tersteeg, 2012; Osler et al., 2013; Young & Mark Williams, 2015). Studies of fall risk in the elderly have shown associations between cognitive motor measures (e.g. concern about falling and poor executive function) and physiological measures of impaired balance (Delbaere et al., 2010a; Hadjistavropoulos et al., 2011). From a healthy ageing perspective there is a need to understand the mechanisms relating fear of falling to balance and mobility in the elderly. In addition, it has been proposed that anxiety increases sensitivity to self-motion, through noradrenergic and serotonergic input to the vestibular nuclei (Balaban, 2002). Therefore, we focus in the present study on the vestibular contributions to human balance and the potential interplay with fear of falling.

As covered in a recent crosstalk debate (Horslen et al., 2015b, a; Reynolds et al., 2015a; Reynolds et al., 2015b; van Dieen et al., 2015), it is currently controversial whether fear of falling influences the vestibular control of balance. Bipolar binaural Galvanic Vestibular Stimulation (GVS) is a frequently employed method to study vestibular balance reflexes (Fitzpatrick & Day, 2004). Cutaneous electrical stimulation at the mastoid processes stimulates the vestibular nerves and creates erroneous feedback of roll rotation. This elicits a lateral body sway response towards the anode electrode. A paradigm of standing at height on a 22 cm narrow walkway to evoke fear of falling, combined with GVS, has shown that fear of falling might differentially affect the feedforward and feedback components of the vestibular-evoked balance response (Osler et al., 2013). Given sufficient time to integrate proprioception of movement with vestibular sensation, vestibular evoked sway is strongly arrested at height compared to ground. However, kinematic data of head and torso showed that fear had no measureable effect on the initial (0-800 ms) vestibular evoked balance response. In contrast, Horslen et al. (2014) have shown increased gain in the initial vestibular reflex response, using a similar height paradigm. However, in their study ground reaction force (GRF) data were used to assess balance responses and a different stimulation paradigm was employed (stochastic vestibular stimulation, SVS) to elicit vestibular balancing reflexes.

Vestibular information is used within a variety of mechanisms related to balance.
Pertinent to this study, vestibular sensory feedback is used to regulate head orientation through the vestibulocolic reflex (VCR) and to regulate balance through responses that control movement of the whole-body CoM. It is possible that fear has differential effects on these vestibular responses, which have different onset latencies to GVS implying distinct neural pathways. Furthermore, extant literature indicates that appendicular reflexes (upper and lower extremities) are governed by different mechanisms than axial (e.g. cervical) reflexes (Forbes et al., 2015). For example, appendicular vestibular reflexes are task-dependent, whereas axial reflexes are more task-independent (Forbes et al., 2015).

EMG data have been used to reveal the latency of vestibular responses and thereby establish the neural pathways that could be involved. For example, the VCR has a latency of approximately 8-10 ms (Watson & Colebatch, 1998; Forbes et al., 2014). When recording lower limb muscles during upright standing, short- and medium-latency vestibular balancing responses were found. The onset of these short-latency responses ranged from 42 to 65 ms, and for medium-latency from 98 to 120 ms post GVS onset (Britton et al., 1993; Fitzpatrick et al., 1994; Ali et al., 2003; Fitzpatrick & Day, 2004; Son et al., 2008; Mian et al., 2010; Muise et al., 2012). In addition, the short- and medium-latency responses are reflected in GRF peaks at approximately 120-200 ms and 290-400 ms latency, respectively, partly due to an electromechanical delay (Mian & Day, 2009; Dakin et al., 2010; Mian et al., 2010; Horslen et al., 2014; Mian & Day, 2014). These short- and medium-latency responses in EMG and/or GRF data are well established since they were replicated in at least 5 different research institutions. According to Fitzpatrick et al. (1994) the short-latency response can produce small segmental movements, but has no effect on the whole-body sway response. It is assumed that the medium-latency response is responsible for the GVS induced sway response, however the neurophysiological origin of the short-latency response and its contribution to balance are still debated (Cathers et al., 2005; Mian et al., 2010). While the short-latency response occurs only in muscles required for balance, the functional relationship with the medium-latency response is unclear.

In general, the relationships between vestibular evoked muscle activity, resulting body movement and physiological function are unclear. For example, it is currently unclear whether the lower extremity short- and medium-latency responses are independent or comprise a coordinated balance response (Mian et al., 2010). Currently, there is
insufficient knowledge of how muscle forces combine to produce movement in a non-rigid, multi-segmental body. Therefore, the movement pattern related to vestibular-evoked balancing reflexes and its mapping to EMG and force plate data are insufficiently understood. Measurement of full-body kinematics can integrate the effect of multiple measured and unmeasured muscle activations and allows us to parse the movement of the whole body centre of mass (CoM) into component parts (cervical, axial trunk, appendices) so as to discriminate effects on head stabilisation (VCR), lower extremity balancing reflexes and whole body balance. GRF measurements in isolation reveal acceleration of the CoM, but do not discriminate segmental movements. While a kinematic analysis of the head, trunk and pelvis response to GVS has been made (Day et al., 1997), a full body kinematic analysis of the GVS response including the extremities has not been conducted to date. This full-body kinematic analysis can be used (a) to differentiate the whole-body centre of mass response (CoM) into component parts (cervical, axial trunk, appendicular short-latency and medium-latency), (b) to unmask component responses which oppose and cancel within the whole body CoM response, (c) to assess the effect of fear of falling on each component, and finally (d) to discern their underlying mechanisms.

