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Postural Responses to Perturbations of the Vestibular System During Walking in Healthy Young and Older Adults

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POSTURAL RESPONSES TO PERTURBATIONS OF THE VESTIBULAR SYSTEM DURING WALKING IN HEALTHY YOUNG AND OLDER ADULTS

by

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ABSTRACT

It has been shown that approximate one-third of US adults aged 40 years and older (69 million US citizens) have some type of vestibular problems. These declining abilities of the vestibular system affect quality of life. Difficulties in performing daily activities (dressing, bathing, getting in and out of the bed and etc.) have been highly correlated to loss of balance due to vestibular disorders. The exact number of people affected by vestibular disorders is still difficult to quantify. This might be because symptoms are difficult to describe and differences exist in the qualifying criteria within and across studies. Thus, it is crucial to develop a valid assessment. To measure how each sensory system contributes to postural control during walking, we developed a novel Locomotor Sensory Organization Test (LSOT).

Our results indicate that the contribution of visual input is significantly increased during locomotion, compared to standing in similar sensory conflict conditions. The increased visual gain in the LSOT conditions reflects the importance of visual input for the control of locomotion. In addition, if we investigated the postural control in walking in time series, the results showed visual input also had an effect but was not as prominent as the somatosensory input. Moreover, while applying Mastoid vibration (MV) on healthy young and older adults combined with LSOT assessment, we found that MV produced a significant increase in the amount of sway variability. Significant changes in the temporal structure of sway variability were only observed in the anterior-posterior direction in both age groups. However, the MV effect on the measure of the temporal structure of variability is opposite where MV produced an increasing effect in young adults. This is a very important finding as vestibular disorders has been difficult to diagnose lacking a systematic assessment leading to speculations that more than 1/3 of adults in the US that are 40 and older may experience vestibular problems that have never been diagnosed. Our experimental design and the results produced could guide a more reliable screening of vestibular system deterioration.

TABLE OF CONTENTS

LIST OF ABBREVIATIONS

SOT: Sensory Organization Test

LSOT: Locomotor Sensory Organization Test

netCOP: et Center of Pressure

CNS: Central Nervous System

AP: Anterior-Posterior

ML: Medial-Lateral

VR: Virtual reality

PI: Performance Index

RHS: right heel strike

LHS: left heel strike

RTO: right toe-off

LTO: left toe-off

Mastoid Vibration: MV

PWS: Preferred walking speed

SampEn: Sample Entropy

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CHAPTER 1

INTRODUCTION TO THE DISSERTATION

Sensory feedback is crucial for postural control during standing and walking. This includes visual, vestibular and proprioceptive feedback. It has been shown that approximate one-third of US adults aged 40 years and older (69 million US citizens) have some type of vestibular problems[1]. These declining abilities of the vestibular system affect quality of life. Difficulties in performing daily activities (dressing, bathing, getting in and out of the bed and etc.) have been highly correlated to the loss of balance due to vestibular disorders[2]. In addition, people with vestibular disorders have a nearly 8-fold increase in the risk of falling in comparison with age-matched controls due to decline in postural control[3] because the deficient vestibular system cannot provide accurate information about the patients' orientation in space in relation to the environment. These patients are forced to rely more on the other two major sensory systems (visual and somatosensory systems) to maintain their postural control. However, when a situation arises that requires information to be processed via the vestibular system (e.g. walking through a dark and slippery sidewalk), these patients show increased sway, which can lead to falls. The exact number of people affected by vestibular disorders is still difficult to quantify[4]. This might be because symptoms are difficult to describe and differences exist in the qualifying criteria within and across studies. Even though Sensory Organization Test (SOT) has widely used to diagnose the vestibular disorders, there are still many vestibular disorders, which are under-diagnosed and under-treated[1]. It might be due to that the SOT only investigates how the vestibular system controls balance during standing. Lack of understanding how vestibular system controls the balance during walking reduces the possibility to early diagnose the vestibular disorders.

How the different sensory systems contribute to postural control during standing can be studied using the SOT. The SOT contains six different conditions to identify abnormalities in the three sensory systems that contribute to postural control during standing. Studies have shown that patients with different vestibular disorders show different responses to sensory perturbed SOT conditions[5-7]. Patients with bilateral vestibular loss demonstrate significant sway differences only when both the visual and the somatosensory systems are perturbed simultaneously[5]. The fact is that patients with well-compensated vestibular losses can use either visual or somatosensory information to orient the body. However, patients who have uncompensated vestibular disorders (e.g. unilateral vestibular disorders) may show increased sway in either the visual or somatosensory perturbed SOT condition. In addition, patients with uncompensated vestibular loss sway significantly more when both the visual and the somatosensory systems are perturbed simultaneously[6]. Incomplete neural adaptation to a vestibular lesion may be a factor that causes these patients with unilateral vestibular disorders to experience a difficulty to select reliable sensory systems to maintain their balance. Some patients, who have distorted but not absent vestibular function such as acute corneal hydrops, show a visually dependent pattern on the SOT results[7]. These patients demonstrate excessive sway when the visual surround is sway-referenced, but normal sway when their eyes are closed. It is as if the central nervous system (CNS) relies on visual information when the eyes are open, even when vision is not providing accurate information about body sway. However, when their eyes are closed, such patients are able to rely on somatosensory information on a firm surface and upon vestibular information when standing on a sway-reference surface. The situation is more complicated with older adults since the vestibular system declines gradually and thus, vestibular system input can be well compensated in a gradual fashion by the other two sensory systems, possible as is the case with the patients with bilateral vestibular loss.

However, all this above information is based on standing posture and not dynamic posture as it occurs during walking, where the majority of falls occur. To measure how each sensory system contributes to postural control during walking, we developed in the second chapter[12] of this dissertation a novel Locomotor Sensory

Organization Test (LSOT). In addition, a novel method, netCOP sway variability, was used to quantify the amount of sway during walking and to quantify ability to balance during walking. Furthermore, we incorporated additional measures to explore variability such as nonlinear measures that capture how movement changes in time series. It has been shown that nonlinear measures derived from SOT conditions significantly revealed unsteady postural control in athletes with cerebral concussion even after 48 hours from the injury while linear measures of amount of sway variability failed to detect this difference[8]. Sample Entropy (SampEn) is a nonlinear measure that quantifies the regularity of a symbolic sequence (time series) by analyzing the presence of similar sub-patterns in the data sequence. Only few studies have used the Entropy measure to investigate the contribution of the sensory systems to postural control during standing among SOT conditions[8-10]. It has been shown that postural sway became more regular when somatosensory information became unreliable than when visual information became unreliable. When both somatosensory and visual information become unreliable simultaneously, the postural sway results are the most regular[8-9]. These results generate several interesting questions with respect to our LSOT experimental paradigm. Does the regularity of postural sway variability demonstrate similar characteristics during walking as in standing? We attempted to answer this question in the third chapter[12] of this dissertation.

Once our novel LSOT assessment is presented, we applied this paradigm combined with vestibular stimulation to investigate how the vestibular system affects postural control during walking. This became the purpose of the fourth chapter (third manuscript) of this dissertation. There are several methods to investigate the role of the vestibular system during walking: 1) using patients with vestibular disorders, 2) stimulating the vestibular system with caloric methods or galvanic current, and 3) stimulating the vestibular system with vibration of selected muscles like the mastoid. It has been quite difficult to identify patients with vestibular disorders here in Omaha. In addition, galvanic vestibular stimulation and caloric irrigation generate uncomfortable feelings for the participants. Therefore, the usability of these approaches to study the true effects of the vestibular system on balance and postural control during walking has been questioned as anxiety due to discomfort may compromise subject responses. We decided to use mastoid vibration to stimulate the vestibular system, because this method does not generate any feelings of discomfort feelings. Furthermore, we wanted to investigate if older adults differed from young adults in the contribution of the vestibular system on dynamic postural control. This was explored in the fifth chapter (fourth manuscript) of this dissertation.

To present the findings of this study, the dissertation was divided into four chapters, each of which was a separate manuscript in itself. The four chapters are:

1. Locomotor Sensory Organization Test: A Novel Paradigm for the Assessment of Sensory Contribution in Gait[11].
2. Locomotor Sensory Organization Test: How Sensory Conflict Affects the Temporal Structure of Sway Variability During Gait[12].
3. Mastoid vibration affects dynamic postural control during gait[13].
4. Mastoid vibration affects dynamic postural control during gait in healthy older adults.

CHAPTER 2

LOCOMOTOR SENSORY ORGANIZATION TEST: A NOVEL PARADIGM FOR THE ASSESSMENT OF SENSORY CONTRIBUTIONS IN GAIT

Chien JH, Eikema DJ, Mukherjee M, Stergiou N. Locomotor sensory organization test: a novel paradigm for the assessment of sensory contributions in gait. Ann Biomed Eng. 42(12): 2512-23, 2014.

ABSTRACT

Feedback based balance control requires the integration of visual, proprioceptive and vestibular input to detect the body's movement within the environment. When the accuracy of sensory signals is compromised, the system reorganizes the relative contributions through a process of sensory recalibration, for upright postural stability to be maintained. Whereas this process has been studied extensively in standing using the Sensory Organization Test (SOT), less is known about these processes in more dynamic tasks such as locomotion. In the present study, ten healthy young adults performed the six conditions of the traditional SOT to quantify standing postural control when exposed to sensory conflict. The same subjects performed these six conditions using a novel experimental paradigm, the Locomotor SOT (LSOT), to study dynamic postural control during walking under similar types of sensory conflict. To quantify postural control during walking, the net Center of Pressure (netCOP) sway variability was used. This corresponds to the performance index of the center of pressure (COP) trajectory, which is used to quantify postural control during standing. Our results indicate that dynamic balance control during locomotion in healthy individuals is affected by the systematic manipulation of multisensory inputs. The sway variability patterns observed during locomotion reflect similar balance performance with standing posture, indicating that similar feedback processes may be involved. However, the contribution of visual input is significantly increased during locomotion, compared to standing in similar sensory conflict conditions. The increased visual gain in the LSOT conditions reflects the importance of visual input for the control of locomotion. Since balance perturbations tend to occur in dynamic tasks and in response to environmental constraints not present during the SOT, the LSOT may provide additional information for clinical evaluation on healthy and deficient sensory processing.

INTRODUCTION

The maintenance of upright posture during standing and walking requires integration of visual, somatosensory and vestibular inputs. Each of these inputs is sensitive to particular characteristics of self-motion and motion within the environment that uniquely contributes to the detection of postural sway. Upon sway detection, the central nervous system initiates corrective postural adjustments by implementing the appropriate muscular responses[14]. Inherent ambiguities in each of the modalities need to be solved before sensory signals provide useful contributions. For example, the somatosensory modality is unable to differentiate between movement of the support surface and movement of the body. This ambiguity can be resolved through access to visual information, which provides self-motion information independent of the support surface. This solution process could be modeled following a Bayesian framework. Sensory ambiguity leads to a broader probability curve of postural sway estimation and uncertainty regarding necessary postural corrections when a single modality is involved. When an additional sensory signal is available, the integrated signal leads to a more precise estimation[15-16] and subsequently more appropriate postural corrections. In conditions of reduced sensory accuracy as a result of internal or external perturbations, the system recalibrates sensory contributions, reciprocally lowering the gain of inaccurate signals and increasing the gain of accurate signals[14]. Body sway and sway variability increase when vision is absent, compared to standing with accurate visual input. However, this increase is significantly lower than the degree of sway observed in individuals with a reduced capacity for sensory reweighting[17]. Whereas the reported reweighting patterns have been observed during standing, similar sensory processes may be involved in locomotion[18].

In order to quantify sensory contributions and the adaptive mechanisms involved in the control of posture during sensory conflict, the Sensory Organization Test (SOT) has been used in patients with vestibular disorder[19-21], concussion[22], stroke[23], and Parkinson's Disease[24]. Through the systematic manipulation of sensory input, the SOT intends to perturb the system and induce adaptive sensory recalibration processes. It can manipulate singly or in combination somatosensory and visual inputs to allow for the assessment of a patient's ability for maintaining balance[24]. It has been found that when healthy adults stand on a firm surface with available visual input, sensory contributions consisted of 70% somatosensory input, 20% vestibular input and 10% visual input[25]. When somatosensory accuracy was reduced through support surface oscillations, sensory recalibration changed the relative contributions to 70% vestibular information, 20% visual information and 10% somatosensory information to maintain postural stability[25]. Based on these results, the somatosensory and vestibular systems seem to be the dominant sensory systems as compared to the visual system to achieve postural control during standing[25]. Whereas this process has been studied extensively in standing, less is known about whether similar strategies are also utilized to resolve sensory conflicts during more dynamic situations of postural control such as walking.

Visual input during walking is uniquely capable of encoding task specific information including travelled distances, navigation, planning walking trajectories and perceiving environmental features[26]. When visual input was manipulated by prism goggles in healthy young adults, subjects demonstrated a significant lateral deviation from their destination[27]. The somatosensory system also provides information about the ground conditions during locomotion, such as the presence of slippery or icy surfaces. Thies and colleagues (2005) indicated that individuals with peripheral neuropathy increased step time and decreased step length when walking on an irregular surface as compared to walking in a dim light condition[28]. These results suggest that the CNS might have to recalibrate multisensory interactions in patients with inaccurate somatosensory perception, by adjusting their gait patterns. Ishikawa and colleagues showed that patients with unilateral vestibular disorders had an asymmetric walking pattern[29-30]. The significantly shorter step length and longer swing time was observed on the side where the vestibular system was affected. The same is observed using vestibular stimulation during locomotion[31]. Adjusting step length and step time was suggested as a strategy to maintain balance and prevent falling during locomotion[32]. Based on the above, it is evident that a deficit in a sensory system can affect gait patterns and balance during locomotion. However, a comprehensive study of how sensory information from all three systems is integrated to achieve dynamic postural control during walking has not been performed. It is possible that the reason for such a knowledge gap is the absence of an experimental apparatus like the SOT for walking.