2.1.1 Aims and approach
In this study we investigated how vestibular balance reflexes are influenced by fear of falling. It is unknown whether, and to what extent, this psychological state modulates the vestibular reflex mechanisms involved in balance control. To challenge the balance system we used GVS to evoke substantial mediolateral sway both at ground level and at a height that is known to invoke fear of falling (Osler et al., 2013). We recorded full-body kinematics to measure the balance response to GVS, in order to discriminate the VCR response from regulation of the CoM (i.e. the balancing response), and to gain insight into the neuro-kinematic progression of the balance response. We analysed our kinematic data using statistical parametric mapping (SPM). SPM is a validated method of statistical analysis for time series data, which is now increasingly being used for kinematic time series (Pataky, 2012; Robinson et al., 2014; Serrien et al., 2015). We focussed on the short- and medium-latency vestibular responses (0 – 400 ms). In our study we compared our full-body kinematic data to known EMG and GRF responses as established in multiple laboratories. Our main research question was: What is the effect of fear of falling on vestibular control of whole body balance? We divided this question into the following sub-questions:
1. What is the kinematic response to GVS of axial and appendicular components, in the short- and medium-latency time domain?
2. What is the effect of fear of falling on each of these components?
3. How do these components relate to each other and to the regulation of head stabilisation and postural balance control?

2.2 Methods

2.2.1 Ethical approval
This study was approved by the local ethics committee of the Science & Engineering faculty, Manchester Metropolitan University. Participants were naïve to the precise purpose of the experiment and gave written informed consent prior to their participation. The study conformed to the standards set by the latest revision of the Declaration of Helsinki.

2.2.2 Participants
Sixteen young healthy adults with no known neurological, musculo-skeletal, balance or vestibular disorder were recruited as a sample of convenience. Ten men and six women were tested. The averaged participant characteristics were as follows (mean (standard deviation): age: 25.9 (5.1) years, height: 1.74 (0.1) m, weight: 69.5 (13.5) kg, BMI: 22.9 (3.5).

2.2.3 Material
Vestibular evoked balance responses were studied in two conditions. In one condition participants stood on a 22-cm-wide walkway placed on the laboratory floor. In the other condition, participants stood on a 22-cm-wide walkway elevated 3.85 m above ground level. The high walkway extended from a mezzanine into a larger neighbouring room (Figure 2.1). Access to the walkway was provided by sliding doors opening the laboratory wall (width 3.57 m). Stimulation and data acquisition devices were stationed on the mezzanine.
2.2.4 Safety system
In both the ground and height conditions participants wore a full-body harness attached to a safety system to prevent a possible fall. The safety system consisted of an inertial reel and a dynamic rope system that was belayed by a certified assistant. Both were attached to a trolley-mounted anchor point positioned directly above the participant to allow walking and standing without creating drag on the participant. This was the same safety system as used by Osler et al. (2013). As the system was attached to the back of the harness, the ropes ran behind the participant outside their visual field. Participants were fully informed of the safety system. However, during data collection, participants could neither see nor feel the safety ropes. Furthermore, they did not test the system prior to the experiment. Verbal, post-experiment debriefing confirmed that knowledge of the safety system provided little comfort to participants who generally reported the experience to be rather testing.

2.2.5 Data collection
Full-body kinematics was collected by means of a 3D motion capture system operating at a sample frequency of 100 Hz using 52 retroreflective passive markers and 9 infrared cameras (Vicon Motion Systems Ltd., Oxford, UK). The marker placement was as follows: 5 on the head (frontal bone, 2 on left and 2 on right zygomatic bone), 2 on sternum, upper back at C7, lower abdomen, 5 on pelvis (ASIS, PSIS and sacrum), upper lateral thigh (iliotibial band), 5 per knee (femoral and tibial condyles, and tibial tuberosity), lower lateral shanks, medial and lateral ankles, 2 per
foot (heel and base of the 3rd metatarsal), shoulders (acromion), upper arms (deltoid insertion), medial and lateral elbows, lateral lower arms (ulna shaft), 2 per wrist (radial and ulnar styloid process), 1 per hand (2nd metacarpal head).

Furthermore, skin conductance (SC) was recorded during all trials as a measure of physiological arousal. SC was measured using two self-adhesive gel electrodes that were placed on the palmar surface of the distal phalanges of the first and third fingers. The electrodes were connected to a GSR Amplifier (ADinstruments Ltd., model ML116, Dunedin, New Zealand). Kinematics and SC data were collected and synchronized using Vicon Nexus software (1.8.5.61009h, Vicon Motion Systems Ltd., Oxford, UK). GVS impulses with a current of 1 mA and 2 s duration were delivered using carbon rubber electrodes (46 by 37 mm) placed in a binaural bipolar configuration similar to the method of Osler et al. (2013). This type of stimulus has shown to evoke significant body sway responses (Day et al., 2010; Osler et al., 2013).

To assess participant’s state of fear, the State-Trait Anxiety Index (STAI) (Rossi & Pourtois, 2012) was used. From the STAI questionnaire only the state anxiety index was used. Moreover, participants were asked to verbally rate their fear of falling on a 1-10 Likert scale anxiety thermometer at several instances of the experiment. The anxiety thermometer has been shown to have fair validity and reproducibility (Houtman & Bakker, 1989). In a more recent study a one-question 5-point Likert anxiety scale was found to be suitable for anxiety measurement (BinDhim et al., 2013).

2.2.6 Procedure

In a repeated measures design participants were tested during the same series of trials in the high and ground walkway conditions in counter-balanced order. Participants were instructed to stand still but relaxed 1.5 m out on the walkway with their head facing forwards and the feet directed along the anterior-posterior axis of the walkway (Figure 2.1). To maximize lateral sway and rule out effects of vision, participants stood with their feet together and eyes closed. After 10 familiarizing GVS stimuli, thirty GVS impulses (15 anode-left, 15 anode-right, randomly ordered) were applied. It is important to note that the direction of body sway evoked by the stimulus was always towards either the right or the left edge of the walkway, depending on GVS polarity (anode left or right). Participants were permitted to open their eyes after each block of 10 trials. These trials were repeated, meaning that all participants completed 3 blocks.
of 10 trials in both the height and the ground condition. Data acquisition for each trial began 3 s prior to and ended 6 s following GVS onset. After each 6\textsuperscript{th} trial in the 1\textsuperscript{st} block, each 8\textsuperscript{th} trial in the 2\textsuperscript{nd} block and each 3\textsuperscript{rd} trial in the 3\textsuperscript{rd} block of trials participants were asked to verbally rate their level of fear of falling for the anxiety thermometer.

\textbf{2.2.7 Data processing}
Baseline SC was calculated as the mean SC level over 2 seconds of quiet standing at ground level. Pre and post GVS onset SC levels were calculated by averaging SC between 3 and 0.5 s before GVS onset, and between 0 and 6 s after GVS onset, respectively. SC signals were normalised by subtracting the baseline signal and dividing by the standard deviation of the pre GVS values in the ground condition.

Using Visual 3D (v5.02.07, C-Motion Inc., Germantown, USA) mediolateral displacement of the following body nodes were calculated: whole-body CoM, head CoM, upper thorax (superior end of thorax segment), pelvis CoM, and the elbows, wrists, knees and ankles. These locations are collectively referred to as nodes. In addition, foot-in-space and head-in-space segment angles as well as ankle, knee, hip, lower back, neck, shoulder, elbow and wrist joint angles in the frontal plane were calculated. A GVS stimulus causes increased mediolateral body sway to the side on which the anode electrode is placed on the head. For half of the GVS trials the anode of the GVS electrodes was on the right side and for the other half of the trials it was on the left side. Therefore, instead of analysing right and left body nodes and angle variables on their own (e.g. right or left knee), these segments were analysed and named based on the anode-cathode configuration, e.g. ‘anode knee’ refers to the knee on the anode side of the body (Figure 2.2).

For each positional and angular variable, the value at GVS onset of a trial was subtracted from all values of the time series of the trial in question. Furthermore, the sign was corrected based on anode electrode location. Analysis of published data shows that the frequency bandwidth of the short- and medium-latency GRF GVS responses averaged over multiple trials and participants does not exceed 3 Hz (Marsden et al., 2005; Mian & Day, 2014). Therefore, we filtered our kinematic data using a 6 Hz low pass Butterworth filter and differentiated twice using a 3rd order Savitsky-Golay filter with a temporal window of 170 ms (Press et al., 1999). As we
were interested in the vestibular reflex response we analysed node acceleration and angle acceleration data in the time domain between 0.2 s before and 0.7 seconds after GVS onset.

![Diagram of body nodes based on GVS electrode configuration](image)

**Figure 2.2: Body nodes based on GVS electrode configuration.** We focussed on mediolateral linear acceleration of the indicated body nodes. These nodes were analysed based on the anode-cathode configuration as the GVS polarity changed between trials.
2.2.8 Statistics

Questionnaire and SC data
Student’s paired t-tests were used to test whether STAI state, anxiety thermometer and SC were increased at height compared to ground. Lastly, correlations between all combinations of SC, anxiety thermometer scores and STAI state scores were calculated using Spearman’s rho. The statistics toolbox in Matlab was used for statistical testing.

Kinematics: Statistical Parametric Mapping (SPM)
To answer our research question all linear and angular acceleration time samples within the first 400 ms after GVS onset were of interest. We therefore used a validated method (SPM) to test at what instances the signals were statistically different from zero and when they were different between conditions. All SPM analyses were implemented using the open-source toolbox SPM-1D (v.M0.1, Todd Pataky 2014, www.spm1d.org,) in Matlab R2014a. SPM regards the whole time series as the unit of observation and is now increasingly used in the analysis of kinematic time series (Pataky, 2012; Robinson et al., 2014; Serrien et al., 2015). This allows time dependence to be incorporated directly in statistical testing.

In this study SPM statistics were calculated of the averaged trials per participant for each condition. A SPM two-tailed one-sample t-test was used separately for the ground and height condition data to test if linear and angular acceleration of previously mentioned body nodes, joints and segments was different from zero ($\alpha=0.05$). Additionally a SPM two-tailed paired samples t-test (Robinson et al., 2014) was used for a ground vs. height comparison of the same dependent variables. The scalar output statistic, SPM{t}, was calculated separately at each individual time sample. To test the null hypothesis the critical threshold was calculated as the value at which only $\alpha$ % (5%) of the analysed trajectories would be expected to traverse. This threshold of significance is based upon estimates of trajectory smoothness (Friston et al., 2007) and Random Field Theory expectations (Adler & Taylor, 2007). Conceptually, a SPM t-test is similar to the calculation and interpretation of a scalar t-test; if the SPM{t} trajectory crosses the critical threshold at any time sample, the null hypothesis is rejected. However, a SPM t-test avoids the false positives of multiple scalar t-tests and avoids the false negatives of scalar t-tests with Bonferroni correction (Adler & Taylor, 2007). Typically, due to interdependence of neighbouring points,
multiple adjacent points of the SPM(t) curve often exceed the critical threshold. We therefore call these “supra-threshold clusters”. SPM then calculates cluster specific p-values which indicate the probability with which supra-threshold clusters could have been produced based on the null hypothesis (Adler & Taylor, 2007).