In the present study we developed and implemented an experimental apparatus, consisting of an integrated instrumented multisensory virtual reality environment: the Locomotor Sensory Organization Test (LSOT). This allowed for the assessment of sensory contributions to the dynamic postural control during walking. We hypothesized that dynamic postural control during walking would be affected by unimodal and multimodal sensory perturbations, inducing sensory recalibration. In addition, we hypothesized that maintaining dynamic postural control during walking shares similar feedback control mechanisms with maintaining postural control in standing, reflected in similar postural sway behavior in the SOT and LSOT. Finally, we hypothesized that the importance of vision in the locomotor task will significantly increase in postural perturbations induced by visual conditions.

METHODS

Subjects

Ten healthy young adults (five males and five females; age 27.20±4.92 years, height 171.30±7.01 cm and weight, 64.70±9.90 kg) participated in this study. Subjects were free from any musculoskeletal impairments, had no history of significant lower extremity injuries which may have affected their posture or gait and had no visual, somatosensory or vestibular deficits. We excluded individuals without normal or corrected to normal vision, scored above zero on the dizziness handicap inventory for a vestibular deficit,[33] and with any type of peripheral neuropathy that can affect somatosensory function. Prior to the experiment, each subject signed an informed consent approved by our University's Medical Center Institutional Review Board.

Protocol

The experiment entailed exposing subjects to sensory perturbations in the SOT and LSOT environments. The SOT was conducted in a quiet room using the Balance Master System 8.4 (NeuroCom International Clackamas, OR, USA) (Figure 2-1). The system contains a moveable visual surround and support surface that rotate in the anterior-posterior (AP) plane. Two 22.9 x 45.7 cm force plates connected by a pin joint are used to collect center of pressure data at 100 Hz. Foot placement is standardized based on subjects' height according to manufacturer guidelines. The SOT contains six conditions to manipulate the combinations of visual, vestibular, and somatosensory information used for postural control during standing. While standing in the Balance Master system, subjects wore a vest according to SOT procedures, attached to the safety harness of the system.

The LSOT apparatus consisted of a virtual reality (VR) environment and an instrumented treadmill containing two embedded force plates (Bertec Corp., Columbus, OH, USA; Figure 2-2), integrated into a single system allowing for synchronized data collection and stimulus presentation. A motion capture system (Optotak Certus; Northern Digital Inc., Waterloo, Canada) was used to capture the three-dimensional marker trajectories at a sampling rate of 100Hz. Active rigid body markers were placed on the toe and heel of each leg. The unfiltered position data for the x, y, z coordinates were exported using Optotrak Certus' proprietary software. Data processing was performed using custom Matlab code (Mathworks Inc., Natick, Massachusetts) for the calculation of step length and step width. Ground reaction force data were acquired from the force plates at 100 Hz. The Heel-Strike was considered to occur at the first frame in which the vertical component of the ground reaction force exceeded a threshold level of 10N and continuously exceeded this threshold for 40 ms. The Toe-Off was considered to occur at the first frame in which the vertical component of the ground reaction force fell below the 10N threshold, sustained continuously for 40ms[34-36]. This 10N threshold was calculated as three times the standard deviation of the vertical ground reaction force during the initial 100 ms (100 frames) of the trial[34-36]. A gait cycle was defined as the time elapsed between two consecutive heel strikes of the ipsilateral leg.

The custom VR environment provided self-motion information through optic flow manipulation and was written in Python using the WorldViz LLC graphics library (Santa Barbara, CA, USA). The virtual environment was projected by three commercial projection systems (Optoma TX 774, Optoma Technology Inc., Milpitas, CA) on three 2.51 m x 1.72 m flat screens that were positioned 1.5 m away from the plane of motion. The angle between side and middle screen was 120 deg. A moving virtual corridor was projected onto the screen to generate the optic flow stimulus. Custom software, written in Visual Basic (Microsoft Corp., Redmond, WA), was utilized to vary the treadmill speed in real time. In order to manipulate vision, we used light intensity goggles (MSA Safety Work, Pittsburgh, PA) which reduced the light intensity from 22 lux to 0.7 lux. The LSOT contained six conditions similar to the SOT to manipulate the visual, vestibular, and somatosensory information during walking (Figure 2-3). In order to increase safety while on the treadmill, subjects also wore the same SOT vest, attached to a LiteGait harness system (Mobility Research, AZ, USA).

Subjects were required to complete all SOT and LSOT conditions in a single session. Subjects first completed the SOT conditions, followed by the LSOT conditions. Experimenters explicitly instructed subjects to “try your best to keep your balance” during the SOT and LSOT conditions. For the SOT, subjects were positioned standing upright on the Balance Master. Each SOT condition followed a standard protocol of three trials lasting 20 seconds each and the sequence of conditions given to subjects followed a predetermined order (conditions 1 - 6). Between the SOT conditions, subjects received a 30 seconds rest period. For the LSOT, prior to the data collection each subject walked for five minutes on the treadmill to determine their preferred walking speed (PWS). Subjects stood on the sides of the treadmill without touching the belts. Subsequently, treadmill belt velocity was incremented from 0 to 0.8 m/s. Then the subjects were asked to step on treadmill while holding the handrail. After the subject started walking on the treadmill, experimenters asked the subject to evaluate the speed as following: “Is this walking speed comfortable like walking around the grocery store?” The treadmill velocity was increased or decreased, following subject directions. Once a comfortable walking velocity was attained, the subject walked continuously for 5 minutes. After the PWS was determined, all subjects walked on the treadmill at their PWS for two minutes in each of the six conditions of the LSOT and each LSOT condition was matched to its respective SOT counterpart and sequence. The LSOT conditions were the following:

1) Normal walking condition: both the speed of the virtual corridor and the treadmill speed were matched with PWS.

2) Reduced visual condition: no VR was presented, the treadmill speed matched with PWS, and the subjects wore vision-reduced goggles.

3) Perturbed visual condition, achieved by manipulating the optic flow speed: the speed of the virtual corridor was pseudo-randomly varied between 80% and 120% (restricted randomization between 80% and 120% in steps of 1) of the selected PWS in pseudo-randomly assigned time intervals within 1 to 10 seconds (restricted randomization between 1 and 10 in steps of 1). Such a range was used in previous studies to manipulate walking speed[37-38]. Moreover, we gave 1 to 10 seconds time intervals of perturbations to reduce adaptation of walking in the perturbed environment. The treadmill speed matched with PWS.

4) Perturbed somatosensory condition by manipulating the treadmill speed: the speed of the virtual corridor matched with PWS, while the treadmill speed was varied between 80% and 120% of the PWS in pseudo-randomly assigned time intervals within 1 to 10 seconds. Walking speed is highly associated with the sensitivity of somatosensory system[39] and is very crucial during stance-to-swing transition[41]. Changing walking speeds immediately affects the time of stance-to-swing transition. This is why fast walking is an excellent selection for quantifying somatosensory impairment[40] and why walking speed has been used in the present study for our somatosensory perturbation[39-41].

5) Perturbed visual and somatosensory condition by reducing vision and manipulating treadmill speed: no VR was presented, the treadmill speed was varied between 80% and 120% of PWS in pseudo-randomly assigned time interval within 1 to 10 seconds, and the subjects wore vision-reduced goggles.

6) Perturbed visual and somatosensory condition by manipulating optic flow and treadmill speed: both the speed of the virtual corridor and the treadmill speed was varied between 80% and 120% of the selected PWS in pseudo-randomly assigned time intervals of 1 to 10 seconds duration. In this condition the velocity of the virtual corridor and treadmill were synchronized with a unitary gain relationship.

Subjects were allowed to rest for one minute with eyes-closed between conditions. Optic flow and treadmill speed were varied between 80 to 120%, as the impact of different walking speeds on gait variability was conventionally investigated in this range[37-38]. Indeed, the amount of gait variability has shown a negative linear correlation with different walking speeds in this range in healthy young adults. However, literature also indicated that over 120% of PWS, muscle activity had a significant jump in comparison with the muscle activity at 120% of PWS[42].

Data Analysis

Postural performance was assessed using the Performance Index (PI). This metric was used to determine the extent to which sway approached the body's stability limits during standing and walking[17]. The calculation method of the PI is conceptually similar to the standard deviation. The PI is calculated by numerically integrating the rectified sway signal (with the steady-state offset removed), and then scaling the result as a percentage of the maximum sway possible during standing. A PI value approaching zero indicates stable postural control. PI values that approach 100 indicate loss of balance. The PI allowed us to compare postural performance and assess sensory contributions during standing[17]. The PIs in both the AP and medial-lateral (ML) directions were calculated in this study for the SOT.

$$\mathrm{PI} = \sum \frac{|\text{COP position in each frame} - \text{origin COP position}|}{\text{Max COP sway position} - \text{origin COP position}} \quad (1)$$

For walking and the LSOT, the ground reaction force data were low-pass filtered at 10Hz (with a 4th order Butterworth filter). The netCOP sway variability metric was calculated using the filtered data. The netCOP is the point where the total sum of a pressure field acts on a body during walking[43]. The netCOP measure allows for a direct comparison of the COP measures between standing and locomotion. The netCOP variable requires the identification of four specific netCOP points: right heel strike (RHS), left heel strike (LHS), right toe-off (RTO), and left toe-off (LTO). These four points were defined by using the data from the instrumented treadmill. The right leg heel strike was defined as the largest positive value in the anterior-posterior direction and largest positive value in the medial-lateral direction per gait cycle. The left leg heel strike was defined as the largest positive value in the anterior-posterior direction and largest negative value in the medial-lateral direction per gait cycle. The right toe off was defined as the largest negative value in the anterior-posterior direction and largest positive value in the medial-lateral position per gait cycle. The left toe off was defined as the largest negative value in the anterior-posterior direction and largest negative value in the medial-lateral position per gait cycle (Figure 2-4). In order to estimate the postural sway during walking, we calculated the netCOP area by calculating the two area triangles created. One triangle consisted of the LHS, LTO, and intersection point between the two triangles. The other consisted of the RHS, RTO, and intersection point. We then added these two triangles to find the total area of netCOP for one gait cycle. The mean and the standard deviation for each subject were calculated by averaging all 90 gait cycles. Then, the netCOP sway variability was calculated as the coefficient of variation for each subject. In the current study, 90 gait cycles were used to calculate the netCOP sway variability for each subject. This was the lowest number of gait cycles performed by the slowest subject within the two minutes of data collection. Thus all data were truncated to 90 gait cycles per subject. The smaller the netCOP sway variability, the better the dynamic postural control during walking. This approach in terms of interpretation, it is the same that is given to the SOT outcome measure. Figures 2-5 and 2-6 include trials of all SOT and LSOT conditions to demonstrate how the variables of interest changed due to the perturbations presented.

Step length and step width were determined based on the heel-strike and toe-off. Step length was defined as the distance between heel strike and subsequent heel strike of the contralateral foot. Step width was defined as the mediolateral distance between heel markers at successive heel strikes. Step length, and step width variability were defined as the coefficient of variation of these spatial parameters to determine how spatial parameters shifted during walking.

One-way repeated measures ANOVA's were performed using SPSS 18.0 (IBM Corporation, Somers, NY) to determine condition effects for the LSOT and SOT. Specifically, the dependent measures were: a) the PI for the SOT in the anterior-posterior (AP) direction, b) the PI for the SOT in the mediolateral (ML) direction, c) the spatial parameters (step length, and step width) for the LSOT, d) the spatial parameters variability (step length and step width variability), and e) the netCOP sway variability for the LSOT (as derived from an area and not a length contains both the AP and ML directions). Pairwise comparisons were performed to determine specific differences between conditions using Bonferroni adjustments. The level of significance was set at 0.05.

RESULTS

Anterior-posterior PI in the SOT

The one-way repeated ANOVA revealed a significant condition effect ($F = 55.38$, $p < 0.001$) (Table 2-1). The post-hoc pairwise comparisons revealed numerous differences between conditions. The conditions 1, 2, and 3 were statistically similar, while the group mean values increased significantly in conditions 4, 5 and 6. The largest group mean value was present in condition 5 (eyes closed with sway-referenced surface), followed by condition 6 (eyes open with sway-referenced surface and visual surroundings). However, there was no significant difference between conditions 5 and 6 ($p = 0.081$).

Medial-lateral PI in the SOT

The one-way repeated ANOVA revealed a significant condition effect ($F = 21.06$, $p < 0.001$) (Table 2-1). The pairwise comparisons revealed similar results with the AP direction, however, this time the largest group mean value by a very small non-significant margin was in the sixth condition. The group mean values were all smaller than the AP.

Spatial parameters in the LSOT

The one-way repeated ANOVA revealed a significant condition effect for step length ($F = 12.7$, $p < 0.001$) and step width ($F = 4.47$, $p = 0.002$). The post-hoc analysis showed that the step length was statistically longer in condition 1 than conditions 2, 5, and 6 (Table 2-1). However, for step width and due to the Bonferroni adjustment the post-hoc pairwise comparisons did not show any statistically differences between conditions.

Spatial parameters variability in the LSOT

The one-way repeated ANOVA showed a significant condition effect in step length ($F = 36.37$, $p < 0.001$) and in step width ($F = 10.52$, $p < 0.001$). The post-hoc pairwise comparisons showed that the step length variability was statistically smaller in condition 1 than conditions 2, 4, 5, and 6 (Table 2-1). For step width variability, condition 1 was statistically smaller than condition 2, 3, 4, 5, and 6 (Table 2-1).