2.3 Results

2.3.1 Questionnaires and SC confirm increased fear of falling at height

STAI, anxiety thermometer and SC data showed that participants had a higher level of fear of falling and physiological arousal in the high walkway condition than in the ground walkway condition (Table 2.1). SC was increased significantly in the height condition both pre (t = -2.709, df = 15, p = 0.016) and post (t = -2.743, df = 15, p = 0.015) GVS onset. In the height condition, the STAI state scores were positively correlated with SC scores (n = 15, rho = 0.506, p < 0.05). For one participant skin conductance was not recorded due to technical malfunction.

Table 2.1: STAI, anxiety thermometer and skin conductance scores. The data are presented as mean (SD). State anxiety scores (STAI) can range between 20 and 80. Anxiety thermometer scores can range between 1 and 10. Skin conductance values are normalised to values of baseline standing.

<table>
<thead>
<tr>
<th></th>
<th>STAI State</th>
<th>Anxiety thermometer</th>
<th>Pre-GVS</th>
<th>Post-GVS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ground</td>
<td>27.4 (5.7)</td>
<td>2.0 (1.1)</td>
<td>-0.53 (1.08)</td>
<td>-0.45 (1.19)</td>
</tr>
<tr>
<td>Height</td>
<td>34.8 (9.3)</td>
<td>4.7 (3.2)</td>
<td>3.91 (6.11)</td>
<td>4.02 (6.08)</td>
</tr>
</tbody>
</table>
2.3.2 Kinematic analysis of vestibular responses to GVS

Representative response of the whole-body CoM
Standing at height has a modest effect on the early sway response (before ~400 ms), and a clear effect on the late GVS body sway response after ~400 ms. Figure 2.3 shows an example of the whole-body CoM mediolateral displacement and acceleration of a representative participant. At ~200 ms after GVS onset the whole-body CoM started to accelerate towards the anode electrode in both the ground and height condition. However peak acceleration was reached at 490 ms at ground level and at 300 ms at height. The amplitudes of this anode-directed (anodal) peak acceleration at ground and height were relatively similar. Whole-body CoM started decelerating at 890 ms at ground level and at 610 ms at height. These changes resulted in a reduced maximum sway displacement at height compared to ground.

Figure 2.3: Effect of height on body COM response to GVS of representative participant. The mediolateral body CoM displacement (A) and acceleration (B) of one participant are shown. GVS onset occurs at 0 seconds and ends at 2 seconds. Lines represent (individual) condition means and shaded areas represent 95% confidence intervals of the trials. The black bar shows the time at which GVS was on. For each trial, CoM displacement was scaled to t = 0, i.e., GVS onset.
**Whole-body CoM group results**

GVS evoked whole-body CoM sway towards the anode (positive) was conventional in that it plateaued at ~1 s, and was preceded by a small cathode-directed (cathodal) peak (negative) at ~250 ms (Figure 2.4A). The whole-body CoM showed a small initial cathodal acceleration and a main anodal acceleration of ~ 20 mm s\(^{-2}\). The timing of cathodal and anodal acceleration responses showing peaks at ~150 ms, and at ~400 ms was comparable to short- and medium-latency vestibular reflex responses found previously in GRF data (Figure 2.4D).

The main effect of height was an increased magnitude of the early cathodal acceleration and a decreased latency of both cathodal and anodal acceleration phases (Figure 2.4D, G). At height, cathodal acceleration was significantly different from zero at 120-140 ms (p = 0.027) followed by significant anodal acceleration at 230-470 ms (p < 0.001). In the ground condition no significant cathodal acceleration was found, however anodal acceleration was significant at 230-670 ms (p < 0.001). At 550-650 ms the ground-height difference was significant (p < 0.001) for body CoM acceleration. The ground-height time difference between anodal acceleration peaks was 110 ms and the body CoM sway terminated more promptly by ~ 300 ms at height (Figure 2.4A). To summarise, the response of the body CoM to GVS had a shorter latency and larger cathodal acceleration at height than on the ground.
Figure 2.4: GVS effects and ground-height difference effects found on acceleration within 0.2 s after GVS. The left, middle, right columns show movement of nodes for: whole-body CoM, head CoM and anode ankle, respectively. A-C, Upper row, shows mediolateral position. D-F, Middle row, shows mediolateral acceleration. Lines represent condition means and shaded areas represent 95% confidence intervals of the ground and height conditions. Anode- and cathode-directed acceleration peaks are indicated by ADA and CDA, respectively. G-I, Bottom row shows statistical parametric maps. Ground, height, and ground-height difference are in blue, green and red, respectively. Lines represent SPM(t) time series of the separate one-sample t-tests for ground and height data and paired t-tests for the ground-height difference. Horizontal dash-dot lines are the thresholds of significance. Shaded areas are supra-threshold clusters that indicate the time domains with significant effects. GVS onset occurs at 0 s. Vertical dashed and dotted lines represent the onset of significant short- and medium-latency acceleration, respectively. These vertical dashed and dotted lines are shown for significant effects in the ground and height conditions, as well as for the ground-height difference.