Sway variability in the LSOT

The one-way repeated ANOVA revealed a significant condition effect ($F = 24.79$, $p < 0.001$) (Table 2-1). Subsequent pairwise comparisons revealed numerous significant differences (Table 2-1). The group mean netCOP value for condition 1 was significantly smaller than the other conditions. In addition, condition 5 (reduced visual information, variable treadmill velocity) had the largest group mean value. Condition 6 (variable optic flow and variable treadmill velocity) displayed the second largest group mean value. The third largest value was for condition 2 (reduced visual information, treadmill speed matched with PWS).

DISCUSSION

In the present study we investigated how individuals recalibrate sensory contributions to locomotion in conditions of ambiguous sensory inputs. The LSOT, a novel experimental paradigm, was developed to study sensory contributions to dynamic postural control during walking. Our results supported our first hypotheses that walking would be affected by unimodal and multimodal sensory perturbations, inducing sensory recalibration. However, our results partially supported our second hypotheses that maintaining dynamic postural control during walking shares similar feedback control mechanisms with maintaining postural control in standing, as postural sway was similar between the two tasks only when visual and somatosensory systems were perturbed simultaneously. Finally, the result supported the hypothesis that vision will be the dominant sensory system during walking.

Specifically, the significant differences found between conditions for the netCOP values in the LSOT supported our first hypothesis (Table 2-1), indicating the LSOT can be used to elicit systematic sensory recalibration processes. Importantly, our results almost mirrored those found at the SOT, particularly in the AP direction (Table 2-1). This direction is the dominant direction of sway movement during the SOT, since the perturbations are presented in the AP direction (see Table 2-1). The PI values in the various perturbation conditions conform to what is commonly reported in the literature[17]. The similarities between the SOT and LSOT results suggest that similar feedback based perceptual mechanisms could be involved. However, contrary to the SOT results, the LSOT also resulted in significantly increased variability when vision was reduced, reflecting the importance of visual input during locomotion.

During standing, our findings showed that the combination of perturbed visual and somatosensory inputs resulted in much larger reliance on the vestibular system resulting in significantly increased levels of COP variability. This also appears to be the case in walking. However, the effect of visual input on walking is more clearly demonstrated when it is reduced (condition 2) while somatosensory input is not perturbed. This condition produced the only practical difference between the SOT and the LSOT and demonstrated a much larger effect in the LSOT. The LSOT conditions 2 and 5 provide a particularly interesting perspective on sensory contributions to locomotion. In the control of upright posture, vision provides indispensable positional information and is the only modality containing the functional organization to allow for this type of contribution. Neither vestibular nor somatosensory input is sufficient to provide positional information during locomotion. In conditions of reduced vision, subjects have limited information of their location on the treadmill. This reduction in positional information may have resulted in a positional drift towards the front or back edges of the treadmill. Theoretically, if subjects walked on the treadmill and had positional drift towards the front and back, the variability should be bigger in the sensory conflicted conditions than the normal conditions. The results we provided in terms of step length and width variability indicated that subjects indeed shift front and back and left and right, in a greater extend in the sensory-conflicted conditions than in the normal walking condition. The corrective motions employed when the limits of the treadmill are reached increased the degree of variability of the netCOP since the netCOP area varies as a function of the stride length on the treadmill. Such large excursions on the treadmill remain unperceived by the vestibular sense, which lacks the sensitivity to detect this type of drift[15]. From a Bayesian perspective, uncertainty in dynamic postural control during walking significantly increases, as vision capacity which is the primary source of stabilizing sensory input, is reduced. Similar observations have been made in step variability patterns in individuals afflicted with peripheral neuropathy under low light environmental conditions[44].

In persons with peripheral neuropathy, gait variability significantly increased on irregular surfaces under the low lighting condition as compared to walking on a level surface under regular lighting condition. The somatosensory perturbation of the irregular support surface increased vestibular gain, which is less effective for the task of feedback control of posture and gait variability. Similarly, in the current study the combined perturbation conditions were implemented to investigate the vestibular control of locomotion. Walking is a complicated behavior involving coordination of multiple systems within the body and the sensory system provides reliable environmental information to these systems[45]. As controlled by visual and vestibular perception, the primary role of intersegmental postural coordination is the stabilization of the head in space. This is why both visual and vestibular rotational stimuli lead to balance responses in the roll plane, the magnitude of which decreases from proximal to distal segments. Subsequently, during constant rotational stimuli the head consistently displays the largest coupled angular deviation, followed by the torso and peripheral effectors[46-47]. We found that netCOP variability significantly increased when walking with both the visual and somatosensory input perturbed as compared to other sensory conflicted conditions. When only the vestibular system was reliable, subjects increased the netCOP area sway variability to maintain dynamic postural control.

Do the mechanisms governing the control of both standing and walking share commonalities in terms of maintaining balance? It has been argued that the control mechanisms used to maintain balance during walking is quite different and complicated from those used during standing because the center of gravity during walking is always outside the base of support[46]. Further, O'Connor and Kuo (2009) stated that the fundamental mechanism to control walking posture may be different from standing posture[48]. They supported this statement with the observation that posture was more sensitive to visual stimuli in the frontal plane than in the sagittal plane during walking.

For standing, the visual stimuli affected the postural control only in the sagittal plane and not in the frontal plane. Our results were line with their study in terms of walking where giving visual perturbation led to higher variability in the frontal plane than in the sagittal plane. However, when multiple sensory systems are perturbed concurrently, the mechanism to control walking and standing posture may be the same since spatial variability increased in both the frontal and sagittal plane in our study. Moreover, the overall netCOP sway variability significantly increased in these multiple sensory conflicting conditions. Based on a Bayesian perspective,[15-16] multiple sensory conflicting conditions resulted in an increased uncertainty of the system to maintain postural control regardless of the task; standing or walking. This is why our results partially supported our second hypothesis that a degree of similarity of control mechanism exists between maintaining dynamic postural control during walking and maintaining postural control in standing.

Interestingly, when we compared conditions 1,2, 3 and 4 during walking, we found no significant differences between conditions 2, 3, and 4, while all three of them were different than condition 1. This result may indicate that for walking both the visual and the somatosensory system have significant contributions when perturbed singly. However, this was not the case during standing where conditions 1, 2, and 3 were not significantly different from each other, while all of them were significantly different from condition 4. This result may indicate that for standing, visual information is not as important as somatosensory information when manipulated singly. This is a very interesting dichotomy between the two tasks that is revealed by the examination of the non-significant results and this is why we have partially supported our second hypothesis. Practically, our results point to the importance of visual information during walking as the continuous assessment of our surroundings is fundamental to maintain postural control. By factoring out vision during walking, we can suggest that the two tasks share similar sensory contributions to postural control.

Our step width results were similar to those reported by Altman et al[49], confirming that a split belt treadmill could cause people to walk with wider steps. In the O'Connor and Kuo study, the authors did not use a split belt treadmill and their dependent measure was a modified step width parameter. This may affect direct comparison between our results and theirs with respect to step width. Furthermore, in the O'Connor and Kuo's study, the dependent measures used were the discrete foot placement during walking and the continuous COP trajectory during standing. The selection of these parameters could be a limitation of their paper, when standing and walking are compared, as these parameters are quite different in nature (discrete versus continuous). In our study, we used in both standing and walking continuous measurements to quantify postural control. To our knowledge this is also the first study that attempted to mimic the SOT paradigm in walking. In the current study, we found that increasing the amount of sway variability seems to be a consistent strategy in standing and walking regarding the sensory conflicting conditions. This was actually similar to O'Connor and Kuo's work. We also found that in conditions 5 and 6, the variability significantly increased in both walking and standing. Thus, we believe that the control mechanisms of standing and walking share a certain degree of similarity.

A possible limitation of the present study is the type of somatosensory perturbation used for the LSOT; variable speeds. This is not identical to the tilting ground perturbation used in the SOT. Thus, it can be argued that changing gait speed not only alters somatosensory input, but also vestibular system input and the mechanical, metabolic and general physiological demand placed on the subjects. However, variable ground tilting during walking would have been a very difficult perturbation to be achieved during walking and such technology is extremely expensive to have any type of clinical applicability at present. Our designed perturbation, namely varying speeds, as we explained in the methods does affect the somatosensory system based on the available literature. On the other hand, tilting the ground, as in the SOT somatosensory condition, could possibly also affect the vestibular system by disturbing the torso dynamics resulting in head movement[50]. Another possible limitation of the present study is that tactile sensation is also available from the safety harness. We attempted to reduce this effect by asking subjects not to hold onto the harness and by adjusting the harness to achieve maximum possible comfort. The safety harness is also included in the standard clinical SOT procedures and thus the utilization of such a harness in our experimental design did improve external validity.

In conclusion, the LSOT results demonstrated that a degree of similarity exists in postural control mechanisms that are active during standing and walking in healthy individuals. The primary difference between them appears to be the nature of the visual contribution. Vision uniquely provides positional information during locomotion. In healthy individuals, compensation by somatosensory mechanisms is more effective during standing, as reflected in a relatively minor increase in COP variability. In locomotion on the other hand, the visual perturbation significantly increased variability. Thus this phenomenon of increased importance of unimodal visual over somatosensory input during locomotion is the inverse of what is observed during standing. SOT has been widely used to examine feedback based postural control during standing and these results have been generalized to infer postural control during walking. However, the LSOT was specifically designed to explore postural control mechanisms during walking and revealed additional patterns of multisensory interactions, not reflected in performance on the SOT. As falls tend to occur in dynamic tasks and in response to environmental constraints not present during the SOT, the LSOT may provide additional information on healthy and deficient sensory processing.

Table 2-1: Group means and standard deviations for all conditions for the 7 dependent measures evaluated. Significant differences between conditions are indicated with superscripts.

Conditions	1	2	3	4	5	6
PI in AP for SOT	7.26(1.41)[$^&]	9.18(2.94)[$^&]	9.36(2.72)[$^&]	17.56(5.01)[*!#^&]	38.10(12.72)[*!#$]	28.64(10.59)[*!#$]
PI in ML for SOT	5.09(2.28)[$^&]	5.27(2.45)[^&]	5.44(2.37)[^&]	8.86(4.04)[*]	11.22(2.09)[*!#]	11.41(2.44)[*!#]
Step Length for LSOT (m)	0.58(0.05)[!^&]	0.49(0.07)[*$]	0.53(0.07)	0.53(0.05)[!^]	0.47(0.05)[*^]	0.46(0.04)[*]
Step Width for LSOT (m)	0.19(0.07)	0.22(0.06)	0.24(0.03)	0.24(0.04)	0.28(0.06)	0.28(0.07)
Step Length Variability for LSOT	2.96(0.87)[!$^&]	4.59(0.89)[*#^&]	2.23(0.48)[!$^&]	5.78(1.12)[*#]	7.92(2.02)[*!#]	6.36(0.69)[*!#]
Step width Variability for LSOT	15.6(2.69)[!#$^&]	27.21(8.79)[*]	24.47(5.51)[*]	25.23(5.63)[*]	31.29(5.74)[*]	30.07(7.55)[*]
netCOP sway variability for LSOT	5.30(0.67)[!#$^&]	13.13(3.74)[*^]	9.21(2.47)[*^&]	10.63(1.99)[*^&]	20.99(6.31)[*!#$]	15.78(5.04)[*#$]

1. *: significant difference exhibited when compared to condition 1.
2. !: significant difference exhibited when compared to condition 2.
3. #: significant difference exhibited when compared to condition 3.
4. $: significant difference exhibited when compared to condition 4.
5. ^: significant difference exhibited when compared to condition 5.
6. &: significant difference exhibited when compared to condition 6.

Figure 2-1. The SMART balance Master (NeuroCom International Clackamas, OR, USA) is used to perform the Sensory Organization Test (SOT). This test contains six conditions: 1) eyes open with fixed surface and fixed visual surrounding; 2) eyes closed with fixed surface; 3) eyes open with fixed surface and sway-referenced visual surroundings; 4) eyes open with sway-referenced surface and fixed visual surroundings; 5) eyes closed with sway-referenced surface; 6) eye open with sway-referenced surface and visual surroundings.

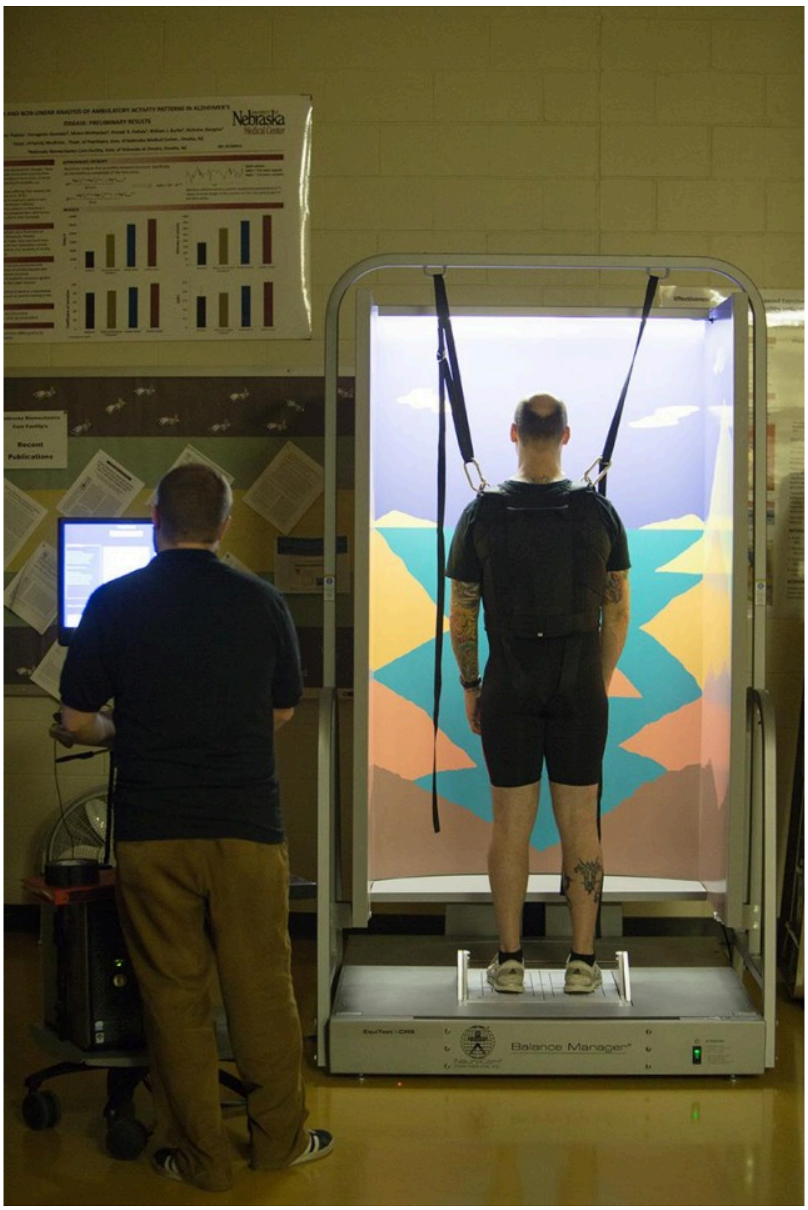


Figure 2-2. The components of Locomotor Sensory Organization Test (LSOT): virtual reality and the instrumented treadmill.

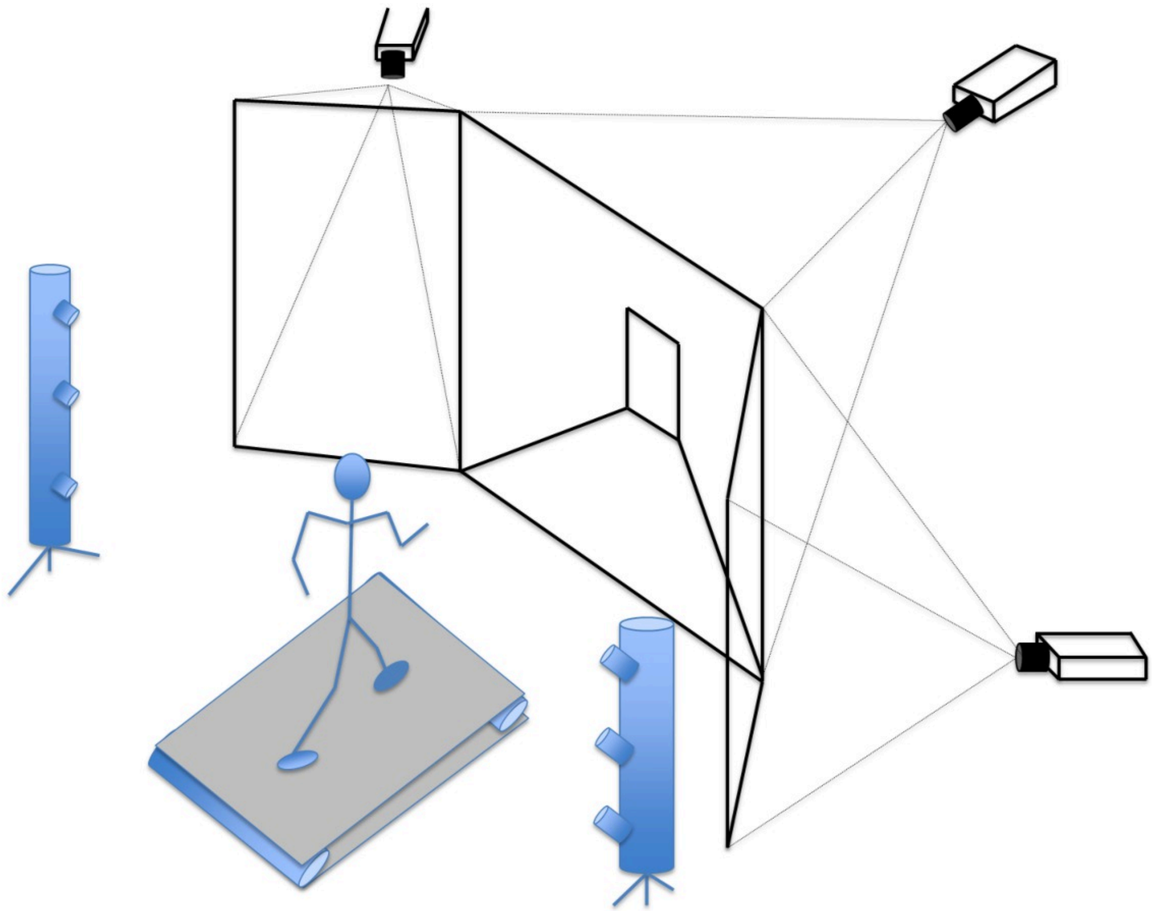


Figure 2-3. The six conditions of Locomotor Sensory Organization Test (LSOT) that mirrors those of the SOT: 1) normal walking condition 2) Reduced visual condition by reducing vision capability condition 3) Perturbed visual condition by manipulating optic flow speed condition 4) Perturbed somatosensory condition by manipulating treadmill speed condition 5) Perturbed visual and somatosensory condition by reducing vision capability and manipulating treadmill speed condition and 6) Perturbed visual and somatosensory condition by manipulating optic flow and treadmill speed condition.

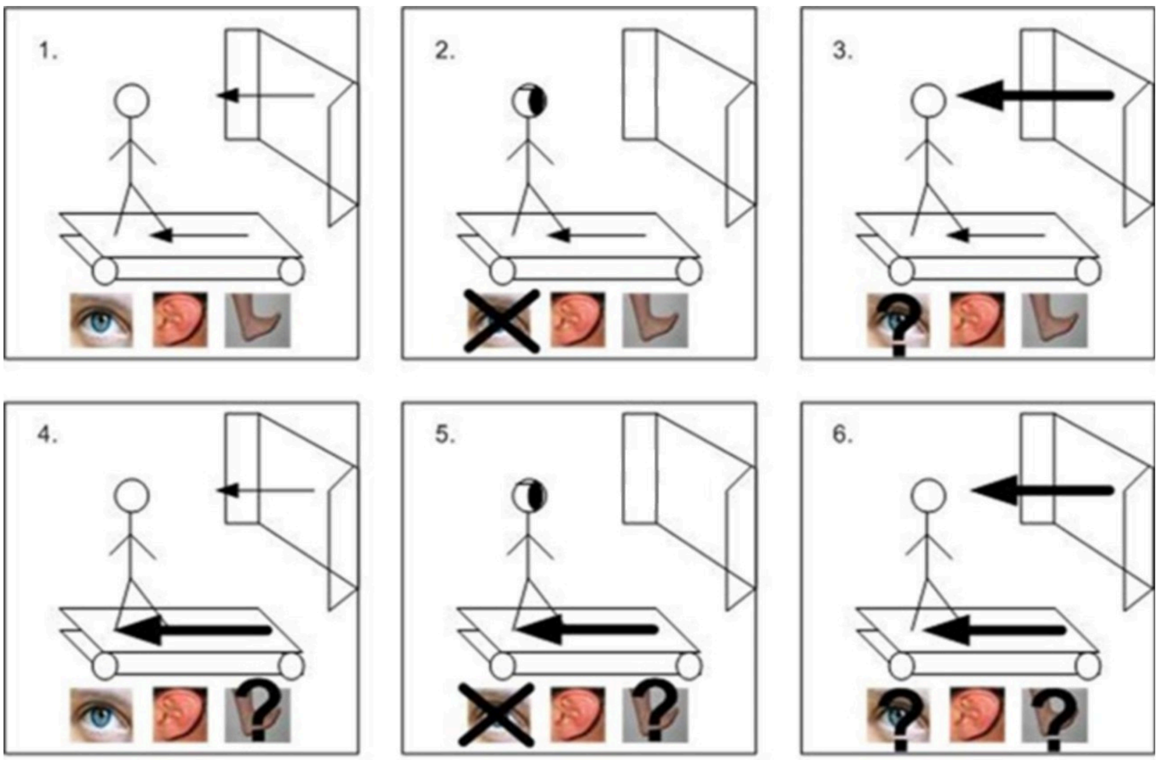


Figure 2-4. The netCOP sway area was composed by two-triangle areas that are represented as the areas with dashed lines. Five points was used to generate these two-triangle areas as following: intersection point, right heel-strike, right toe-off, left heel-strike, left toe-off.

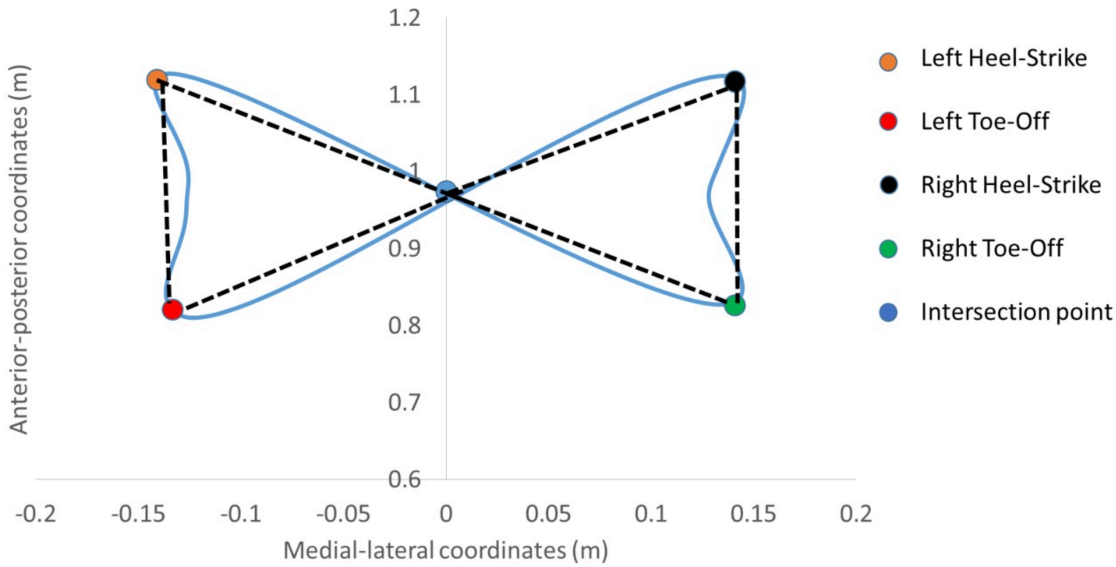


Figure 2-5. Representative trials from a single subject from the six SOT conditions -- the COP sway in the six conditions for the SOT during standing.

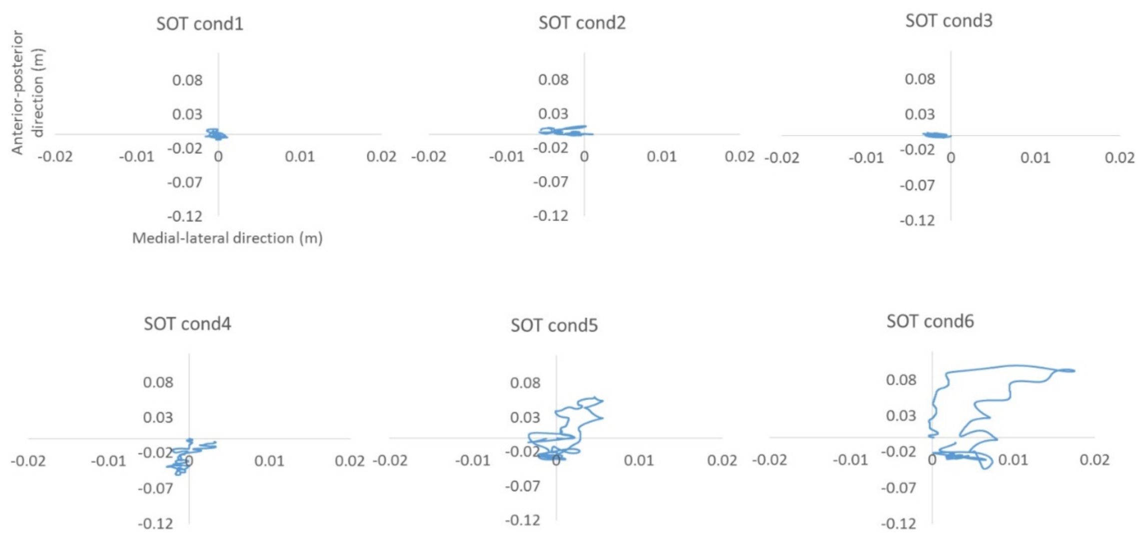
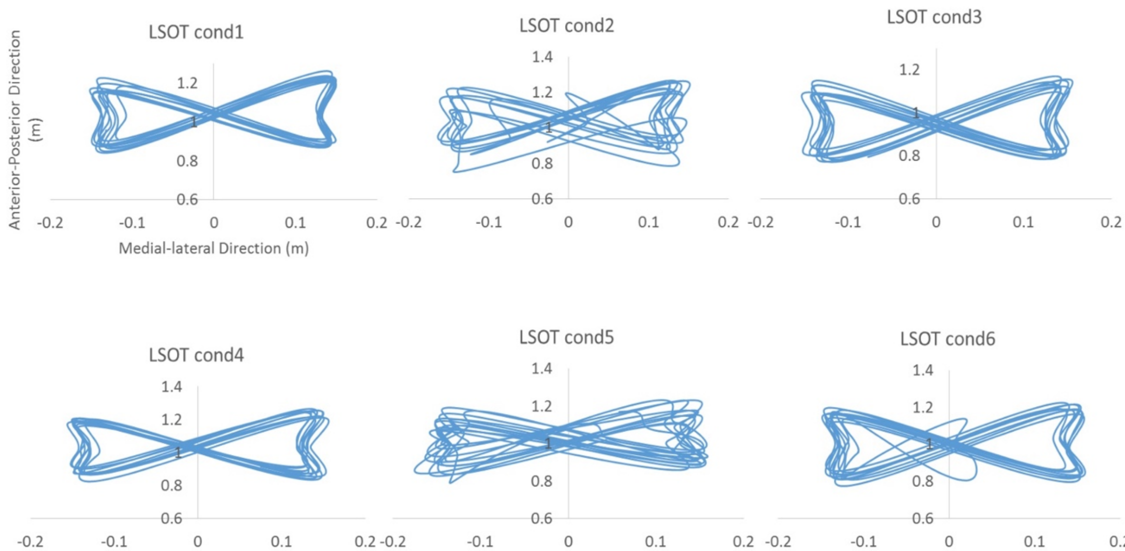


Figure 2-6. Representative trials from a single subject from the six LSOT conditions -- the netCOP sway in the six conditions for the LSOT during walking.