Head CoM & upper thorax nodes
Following GVS, the head node swayed consistently to the anode before plateauing at ~1 s (Figure 2.4B). Initial acceleration of the head CoM and upper thorax node was anodal (Figure 2.4E, 2.5). Head CoM acceleration was significant from 70 ms (p <
0.001, Figure 2.4H) and upper thorax acceleration was significant from 160 ms (Figure 2.5).

The anodal acceleration of the head and upper thorax nodes were unaffected by height. No significant ground-height difference was found for head CoM or upper thorax within the first 0.4 s (Figure 2.4H, 2.5). This lack of difference between height and ground replicates the head and trunk kinematics collected by Osler et al. (2013).

**Response of the lower extremities: pelvis, knee and ankle nodes**

Initial cathodal acceleration was observed in the pelvis and lower limbs. This response occurred at short-latency and was followed by anodal acceleration at medium-latency (Figure 2.4, 2.5). For the pelvis, both knees and ankles, cathodal acceleration was significant from 100-150 ms (Figure 2.4F, 2.5). These short-latency cathodal acceleration clusters were followed by significant medium-latency anodal acceleration clusters (pelvis and knees), which started between 270 and 370 ms (Figure 2.5).

The effect of height was an increase in the magnitude of the initial cathodal acceleration in the lower limbs. Inspection of Figure 2.4F and Figure 2.5 shows this increase was largest for the knee and ankle nodes, as confirmed by the significant ground-height difference in the initial cathodal acceleration. Cathodal acceleration was also observed earlier at height (Figure 2.4F, 2.5).
Figure 2.5: Cathodal acceleration around ~0.2 s in pelvis and lower extremities only. Data is shown of all nodes that are not included in Figure 2.4. Nodes are ordered from superior to inferior. Lines represent condition means and shaded areas represent 95% confidence intervals of the ground and height conditions. Positive values are mediolateral anodal acceleration and negative values are mediolateral cathodal acceleration. Vertical dashed and dotted lines represent the onset of significant short- and medium-latency acceleration, respectively. These vertical dashed and dotted lines are shown for significant effects in the ground and height conditions, as well as for the ground-height difference.

Response of the upper limbs: elbow and wrist nodes
The upper limbs showed a clear anodal acceleration at medium-latency and they were notable for their absence of response at short-latency timescales (Figure 2.5). Only the cathode wrist showed a significant cathodal response at short-latency. The amplitude was similar to the pelvis CoM, therefore the pelvis acceleration could have been transferred mechanically to the cathode wrist. No significant difference between ground and height was found (Figure 2.5).
Summary of GVS response revealed by node movements

Figure 2.6 provides a sequential overview of the GVS response and the effect of height for all body nodes. The GVS response comprises an early anodal acceleration of the head and upper thorax, a short-latency cathodal acceleration of the pelvis and lower limbs and a medium-latency anodal acceleration of the whole-body CoM resulting in sustained anodal sway of the whole body. Cathodal acceleration had a short-latency origin and was restricted to the pelvis and lower limbs. The effect of height-induced fear of falling on vestibular reflexes was only significant in acceleration of lower extremity nodes.

Figure 2.7 shows the mean displacement and acceleration at key time points. A video of the GVS response showing movement of stick figures comparable to Figure 2.7 can be found in Supplementary Material. At 170 ms, comparable with the GRF short-latency response, the cathodal acceleration and increased magnitude at height is evident at the ankle, knee and pelvis nodes. At 330 ms, comparable with the GRF medium-latency response, it seems that the acceleration and displacement of the whole body towards the anode is associated with cathodal buckling of the lower limbs centred at the knee, and that this effect was increased at height.
Figure 2.6: Body node acceleration: Significant time domains at ground vs. height.

The bars show significant time domains of the SPM one-sample t-tests for ground and height, and the SPM paired t-tests on the ground-height difference. Vertical lines within each supra-threshold cluster bar indicate the time of maximum significance. The p-value of each cluster is shown left of each bar. Significant short-latency ground-height differences within 0.14 – 0.2 s was found in acceleration of lower extremity nodes only. A significant medium-latency ground-height difference was found for cathode knee only from 0.27 s to 0.29 s.
Figure 2.7: Nodes at different times after GVS onset. Dots and stick figures show mediolateral displacement of the head, trunk and lower extremity body nodes with respect to the position at GVS onset.
Joint and segment angle acceleration

Node movements result from a combination of joint rotations. For example head node movement summarises the cumulative rotation of joints from the ankles to the neck. The following results remove ambiguity regarding the source of the head and trunk node accelerations.

Initial linear anodal acceleration of the head (50-100 ms) and upper thorax nodes (100-150 ms), (Figure 2.6) were confirmed as arising from joint rotations at the neck and subsequently the lower back (Figure 2.8 A, B). In both conditions the VCR was faster than the vestibular reflex in any of the other joints. Height had no significant effect on the magnitude of these axial reflexes (Figure 2.8 E, F), which were remarkably consistent at ground and height (Figure 2.8 A, B).
Figure 2.8: GVS effects in both conditions for angle accelerations, no ground-height difference effects. The left and right columns of graphs represent neck lateral flexion and lower back lateral flexion, respectively. Positive values represent anode flexion, i.e. folding together of the proximal and distal segments of the joint towards the lateral side on which the anode electrode is placed. The first row (A&B) shows lateral flexion angles and the second row (C&D) shows angle acceleration. Lines represent condition means, and shaded areas represent 95% confidence intervals of the conditions (ground and height). Positive values are lateral flexion towards anode and negative values are lateral flexion towards cathode. The bottom row (E&F) shows statistical parametric maps. Lines represent SPM(t) time series of the separate one-sample \( t \)-tests for ground and height data and paired \( t \)-tests for the ground-height difference. Horizontal dash-dot lines are the thresholds of significance and shaded areas are supra-threshold clusters that indicate the time domains with significant effects. GVS onset occurs at 0 s. Vertical dashed and dotted lines represent the onset of significant short- and medium-latency acceleration, respectively. These vertical dashed and dotted lines are shown for significant effects in the ground and height conditions. No significant ground-height difference effect was found in any of the measured angles.
2.4 Discussion

The goal of this study was to investigate the effects of fear of falling on vestibular control of whole body balance with the following sub-questions:

1. What is the kinematic response to GVS of axial and appendicular components, in the short- and medium-latency time domain?
2. What is the effect of fear of falling on each of these components?
3. How do these components relate to each other and to the regulation of head stabilisation and postural balance control?

2.4.1 Short- and medium-latency vestibular reflexes are reflected in full-body kinematics

Our results show a unidirectional, anodal acceleration of the head CoM and upper thorax in response to GVS. This is consistent with previous findings (Osler et al., 2013). Our novel findings in the body CoM, pelvis and lower limbs show a pattern of cathodal acceleration followed by anodal acceleration (Figure 2.6). This biphasic pattern is consistent with the well-established short- and medium-latency GRF and EMG responses to vestibular stimulation (Britton et al., 1993; Fitzpatrick et al., 1994; Ali et al., 2003; Fitzpatrick & Day, 2004; Son et al., 2008; Mian & Day, 2009; Dakin et al., 2010; Mian et al., 2010; Muise et al., 2012; Horslen et al., 2014; Mian & Day, 2014). In addition, this pattern is also consistent with a small cathodal sway preceding the larger anodal sway of the pelvis shown previously by Cathers et al. (2005) in their Figure 2. For reference, Figure 2.9 shows published GRF records of the short- and medium-latency responses and confirms that the established timing of short- and medium-latency responses is consistent with our acceleration data. The short-latency cathodal acceleration is part of a lateral, buckling movement of the lower limbs (Figure 2.7) supporting the idea that the source of force generation moving the whole body towards the anode arises in the lower limbs.
Figure 2.9: **Short- (SL) and medium-latency (ML) responses in different publications.**

**A. Body CoM - GVS**
- Mediolateral acceleration of body CoM from this study at ground and height is shown. Acceleration towards the anode GVS electrode (ADA) is positive and cathode directed acceleration (CDA) is negative. 1mA GVS stimulation starts at 0 s with 2 seconds in duration.

**B. GRF - GVS**
- This graph is redrawn from Marsden et al. (2005). A 1 mA GVS of 3 seconds duration starts at 0s and the shear GRF is plotted. GRF towards anode is positive and towards cathode is negative. Participants stood at ground level.

**C. GRF - SVS**
- SVS-GRF coupling (cumulant density) is shown as a function of the SVS-GRF time lag. GRF-SVS (2-25 Hz) cumulant density of participants standing at low and at high altitude is shown by the thick lines. This data is redrawn from Horslen et al. (2014) so that positive values indicate coupling of vestibular stimulation (SVS) with shear GRF towards anode and negative values indicate coupling of SVS with shear GRF towards cathode. The thin line shows GRF-SVS (1-20 Hz) cumulant density data at ground level redrawn from Mian et al. (2010). The short- and medium-latency (SL and ML) responses follow a pattern that is comparable to the short- (CDA) and medium-latency (ADA) responses found in the body CoM and lower body nodes with GVS in this study.
2.4.2 The short-latency response contributes to balance control

Authors have questioned the origin and role of the short-latency response and have suggested that it is independent of the medium-latency response (Fitzpatrick & Day, 2004; Mian et al., 2010). However, the principle of craniocentricity holds for both the short- and medium-latency responses (Mian et al., 2010; Horslen et al., 2014). The principle of craniocentricity states that the direction of the sway response to GVS is determined by head orientation. Consistent with a semi-circular canal origin, we propose that the short- and medium-latency responses comprise a coordinated balance response. We see the short-latency response as the fastest component of this response, which generates whole-body sway towards the anode electrode.

In both ground and height conditions, GVS caused a rapid generation of lateral anodal body sway. Biomechanically, acceleration of the whole body CoM requires rapid, active generation of an internal muscular moment on the trunk relative to the ground. Generation of a moment on the trunk relative to the ground occurs via muscles distributed across ankles, knees, hips and lower back. Acceleration of the linked segments is inversely proportional to their inertia, therefore the lightest segments show largest acceleration and the cathodal ‘buckling’ is most visible at the knee (Figure 2.7). Furthermore, the observed cathodal displacement of the ankle, knee and hip (caused by the short-latency response) increases the gravitational moment relative to the ground. This gravitational moment induces acceleration of the whole body in the anodal direction, as shown by the medium-latency acceleration. To illustrate, one could compare this method by balancing an upright stick on the palm of the hand by moving the hand in the horizontal plane to change the base of support and accelerate the stick in the opposite direction. Hence, the short-latency cathodal acceleration of pelvis and lower extremities is the earliest part of the attempt to rapidly generate anodal movement of the whole body CoM. The associated expression in GRF and EMG data likely reflects the same mechanism.