CHAPTER 3

Locomotor sensory organization test: how sensory conflict affects the temporal structure of sway variability during gait

Chien JH, Mukherjee M, Siu KC, Stergiou N. Locomotor sensory organization test: how sensory conflict affects the temporal structure of sway variability during gait. Ann Biomed Eng (IN PRESS).

ABSTRACT

When maintaining postural stability temporally under increased sensory conflict, a more rigid response is used where the available degrees of freedom are essentially frozen. The current study investigated if such a strategy is also utilized during more dynamic situations of postural control as is the case with walking. This study attempted to answer this question by using the Locomotor Sensory Organization Test (LSOT). This apparatus incorporates SOT inspired perturbations of the visual and the somatosensory system. Ten healthy young adults performed the six conditions of the traditional SOT and the corresponding six conditions on the LSOT. The temporal structure of sway variability was evaluated from all conditions. The results showed that in the anterior posterior direction somatosensory input is crucial for postural control for both walking and standing; visual input also had an effect but was not as prominent as the somatosensory input. In the medial lateral direction and with respect to walking, visual input has a much larger effect than somatosensory input. This is possibly due to the added contributions by peripheral vision during walking; in standing such contributions may not be as significant for postural control. In sum, as sensory conflict increases more rigid and regular sway patterns are found during standing confirming the previous results presented in the literature, however the opposite was the case with walking where more exploratory and adaptive movement patterns are present.

INTRODUCTION

Successfully maintaining postural control during standing and walking requires integration of three major sensory systems: visual, vestibular and somatosensory systems[11]. It has been suggested that each sensory system monitors postural changes through independent sensorimotor pathways. The central nervous system (CNS) responds by implementing the appropriate corrective muscle synergies based on the integrated input from these three sensory systems[14]. If only one sensory system is intact, the CNS determines the response completely based on that particular sensory system; and if two or more sensory systems are intact, the CNS evaluates all signals from the available sensory systems and makes adequate responses[14]. Based on this theoretical framework when conditions of reduced perceptual accuracy exist, the CNS recalibrates by reducing inaccurate sensory gains and increasing the functional gain of accurate sensory modalities. During this recalibration process, humans demonstrate difficulties to maintain balance and alter postural control, such as increasing body sway without vision in standing[14]. Successful recalibration leads to functional adaptation to the perceived environmental perturbation, as observed for example in the shortening of the stride length on a slippery ground in locomotion[14].

In order to quantify the adaptive mechanisms involved in the control of standing posture during sensory conflict, the Sensory Organization Test (SOT) has been widely used in patients with vestibular disorder[17,19], concussion[22], stroke[23], and Parkinson's Disease[24], among others. The design of the SOT is intended to challenge postural control through manipulations of the sensory input. It can manipulate somatosensory and visual inputs individually or in combination to allow assessment of a patient's ability for maintaining balance. The SOT has allowed scientists to investigate amount of sway variability under these conditions and make inferences about sensory contributions to postural control. In summary these studies found that the amount of sway variability increased as postural control was challenged by manipulating sensory inputs in the SOT[51]. These increases have been interpreted as increased noise in the system that could lead to instability[51].

To further explore this interpretation, researchers have recently shown interest in the temporal structure of sway variability or in other words how sway variability changes over time while performing the SOT[8-9, 52]. This work, which encompasses several different areas including brain function and disease dynamics, has shown that many apparently “noisy” phenomena are the result of nonlinear interactions and have deterministic origins[53-55]. As such, the measured signal, including its “noisy” component, may provide important information regarding the function of the system that produced it. Therefore, new innovative clinical methods that use nonlinear mathematical analysis and investigate the temporal structure of variability have been proposed. These nonlinear methods are being used increasingly to describe complex conditions. For example, nonlinear analysis of the temporal structure of the variability has recently been used to study heart rate irregularities, sudden cardiac death syndrome, blood pressure control, brain ischemia, epileptic seizures, and several other conditions[53, 56-61]. Such research has allowed for a better understanding of the complexity of these pathologies and eventually led to the development of better prognostic and diagnostic tools in other areas (i.e. cardiology, neurology). Thus, it is fair to assume that nonlinear analysis of the sway variability could allow insight into the complex strategies used to control movement and posture informing clinical practice with respect to movement related disorders.

Such an assumption led investigators to explore the temporal structure of sway variability while performing the SOT[9-12]. Riley at al. (2003) used recurrence quantification analysis to investigate the temporal structure of sway variability[52]. They found that the temporal structure of postural sway tended to become increasingly regular as the SOT condition increased in difficulty (i.e. as the SOT condition moved from eyes open to eyes closed, to sway-referenced visual surround or support surface, and to sway-reference surface and visual surround). Entropy analysis has also been shown to detect changes in postural control dynamics and results have highlighted the role of such analysis to evaluate postural stability with the SOT condition[22, 8-10]. Specifically, an overall decrease in entropy values (i.e. more regular sway patterns) with the SOT condition was found even though these studies were not focused on the SOT condition per se but on the effects of vibrating the Achilles tendon[10, 62]. Similar results were found with entropy values decreasing as the SOT condition increased in difficulty indicating more regular sway patterns[8-9, 22]. Therefore, from all the above mentioned studies it can be concluded that sensory manipulation through the SOT condition leads to a more regular and repeatable sway movement pattern.

This strategy could be interpreted as an effort to temporally maintain postural stability under increased sensory conflict. A more rigid (i.e. more regular and repeatable) response has been considered as a freeze of the available degrees of freedom, a phenomenon that is also observed when dealing with novel situations and learning the new skill[67]. Will such a strategy be also utilized during more dynamic situations of postural control as in the case with walking? Here this study attempted to answer this question by using an experimental apparatus that combines a treadmill, instrumented with force platform technology, and virtual reality; the Locomotor Sensory Organization Test[1]. This study hypothesized that a more rigid response will also characterize dynamic postural control during walking on our apparatus that incorporates SOT inspired perturbations of the visual and the somatosensory system.

METHODS

Subjects

Ten healthy young adults (five males and five females; age 27.20±4.92 years, height 171.30±7.01 cm and weight, 64.70±9.90 kg) participated in this study. Subjects were free from any musculoskeletal impairment, had no history of significant lower extremity injuries, which may have affected their posture or gait, and had no visual, somatosensory or vestibular deficits. We excluded individuals without normal or corrected to normal vision, scored above zero on the dizziness handicap inventory for a vestibular deficit[33] and with any type of peripheral neuropathy that can affect somatosensory function. Prior to the experiment, each subject signed an informed consent approved by our University's Medical Center Institutional Review Board.

Protocol

The experiment entailed exposing subjects to sensory perturbations in the SOT and LSOT environments. The SOT was conducted in a quiet room using the Balance Master System 8.4 (NeuroCom International Clackamas, OR, USA). The system contains a moveable visual surround and support surface that rotate in the anterior-posterior (AP) plane. Two 22.9 x 45.7 cm force plates connected by a pin joint are used to collect center of pressure data at 100 Hz. Foot placement is standardized based on subjects' height according to manufacturer guidelines. While standing in the Balance Master system, subjects wore a vest attached to the safety harness of the system (Figure 3-1).

The Locomotor Sensory Organization Test (LSOT) consisted of two components: a virtual reality environment, and an instrumented treadmill (Bertec Corp., Columbus, OH, USA) (Figure 3-2)[1]. The LSOT contained six conditions similar to the Sensory Organization Test to manipulate the sensory information during walking (Figure 3-3)[11]. Prior to the data collection, each subject walked for five minutes on the treadmill to determine their preferred walking speed (PWS). After the PWS was determined, all subjects walked on the treadmill with the PWS for two minutes in each of the six conditions of the LSOT test. The LSOT conditions from 1 to 3 required the subject to walk on the treadmill set to the Preferred Walking Speed (PWS). This was done with matching optic flow in condition LSOT 1 (none of the sensory systems was challenged as in SOT 1), vision reduced in condition LSOT 2 (visual blocked as in SOT 2), and eyes open but random optic flow in condition LSOT 3 (visual perturbation matched to SOT 3). The visual perturbation was created by varying the optic flow between 80% and 120% of PWS in randomly assigned time intervals of 1 to 10 seconds. The LSOT conditions 4-6 all had random perturbation of the treadmill speed. The random treadmill perturbations was created by varying the treadmill speed between 80% and 120% of PWS in randomly assigned time intervals of 1 to 10 seconds. This was done with optic flow matched to PWS in condition LSOT 4 (somatosensory perturbation as in SOT 4), vision reduced in condition LSOT 5 (visual blocked and somatosensory perturbation as in SOT 5) and finally, eyes open with matching random optic flow condition LSOT 6 (simultaneous visual and somatosensory perturbation as in SOT 6). In between conditions, the subjects were allowed to rest for one minute with closed eyes.

Data Reduction

For the SOT, we investigated the temporal structure of sway variability using the COP trajectory in the AP and the medial-lateral (ML) direction. In addition, we only selected the first trial of each SOT condition to reduce the effect of condition adaptation. A similar approach has been used in previous studies[8-9], [64]. For the LSOT, we investigated the temporal structure of sway variability using the netCOP trajectory in the AP and the ML direction. This measure allows for a direct comparison of the COP measures between standing and locomotion. The netCOP is the point where the total sum of a pressure field acts on a body during walking. The total force vector acting at the netCOP is the value of the integrated vector pressure field[43]. The netCOP as is the case with the COP, provides with a net representation of the movement generated by the entire body and all available degrees of freedom[65]. Before calculating the temporal structure of the variability present in the COP and netCOP data, the original data was down sampled from 100Hz to 10Hz to reduce the irrelevant noise present in the data since there was no physiological signal above 10 Hz in the COP data of both tasks[66].

Sample Entropy (SampEn): For all the COP and netCOP time series, the SampEn values were calculated using a customized script in MatLab R2011a (Mathworks, Natick, MA). The SampEn algorithm is defined as the negative natural logarithm for conditional properties that a series of data points a certain distance apart, m, would repeat itself at m + 1. SampEn takes the logarithm of the sum of conditional probabilities. Given the time series g(n) = g(1), g(2), …, g(N), where N is the total number of data points, a sequence of m-length vectors is formed. Vectors are considered alike if the tail and head of the vector are within the set tolerance level. The sum of the total number of like vectors is divided by m+1 and defined as A or by N-m+1 and defined as B. SampEn is then calculated as –ln(A/B). A perfectly repeatable time series has a SampEn value ~0 and a perfectly random time series has a SampEn value converging toward infinity. In the current study, the following parameters were selected and used in the determination of SampEn values in SOT and LSOT: (a) a pattern length (m) of 2, (b) and error tolerance (r) of 0.2[67]. The time series length in the SOT trials was 200 data points. The time series length in the LSOT trials was 1200 data points. These data lengths should be sufficient according to the literature[67].

Four one-way repeated measure ANOVAs were performed using SPSS (18.0, IBM Corporation, Somers, NY) to determine condition effects of the LSOT and SOT. Specifically, the dependent measures were: the SampEn calculated from the COP data for the SOT in the (1) AP and in the (2) ML direction, and the SampEn calculated from the netCOP data for the LSOT in the (3) AP and in the (4) ML direction. Pairwise comparisons were performed to determine specific differences between conditions using Bonferroni adjustments. The adjusted significance level for the pairwise comparisons was 0.0083.

RESULTS

Anterior-posterior SampEn values in the SOT

The one-way repeated ANOVA revealed a significant condition effect ($F = 17.79$, $p < 0.001$) (Table 3-1; Figure 3-4A). The post-hoc pairwise comparisons revealed numerous significant differences between conditions. The first three conditions had all significantly larger values than the last three, however, there were no differences between them. The last three conditions had also no differences between them. The largest group mean value was present in condition 1, while the smallest group mean value was present in condition 5 (eyes closed with sway-referenced surface), followed by condition 6 (eyes open with sway-referenced surface and visual surroundings).

Anterior-posterior SampEn values in the LSOT

The one-way repeated ANOVA revealed a significant condition effect ($F = 292.96$, $p < 0.001$) (Table 3-1; Figure 3-4B). The post-hoc pairwise comparisons revealed that all possible comparisons between conditions were significant. The smallest group mean value was present in condition 3 (variable optic flow), followed by condition 1. The largest group mean value was present in condition 5 (reduced visual information, variable treadmill velocity), followed by condition 6 (variable optic flow and variable treadmill velocity).

Medial-lateral SampEn values in the SOT

The one-way repeated ANOVA revealed a significant condition effect ($F = 19.49$, $p < 0.001$) (Figure 3-5A). The post-hoc pairwise comparisons revealed numerous significant differences between conditions. Conditions 1 and 2 had significantly larger values than conditions 4, 5 and 6. Conditions 3 and 4 had also significantly larger values than condition 6. In general, the group mean values decreased from condition 1 to condition 6 with the smallest group mean value be present in condition 6 (eyes open with sway-referenced surface and visual surroundings), followed by condition 5 (eyes closed with sway-referenced surface). However, there was no significant difference between conditions 5 and 6.