Previous evidence from Mian et al. (2010) suggests the short- and medium-latency responses might be independent. Among other conditions, these authors applied SVS to participants in a standing posture with the head pitched down (facing downwards) and in a more normal standing posture with the head upright facing forwards. In this head upright posture, SVS induced vestibular feedback of rotation around a horizontal axis pointing in the anterior/posterior direction. Because of the
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craniocentric response this axis of rotation was vertical in the head down posture. The short- and medium-latency responses were measured with gastrocnemius medialis EMG and GRF data. Their results showed that in the head down posture, the medium-latency SVS-EMG response was attenuated, whereas the short-latency SVS-EMG response seemed unaffected compared to head upright. They interpreted the short- and medium-latency responses as independent rather than comprising a coordinated response to a common purpose.

Following the insight of our results, we show that these authors’ data (2010) are consistent with short- and medium-latency responses comprising a coordinated response to regulate CoM location (balance). The authors assumed that the SVS-induced feedback of yaw rotation about the earth vertical axis in the head down posture does not contribute to balance control. For their interpretation to be correct, this vertical axis of rotation should intersect the whole body CoM. In reality, their Figure 2 indicates that for the head down position the vertically oriented axis of rotation does not intersect with the participant’s CoM but passes in front of it (Mian et al., 2010). Consequently, in this head down configuration one would expect an initial lateral acceleration of the whole body CoM, along the circumference of its arc around the SVS-evoked vertical axis of rotation. The direction of this CoM acceleration in the head down position should therefore be the same as for the head upright position. Since CoM acceleration is proportional to GRF data, this explains why the observed short-latency GRF response pattern (Mian et al., 2010) was similar in both conditions.

We conclude the short- and medium-latency responses comprise a coordinated regulation of balance. If correct, this insight updates the preceding observation that the short-latency response has no effect on the GVS-induced whole body movements (Fitzpatrick & Day, 2004). Our study measured vestibular reflexes in one postural configuration. We predict that for different body configurations, the expression in EMG, GRF and movement at short- and medium-latency will reflect the coordinated pattern needed to regulate whole-body CoM in that configuration.

2.4.3 Fear of falling influences vestibular balancing reflexes, but not the VCR

Whether and how fear of falling influences vestibular reflexes is currently debated (Horslen et al., 2015b, a; Reynolds et al., 2015a; Reynolds et al., 2015b). Our results
show that neck-generated head movement (VCR) was highly consistent between repetitions and between conditions (Figure 2.8A). The early acceleration response of the head and upper thorax were unaffected by fear of falling. Only for the lower limbs was early GVS-induced acceleration increased significantly by fear of falling. Statistical significance was reached in movements of remarkably small amplitude (Figure 2.4C). This confirms the sensitivity of our experiment and underscores that early acceleration of the head and upper thorax arising from angular acceleration of the neck and lower back were not influenced by fear. This study confirms that height-induced fear of falling accentuates the short- and medium-latency balance response and hence increases vestibular reflex gain of whole-body stabilisation. The functional effect of fear of falling is an earlier arrest of anodal sway, halving the distance moved by the whole-body CoM towards the dangerous edge (Figure 2.3).

Our findings are consistent with those of Horslen et al. (2014) who found an increased gain of the GRF-SVS response at short- and medium-latency during postural threat. Our findings are also consistent with the seemingly opposing results of Osler et al. (2013) who found no effect of postural threat on early acceleration of the head and upper trunk. As they collected kinematics of head and trunk but not of the lower limbs, they concluded that fear of falling does not affect the vestibular balance reflex. Our study shows that fear of falling accentuates the vestibular balance reflex, as the reflex gain of short- and medium-latency responses found in lower limb kinematics was increased at height. Our study also shows that early CoM acceleration comprises the integration of anodal head acceleration and cathodal lower limb acceleration (Figure 2.6). These opposing accelerations would mutually cancel and tend to reduce the early CoM acceleration signal, which was significant only at height. Hence a contribution of this study is a demonstration of limitations of CoM acceleration (and hence ground reaction force) to reveal GVS responses, and demonstrates the power of kinematic analysis to reveal opposing components of the GVS response.

### 2.4.4 Axial head-in-space stabilisation is task-independent

Vestibular afferents are used in multiple feedback pathways for a variety of functional purposes. Regulating head-in-space orientation and regulating the whole-body CoM to maintain balance can be distinguished as separate goals with different underlying mechanisms (Day et al., 1997). These goals are related hierarchically in the sense that balance of the whole body depends upon integration of vestibular with proprioceptive
information, which depends upon vestibular regulation of the head (VCR). Our results are consistent with others who see a distinction between vestibular mechanisms that govern axial and appendicular reflexes (2015).

Vestibulocollic neural pathways regulating head-in-space mostly comprise three-neuron-arcs. They primarily originate from medial vestibular nuclei, and response latencies of these pathways are short (~8-10 ms) (Watson & Colebatch, 1998; Forbes et al., 2014). Additionally, the VCR latency response of the sternocleidomastoid (SCM) muscle response was found to be unaltered by manipulation of vision, external support, stance width and posture (Watson & Colebatch, 1998; Welgampola & Colebatch, 2001). Forbes et al. (2014) tested the effect of fixating the trunk and head position on the VCR with the idea that this fixation rendered the neck muscles irrelevant to head posture. The VCR was still present in the fixed condition and was therefore concluded to be task independent.