Medial-lateral SampEn values in the LSOT

The one-way repeated ANOVA revealed a significant condition effect ($F = 14.03$, $p < 0.001$) (Figure 3-5B). The post-hoc pairwise comparisons revealed several significant differences between conditions. The group mean value for condition 1 was significantly smaller than condition 2 (reduced visual information) and condition 5 (reduced visual information, variable treadmill velocity). Condition 2 (reduced visual information) had a significantly larger value than conditions 3 (variable optic flow) and 4 (variable treadmill speed).

DISCUSSION

This current study investigated how increased sensory conflict affects the temporal structure of sway variability during standing and walking. Based on previous studies that have used the SOT and found a more rigid (i.e. more regular and repeatable) response during standing posture in conditions with increased sensory conflict, we hypothesized that a more rigid response will also characterize dynamic postural control during walking in such conditions. To test this hypothesis an apparatus that uses SOT inspired perturbations of the visual and the somatosensory system[11] was used. The apparatus combined a treadmill, instrumented with force platform technology, and virtual reality, to create the Locomotor Sensory Organization Test (LSOT)[11]. The results verified the findings presented in the literature regarding the SOT and revealed a more rigid (i.e. more regular and repeatable) response during standing posture in conditions with increased sensory conflict. They also revealed that the LSOT was successful in producing significant differences between conditions with increased sensory conflict during walking. However, the results did not support our hypothesis as we found a less rigid and more irregular response for dynamic postural control during walking with increased sensory conflict.

As mentioned above, the SOT results were in agreement with the literature. The entropy values decreased as the SOT conditions increased in difficulty indicating more regular sway patterns[8-10]. One notable difference is that in previous studies that have used the SOT, a different entropy algorithm was utilized, the Approximate Entropy. However, this algorithm has been found to exhibit certain limitations while Sample Entropy was identified as more reliable for short data sets[67]. For this reason, the Sample Entropy algorithm was used and to the best of our knowledge, our study is the first study to perform such an analysis with SOT derived data sets. The only direct comparison that could possibly attempt to make is with two studies that have used the Sample Entropy algorithm in investigating questions related with postural control[68-69]. In these two studies healthy subjects stood on a solid surface with either eyes open or closed. The results of the study by Rigoldi and colleagues were comparable to the present study (referring to the first two SOT conditions) in terms of the AP direction but not the ML direction where our values were smaller[69]. The differences in the ML direction could be due to the fact that the SOT test is performed mainly in the AP direction - both visual surround and sway reference are manipulated in the AP direction. The results of the study by Ramdani and colleagues were much larger than the present study but these values may be influenced by the fact that we used different m and r parameters (ours were 2 and 0.2, while Ramdani et al had 3 and 0.3)[68]. No values on these parameters were reported in the Rigoldi et al study. In sum, we feel confident about the values of our results at least with respect to the SOT test, since no such comparisons could be made for the LSOT due to lack of related literature.

How is dynamic postural control affected in the AP direction? In our previous work using the LSOT to explore amount of sway variability during locomotion, we found that the contribution of visual input was significantly increased during locomotion compared to standing in similar sensory conflict conditions[11]. Thus, it is not surprising that in this study we found that manipulating vision would also alter the temporal structure of sway variability during locomotion. However, the interesting result was that two different kinds of visual manipulation (reduced vision as in condition 2 and perturbed vision as in condition 3) produced completely opposite results. Reduced vision resulted in a significantly more irregular response, while perturbed vision produced a significantly more regular response. It is possible that reduced vision resulted in more uncertainty and larger need to explore the available stepping space leading to more irregular movement patterns. This deduction is supported by Perry et al. (2001) who found that when visual information was occluded using special glasses[70], the COM moved closer to the base of support during double support along with more variability in the COM movement, as the subjects were attempting to achieve a final stable position. Further support is provided by our previous findings using the LSOT[11] where amount of variability for step length, step width, and netCOP increased significantly when vision was reduced. However, in the perturbed vision condition, where we observed a more regular response, the visual input was in conflict with the treadmill moving at PWS resulting in a freeze of the available degrees of freedom as the subjects were learning to walk in a visually unreliable and an unfamiliar condition[71]. Additional support is provided by our previous study[11] where we found that step length variability decreased in the visual conflict condition and increased in the vision reduced condition. However, in the perturbed vision condition, where we observed a more regular response, the visual input was in conflict with the treadmill moving at PWS resulting in a freeze of the available degrees of freedom as the subjects were learning to walk in a visually unreliable and an unfamiliar condition. Such an interpretation is supported by Katsavelis et al. (2010) where was found that optic flow manipulation resulted in decreases in measures of the temporal structure of gait variability as compared to normal unperturbed walking[72]. Further support is provided by our previous LSOT study[11] where we found that step length variability decreased while the increase in netCOP variability was relatively smaller, in comparison with condition 1 of the LSOT.

Beyond the differential effect of visual manipulation on our results, another interesting result from the present study is that altering only the somatosensory input (as in condition 4) produced a larger effect on the temporal structure of sway variability while walking than only reducing the visual input (as in condition 2). This was not expected, as results for the amount of variability in our previous study were different[11]. Importantly when perturbed somatosensory input was added to reduced visual input (as in condition 5), an almost linear additive effect was produced on the temporal structure of sway variability. There was also a large effect when perturbed somatosensory input was added to the perturbed visual input (as in condition 6) reversing the decreasing effect observed in condition 3. These results suggest that somatosensory input has a very prominent effect on the temporal structure of sway variability and is even more influential than visual input. It is possible that visual input has a larger effect on amount of variability during locomotion as observed in previous work[11], but somatosensory input may play a bigger role when dealing with the temporal structure of variability in the anterior posterior direction. This interpretation is supported by Clark et al. (2014) that found that altered somatosensation can affect prefrontal activity during walking[73]. Moreover, investigations of kinesthetic distance perception have shown that perception of distance traveled while blindfolded depends upon the way in which the legs are coordinated[76].

The results for dynamic postural control in the AP were not replicated for the ML direction. Interestingly, the only condition that produced significant effects was the reduced visual input (condition 2). Neither perturbed visual (condition 3) nor perturbed somatosensory input (condition 4) had a significant effect and even when these two conditions were combined (as in condition 6), we did not observe any significant results. These results suggest that in the ML direction, control as evaluated through the temporal structure of variability mostly depends on contributions from peripheral vision since it is the reduced visual condition that actually had an effect and not the perturbed vision condition. This interpretation is supported by Graci et al. (2009; 2010) who found that proprioceptive information as provided by the peripheral visual field is used online to fine tune adaptive gait[71,75]. Importantly, these results demonstrate that sensory inputs have directionally dependent contributions.

There are certain interesting observations when comparing SOT and LSOT results. First, in the AP direction during standing, significant differences occurred as soon as the perturbed somatosensory condition was introduced (SOT condition 4). Before this condition and in conditions 2 and 3, there were no effects. Something similar was observed with walking where we found a strong somatosensory effect as described above. In walking we also have a secondary result, which is the differential effect of reduced vision versus perturbed vision. In the medial lateral direction, we again have a significant effect of the somatosensory input in the SOT results which is similar with the anterior posterior results. However, this is not the case during walking where we found reduced vision to be the most significant sensory condition. Thus, here we have a true difference between the two tasks in terms of sensory systems contributions as observed through analysis of the temporal structure of sway variability. It also might be due to the attentional demands of balance control vary depending on the complexity of the task[74].

Another important result is that during standing as sensory conflict increases, in general the values decrease while in walking they increase. These results could suggest that while standing with our feet stationary, we do not have many options or solutions for postural control when we are faced with sensory conflict. Being more rigid and freezing the degrees of freedom is what we always do when we are faced with the unknown especially if we have no options. However, while walking we have more options that allow us further exploration and adaptations in order to compensate for increased sensory conflict conditions.

In conclusion, our results allowed us to identify how increased sensory conflict affects the temporal structure of sway variability during standing and walking. In general, we observed that somatosensory input is crucial for the control of the temporal structure of sway variability for both waking and standing in the anterior posterior direction. Visual input also has an effect but is not as prominent as the somatosensory input. It could also have a different effect based on the way it is manipulated. However, in the medial lateral direction reduced visual input has a much larger effect during walking than in standing possibly due to decreased contribution from peripheral visual inputs. Furthermore, and regardless of direction, as sensory conflict increases we observe more rigid and regular sway patterns during standing, while the opposite is the case with walking where we observe more exploratory and adaptive movement patterns. This information could enable more comprehensive decision making processes to be made using the LSOT, possibly in parallel with the SOT that is presently readily available in clinics. Such information could allow us to assist patients with sensory and motor disorders by guiding diagnosis and rehabilitation. The present paper provides the foundation for the establishment of the normative data needed for nonlinear measures and further evidence for adaptation of this technology by the biomedical industry.

Table 3-1. Group means and standard deviations for all conditions for the dependent measures evaluated. Significant differences between conditions are indicated with superscripts.

Conditions	1	2	3	4	5	6
SampEn for SOT in anterior-posterior direction	0.217(0.043)[$%^]	0.185(0.032)[$%^]	0.199(0.058)[$%^]	0.108(0.036)[!@#]	0.094(0.034)[!@#]	0.092(0.045)[!@#]
SampEn for LSOT in anterior-posterior direction	0.259(0.009)[@#$%^]	0.314(0.009)[!#$%^]	0.183(0.016)[!@$%^]	0.346(0.023)[!@#%^]	0.402(0.024)[!@#$^]	0.380(0.018)[!@#$%]
SampEn for SOT in medial-lateral direction	0.096(0.030)[$%^]	0.082(0.012)[$%^]	0.065(0.012)[^]	0.059(0.010)[!@^]	0.057(0.013)[!@]	0.048(0.012)[!@#$]
SampEn for LSOT in medial-lateral direction	0.071(0.006)[@%]	0.105(0.017)[!#$]	0.078(0.012)[@]	0.075(0.009)[@]	0.093(0.016)[!]	0.081(0.016)

7. [!]: significant difference exhibited when compared to condition 1.
8. [@]: significant difference exhibited when compared to condition 2.
9. [#]: significant difference exhibited when compared to condition 3.
10. [$]: significant difference exhibited when compared to condition 4.
11. [%]: significant difference exhibited when compared to condition 5.
12. [^]: significant difference exhibited when compared to condition 6.

Figure 3-1. The SMART balance Master (NeuroCom International Clackamas, OR, USA) is used to perform the Sensory Organization Test (SOT). This test contains six conditions: 1) eyes open with fixed surface and fixed visual surrounding; 2) eyes closed with fixed surface; 3) eyes open with fixed surface and sway-referenced visual surroundings; 4) eyes open with sway-referenced surface and fixed visual surroundings; 5) eyes closed with sway-referenced surface; 6) eye open with sway-referenced surface and visual surroundings.

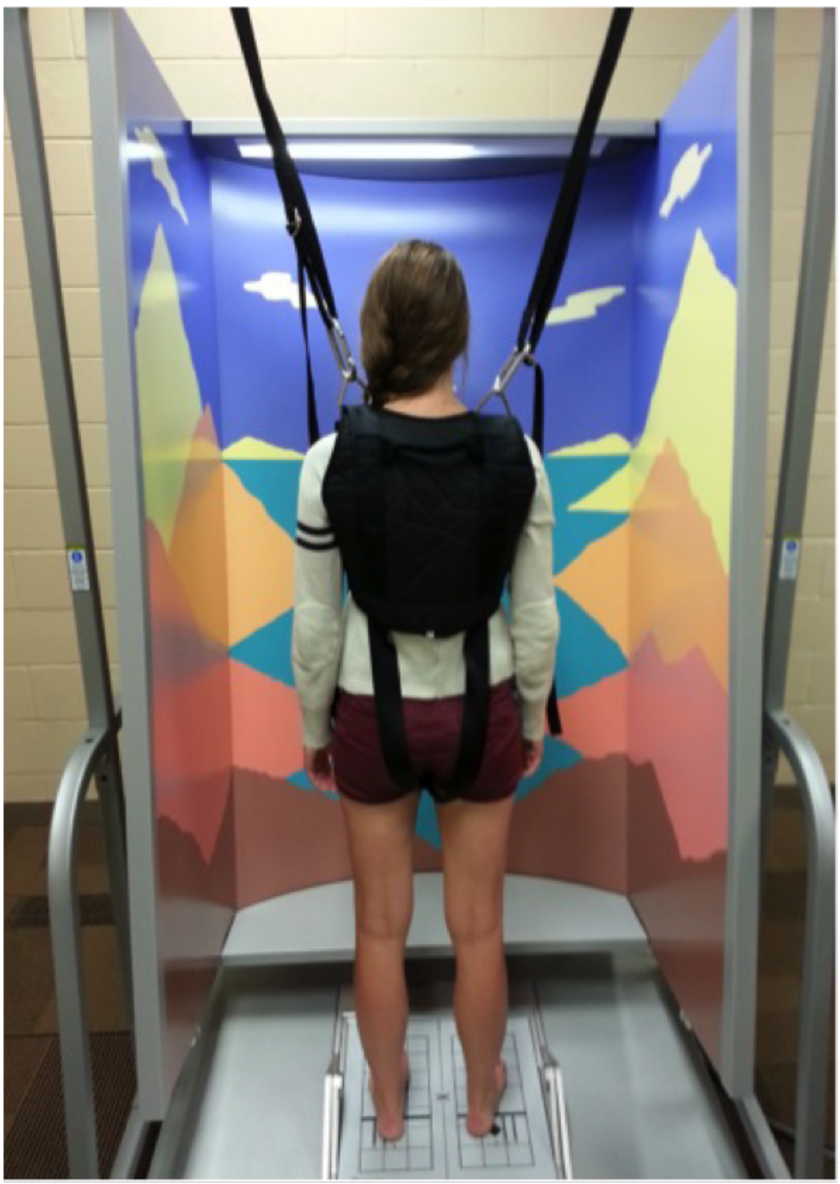


Figure 3-2. The components of Locomotor Sensory Organization Test (LSOT): virtual reality and the instrumented treadmill.

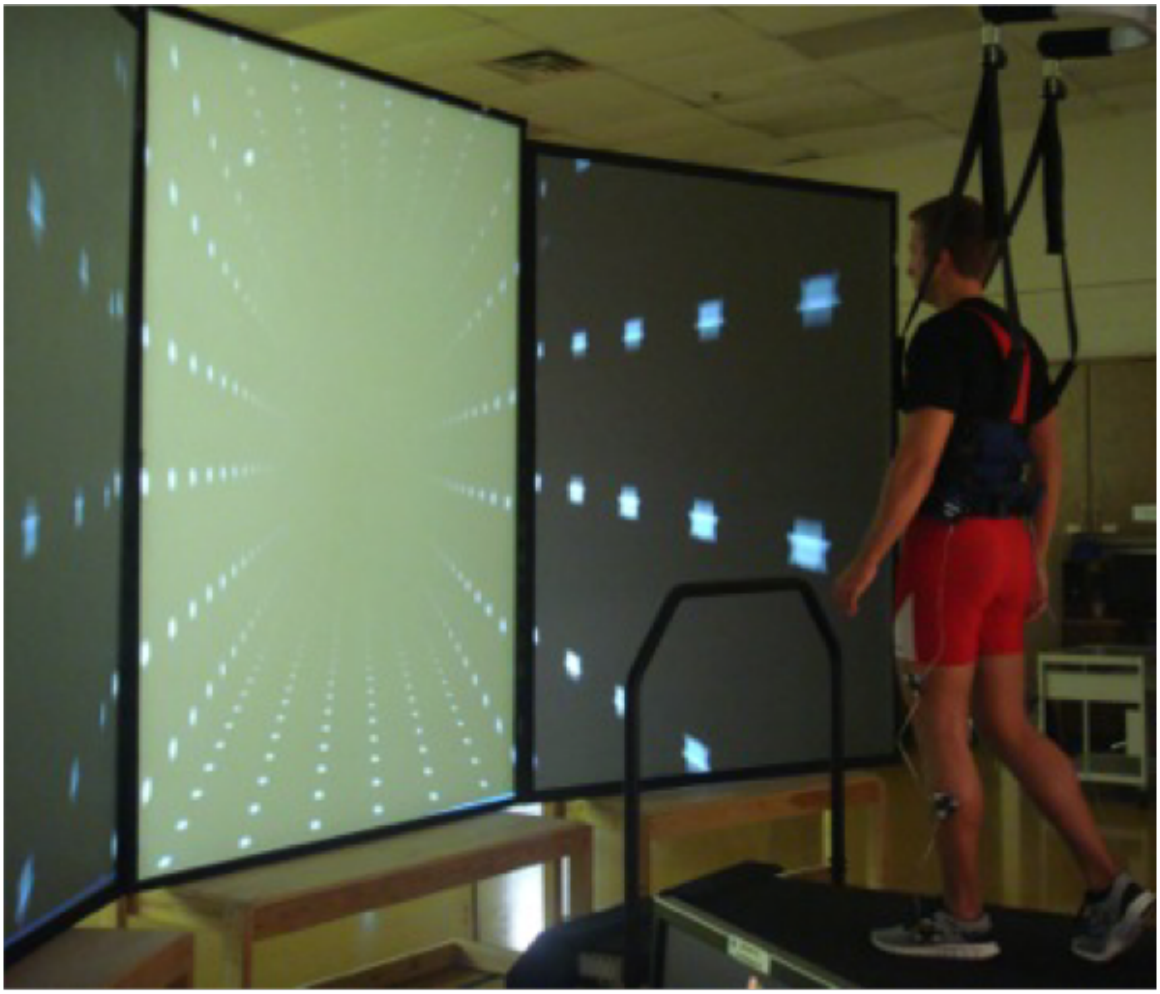


Figure 3-3. The six conditions of Locomotor Sensory Organization Test (LSOT) that mirrors those of the SOT: 1) normal walking condition 2) Reduced visual condition by reducing vision capability condition 3) Perturbed visual condition by manipulating optic flow speed condition 4) Perturbed somatosensory condition by manipulating treadmill speed condition 5) Perturbed visual and somatosensory condition by reducing vision capability and manipulating treadmill speed condition and 6) Perturbed visual and somatosensory condition by manipulating optic flow and treadmill speed condition.

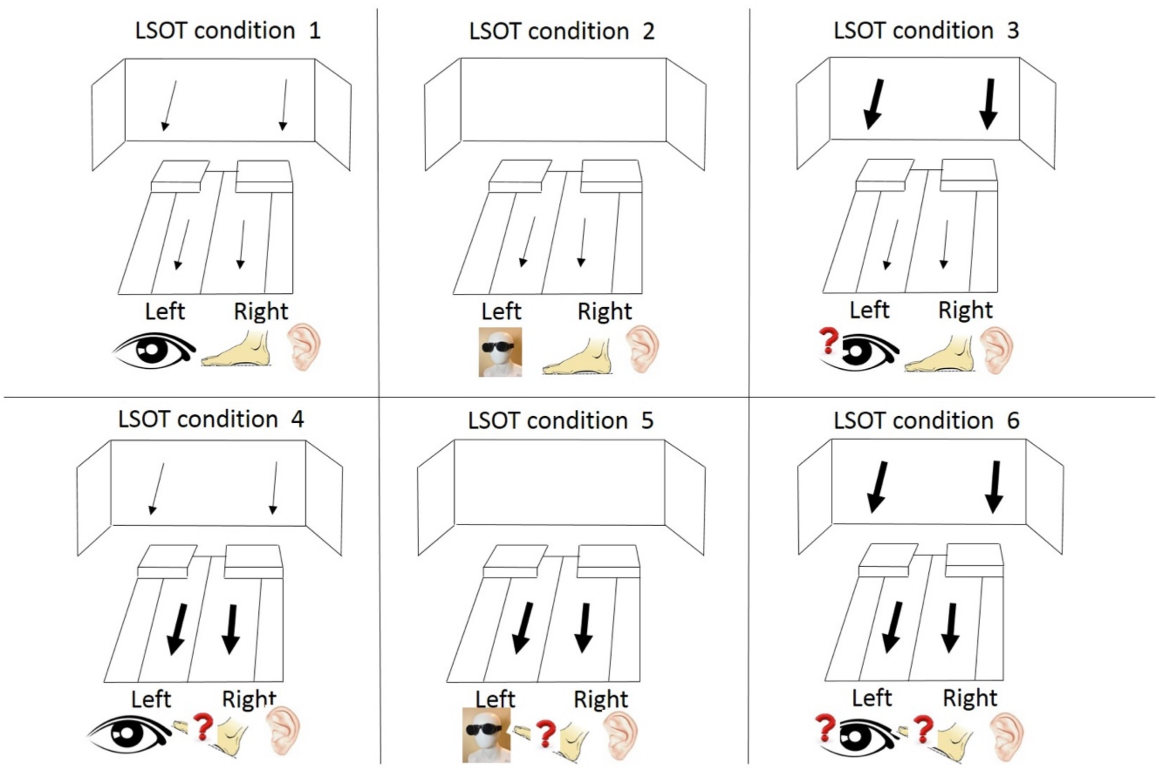
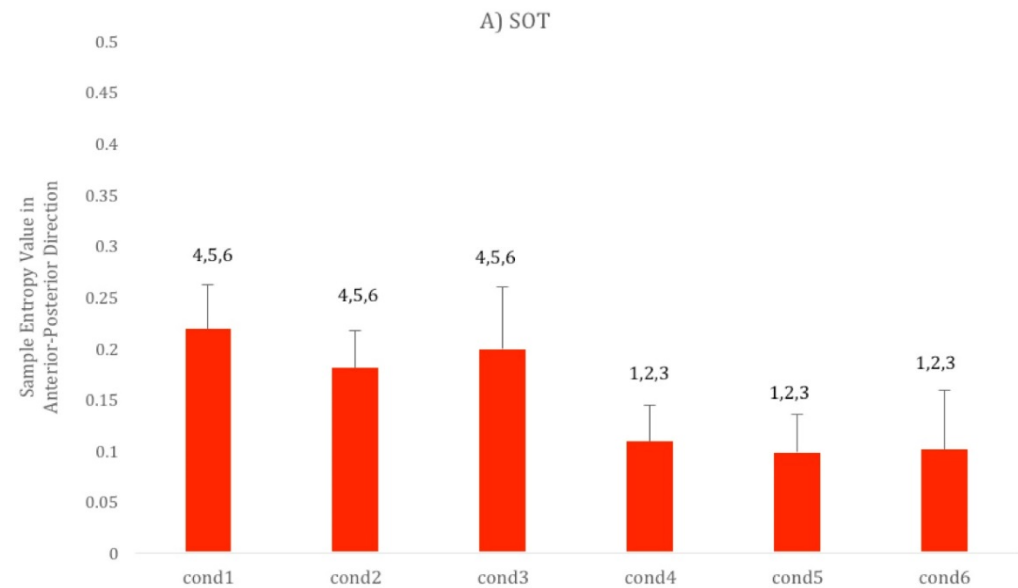


Figure 3-4. Bar chart showing the mean of the Sample Entropy values of all the subjects for the SOT (red; Figure 3-4A) and the LSOT (blue; Figure 3-4B) groups across the six experimental conditions. Error bars are standard deviation. For each condition the *post hoc* differences are indicated over the bars with the number of the condition found to be significantly different with.



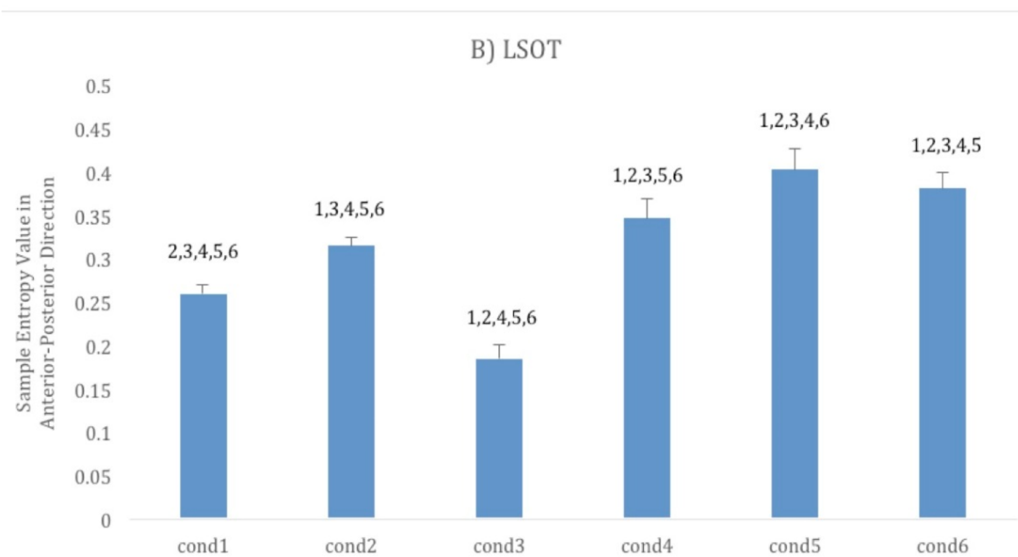
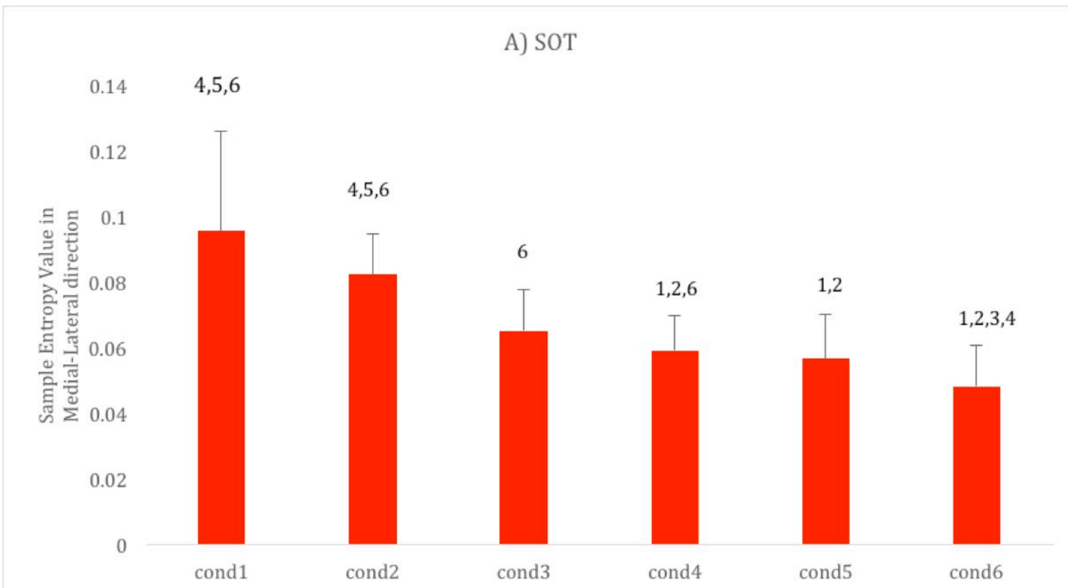
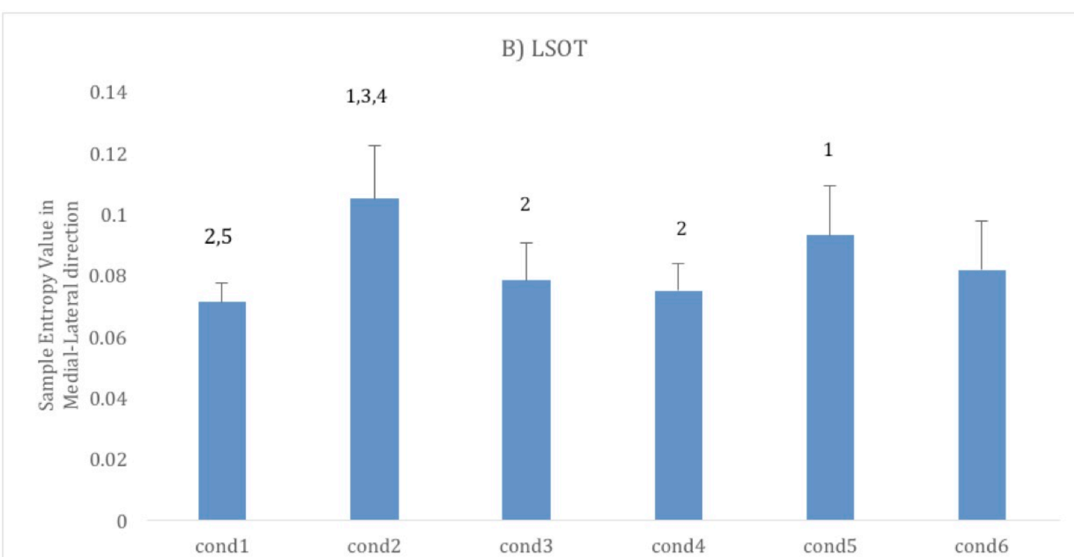


Figure 3-5. Bar chart showing the mean of the Sample Entropy values of all the subjects for the SOT (red; Figure 3-5A) and the LSOT (blue; Figure 3-5B) groups across the six experimental conditions. Error bars are standard deviation. For each condition the *post hoc* differences are indicated over the bars with the number of the condition found to be significantly different with.