2.4.5 Appendicular whole body stabilisation is task-dependent

The whole body sway response is task-dependent and more flexible than the VCR. Day et al. (1997) studied the effects of changes in posture on the GVS response and concluded that the vestibular response is organised to stabilise the body rather than the head in space. Appendicular muscles are innervated through vestibulospinal tracts originating from the lateral vestibular nuclei. Direct and indirect connections via spinal interneurons to motor neurons of extremities have been found in animal studies (Lund & Pompeiano, 1968; Shinoda et al., 1986). In humans, response latencies of ~50–60 ms were found for appendicular vestibular reflexes (Britton et al., 1993; Fitzpatrick et al., 1994; Day et al., 1997; Ali et al., 2003; Son et al., 2008). These latencies are longer than expected for the presence of direct vestibulospinal connections and are consistent with the additional processes of postural gating and coordinate transformation associated with appendicular balance responses (Fitzpatrick & Day, 2004). As discussed by Fitzpatrick and Day (2004), between immediate vestibular processing and regulation of balance there is a process of coordinate transformation from head-in-space to body-in-space and a process of gating or selection of biomechanically appropriate muscles. While previous work has established postural gating of the balance and not the cervical response (Forbes et al., 2015), our contribution confirms the differential effect of perception of risk on balance, but not the cervical response.
In our study, the GVS response direction was dependent on the randomly ordered GVS electrode polarities (anode left or right) and effects of height-induced fear of falling were not found in axial vestibular reflexes. Therefore, a general over-excitation of the motor neuron pool as a result of increased fear of falling would be unlikely given the focal and polar nature of the changes.

Recently, authors have found that vestibular evoked myogenic potentials (VEMPs) in the neck (sternocleidomastoid) and soleus were increased marginally (9%, 12%) by height-induced fear of falling whereas other muscles including upper limb muscles were not enhanced by fear of falling (Naranjo et al., 2015).

VEMPs arise from stimulation of the saccule (Rosengren et al., 2010). The saccule predominantly registers linear acceleration and pitch within the head defined sagittal plane (Fitzpatrick & Day, 2004). Within the posture studied by Naranjo et al. (Naranjo et al., 2015; Naranjo et al., 2016) stimulation of the saccule would evoke sensations of vertical and horizontal acceleration. Horizontal acceleration would challenge balance (horizontal location of CoM relative to feet), and would require a response within muscles regulating horizontal location of CoM. Vertical acceleration would require a vertical postural response but would not challenge balance. Fear of falling would be expected to accentuate the balance response and not the vertical postural response. Naranjo et al. (2015) show precisely a general response unmodulated by fear, and a response in muscles regulating horizontal translation of the head and body that is accentuated by fear, namely soleus and sternocleidomastoid within their setup.

The GVS response arises from artificial vestibular feedback from the labyrinths (Fitzpatrick & Day, 2004), which register rotation of the head in space. Head-in-space rotation requires a response to regulate the angle of head in space and, depending upon posture of the head relative to the feet, a response to regulate horizontal movement of the whole-body CoM. Head rotation, per se (without translation), does not challenge balance whereas horizontal movement of CoM does challenge balance. Hence, fear of falling would be expected to accentuate the balance response while the effect on the head rotation response is more of an open question. Our results show a
differential influence of fear of falling on the balance response to GVS as opposed to the head rotation response.

Combined, our results and those of Naranjo et al. (Naranjo et al., 2015; Naranjo et al., 2016) both support a thesis that vestibular feedback gain of balance responses is accentuated by fear of falling, and both support a thesis that modulation of response depends upon the function of the reflex pathway. Therefore, our results and those of Naranjo et al. (Naranjo et al., 2015; Naranjo et al., 2016), contradict the thesis of a common central mechanism, where fear of falling influences all vestibular feedback mechanisms (Naranjo et al., 2016).

To summarize, axial and appendicular GVS reflexes were distinguished by several features. These include invariance of latency and magnitude of the response to fear of falling, and absence of cathodal acceleration at short-latency. These different properties may reflect differences in innervation (medial vs. lateral vestibulospinal tracts) and different functional goals (head stabilisation vs. whole body balance).

### 2.4.6 Implications for fear of falling

Clinically, important questions are the extent and mechanisms by which balance responses are influenced by fear (van Dieen et al., 2015). Our findings show that fear influences vestibular balancing reflexes. However, it is important to note that while fear of falling increases the gain of this balance reflex, it remains undetermined whether this leads to an increase or decrease in the risk of falling in the general population, and in elderly persons with a persistent fear of falling. Efficient balance control enables mobility. Hence, future studies could investigate whether the effect fear of falling on vestibular reflexes increases or decreases mobility in the general population, and in the elderly population in particular. Additionally, the asymmetric decline of sensory and vestibular function with ageing may leave individuals vulnerable to the influence of fear on vestibular processing (Horak et al., 1989; Baloh et al., 1993; Kristinsdottir et al., 2000). Patient-specific identification of the origin of balance performance decline is required and follow-up studies with elderly persons and clinical subgroups could clarify mechanisms relating fear of falling to balance and mobility.
2.4.7 Conclusion

To our knowledge, the present study provides the most detailed full-body kinematic analysis of the GVS evoked response to date. We parsed the whole body response (CoM) into its component parts (cervical, axial trunk, short- and medium-latency lower extremity) and assessed the effect of fear of falling on each component. Results demonstrated the ability of kinematic analysis to reveal small responses, believed marginal through EMG and also demonstrated opposing responses cancelling their effect within centre of mass and force plate data. This new evidence suggests the short- and medium-latency reflexes are not independent but in fact comprise a coordinated balance response. Results also indicated that fear differentially accentuates the appendicular balance response without influencing the axial vestibulocollic reflex.