CHAPTER 4

Mastoid vibration affects dynamic postural control during gait

Chien JH, Mukherjee M, Stergiou N. Mastoid vibration affects dynamic postural control during gait. Ann Biomed Eng. [Under Review].

ABSTRACT

Our objective was to investigate how manipulating sensory input through mastoid vibration (MV) could affect dynamic postural control during walking, with and without simultaneous manipulation of the visual and the somatosensory systems. We used three levels of MV (none, unilateral, and bilateral) via vibrating elements placed on the mastoid processes. We combined this with the six conditions of the Locomotor Sensory Organization Test (LSOT) paradigm to challenge the visual and somatosensory systems. We hypothesized that MV would affect both amount and temporal structure measures of sway variability during walking and that, in combination with manipulations of the visual and the somatosensory inputs, MV would augment the effects previously observed. The results confirmed that MV produced a significant increase in the amount of sway variability in both anterior-posterior and medial-lateral directions. Significant changes in the temporal structure of sway variability were only observed in the anterior-posterior direction. Bilateral MV produced larger effects than unilateral stimulation. We concluded that sensory input while walking could be affected through MV and such changes are in the direction of motion. Combining MV with manipulations of visual and somatosensory input could allow us to better understand sensory system contributions during locomotion.

INTRODUCTION

Recent epidemiological evidence estimates that approximately 30% of adults above the age of 40 (approximately 69 million Americans) might experience some form of vestibular dysfunction[1]. Such dysfunction could eventually lead to chronic dizziness and imbalance that can have significant impact on activities of daily life such as walking[77]. To reduce the economic and societal burden it is important to be able to diagnose vestibular problems and treat them appropriately. However, our knowledge of how the vestibular system affects balance and postural control during walking is limited.

Few studies have investigated how patients with vestibular disorders maintain balance during walking[78-80]. The limited research has revealed that patients with a bilateral vestibular disorder were able to walk successfully blindfolded over a short distance without any lateral deviation, even though these patients were much slower than controls. However, blindfolded patients with a unilateral vestibular disorder walked with significant lateral deviations in the direction of the lesion. These findings suggest that the contribution of the vestibular system to postural control during walking could be of great importance.

To avoid unnecessary exposure of patients with vestibular disorders to untested methodological procedures, several investigators have instead tested healthy individuals that were subjected to caloric and galvanic stimulation to study the role of the vestibular system in postural control during gait. The caloric method tests the function of the vestibular system using air or water irrigation on the external ear canals[80]. With caloric vestibular stimulation, subjects showed increased lateral deviation at the hip but not at the foot, neck or head during treadmill walking with eyes open[81]. In galvanic vestibular stimulation a small amount of galvanic current is applied to the mastoid process to modulate the continuous firing level of the peripheral vestibular afferents[82]. This causes participants to lean in different directions during walking depending upon the polarity of the current. The effect of galvanic vestibular stimulation depends on the walking speed[83], however, such that when walking speed increases, the effect is attenuated and the lateral deviation diminishes. Importantly, both galvanic vestibular stimulation and caloric irrigation induce discomfort[84-85]. Therefore, the usability of these approaches to study the true effects of the vestibular system on balance and postural control during walking is questionable as anxiety due to discomfort may compromise subject responses.

To overcome the limitations with these techniques, scientists have employed vibration stimulation as an alternative method of vestibular manipulation. Specifically, Karlberg et al. (2003) showed that abnormal eye movements (nystagmus) induced by mastoid vibration (MV) are similar to those observed in patients with acute unilateral vestibular deficit[86]. Further, vibrating the neck muscles can cause significantly more nystagmus in patients with unilateral vestibular lesion[86]. This suggests that the vestibular system is sensitive and responsive to MV[87]. Moreover, MV is considerably more comfortable than the caloric test[87]. For these reasons, MV presents a viable alternative method for the investigation of the effects of the vestibular system on postural control.

Research has shown that MV induces dizziness or unsteadiness and further influences postural control by affecting the body-centered coordination system[88-90]. Furthermore, in a previous study during which healthy subjects underwent PET assessments whilst receiving MV, it was found that the areas of the perisylvian cortex, temporoparietal junction and somatosensory area II were the common activation regions. These areas are those involved for vestibular and neck muscle representations of body orientation in space[91]. MV was also found to affect body orientation in healthy controls but not in patients with cervical dystonia during stepping-in-place[92]. This study confirmed that neck sensation is crucial for combining the information from the vestibular system and the neck muscle spindles for controlling posture. Vestibular input cannot identify if the head or the entire body is progressing especially when the head is moving over a stationary torso. Thus, input from the neck muscles is fundamental in informing the nervous system regarding movements of the head with respect to the torso and the head yaw rotation[93].

Current clinical testing using the Sensory Organization Test (SOT) manipulates only the visual and somatosensory inputs to study their effects on postural control during standing; the vestibular system is not manipulated. Recently, our group has developed the Locomotor Sensory Organization Test (LSOT)[11-12] as a parallel to the SOT. The LSOT uses sequential manipulations of different sensory systems to study the effects of sensory inputs on dynamic postural control during walking. Our previous research with the LSOT has shown that dynamic balance control during walking in healthy individuals is affected by the manipulation of multisensory inputs. The amount of sway variability observed during walking reflects similar balance performance with standing posture, indicating that similar feedback processes may be involved. However, the contribution of visual input is significantly increased during walking in comparison to standing. Our results with respect to the temporal structure of sway variability also revealed that as sensory conflict increases, more rigid and regular sway patterns are found during standing. However, the opposite is the case with walking where more exploratory and adaptive movement patterns are present. In these experiments, an obvious unknown is the involvement of any type of input from vestibular signals, as such contributions were not manipulated systematically.

Therefore, the purpose of the present study was to combine MV with the LSOT paradigm to determine the contributions of the vestibular system to dynamic postural control during walking. Sway variability measures were used as previously described to investigate dynamic postural control[11-12]. We hypothesized that the MV would affect both the amount and the temporal structure of sway variability during walking and, when applied in combination with manipulations of the visual and the somatosensory inputs, would further augment the observations from in our previous work.

METHODS

Subjects: Twenty healthy young adults (ten males and ten females; age 24.05±5.34 years, height 1.70±0.09 m and weight, 69.7±15.3 kg) participated in this study. The average of their preferred walking speed (PWS) was 1.02±0.08 m/s. They were free from any neural or musculoskeletal problems and had no recent history of lower extremity injures that might have affected their gait. In addition, subjects were excluded from the study if they had a history of visual or vestibular deficits and scored above zero on the dizziness handicap inventory for a vestibular deficit[33]. Prior to the experiment, each subject gave informed consent as approved by our university's Institutional Review Board.

Instrumentation: The Locomotor Sensory Organization Test (LSOT) consists of two components: a virtual reality (VR) environment with a virtual corridor, and an instrumented treadmill (Bertec Corp., Columbus, OH, USA)[11-12]. The LSOT contains six conditions similar to the Sensory Organization Test to manipulate sensory information during walking:

1) Normal walking condition: both the speed of the virtual corridor and the treadmill speed are matched with the PWS.

2) Reduced visual condition: no VR is presented, the treadmill speed is matched with the PWS, and the subjects wear vision-reduced goggles.

3) Perturbed visual condition: achieved by manipulating the optic flow speed. The speed of the virtual corridor is pseudo-randomly varied between 80% and 120% (restricted randomization between 80% and 120% in steps of 1%) of the selected PWS. Furthermore, these variations occur in pseudo-randomly assigned time intervals within 1 to 10 seconds (restricted randomization between 1 and 10 seconds in steps of 1 second)[11-12, 37-38] in order to reduce likelihood of adaptation of walking in the perturbed environment. The treadmill speed is matched with the PWS.

4) Perturbed somatosensory condition: achieved by manipulating the treadmill speed. The speed of the virtual corridor is matched with the PWS. The treadmill speed is varied between 80% and 120% of the PWS in pseudo-randomly assigned time intervals within 1 to 10 seconds. This experimental design is justified as walking speed is highly associated with the sensitivity of the somatosensory system and is crucial during stance-to-swing transition[39-40].

5) Perturbed visual and somatosensory condition: achieved by reducing vision and manipulating the treadmill speed. No VR is presented. The treadmill speed is varied between 80% and 120% of PWS in pseudo-randomly assigned time intervals within 1 to 10 seconds, and the subjects wear vision-reduced goggles.

6) Perturbed visual and somatosensory condition: achieved by manipulating optic flow and treadmill speed. Both the speed of the virtual corridor and the treadmill speed are varied between 80% and 120% of the selected PWS in pseudo-randomly assigned time intervals of 1 to 10 seconds duration. In this condition the velocity of the virtual corridor and treadmill are synchronized with a unitary gain relationship.

The MV used in the present study contained two vibrating elements, called EMS tactors (Engineering Acoustics, FL, USA.), that were placed on the mastoid processes bilaterally to perturb the vestibular feedback signals (Figure 4-1). The frequency and amplitude of the stimulation were communicated wirelessly from a computer to the tactor controller unit, which transmitted the signals through cables to the tactors. The frequency and amplitude of MV were set to 100 Hz and 17.5 db respectively. These specific settings were selected based on our pilot studies and on previous literature[92, 95] as they were found to be large enough to consistently induce changes in eye movement and in postural control during standing. A pulsed firing pattern with an active period duration of 0.3 s and a resting period duration of 0.6 s was used in order to prevent saturating the sensation of the vestibular system. Three conditions of MV were given to the participants:

bilateral, unilateral or none (control). For unilateral stimulation, one side was randomly selected for each subject at the beginning of the experiment and this side was used consistently for all of the unilateral trials.

Subjects wore a safety harness attached to a LiteGait system (Mobility Research, AZ, USA) in order to increase safety whilst on the treadmill.

Procedures: Participants were required to complete 18 randomly presented conditions (3 MV conditions by 6 LSOT conditions) on the same visit. Prior to the data collection each subject walked for five minutes on the treadmill to determine their PWS. This commenced with the subject standing on the sides of the treadmill without touching the belts. The belt velocity was incremented from 0 to 0.8 m/s and the subject was asked to step onto the treadmill whilst holding the handrail. After the subject had started walking on the treadmill, experimenters asked the subject to evaluate the speed: "Is this walking speed comfortable, like walking around the grocery store?" The treadmill velocity was increased or decreased, based on subject directions. After a comfortable walking velocity had been attained, the subject walked continuously for 5 minutes. After the PWS had been determined, all subjects walked on the treadmill at their PWS for two minutes for each condition while data were captured. Between conditions, the subjects were asked to rest with closed eyes for one minute.

Data Reduction: The ground reaction force data acquired from the instrumented treadmill were low-pass filtered at 10Hz (with a 4^{th} order Butterworth filter). The net center of pressure sway variability metric was calculated using the filtered data. The net center of pressure (netCOP) is the point at which the total sum of a pressure field acts on a body during walking[43]. The netCOP variable requires the identification of four specific netCOP points: right heel strike (RHS), left heel strike (LHS), right toe-off (RTO), and left toe-off (LTO). These four points were defined by using the data from the instrumented treadmill. In order to estimate the postural sway during walking, we calculated the netCOP area by calculating the two area triangles created. One triangle consisted of the LHS, LTO, and intersection point. The other consisted of the RHS, RTO, and intersection point. We then added these two triangles to find the total area of netCOP for one gait cycle (Figure 4-2). The mean and the standard deviation for each subject were calculated by averaging all available gait cycles. Then, the netCOP sway variability was calculated as the coefficient of variation of netCOP sway area for each subject and was used as a metric of the amount of variability. In the current study, 85 gait cycles, which was the lowest number of gait cycles performed by these twenty participants in two minutes, was used to calculate the netCOP sway variability.

The temporal structure of sway variability was quantified using Sample Entropy (SampEn), calculated using a customized script in MatLab R2011a (Mathworks, Natick, MA). The SampEn was computed from the netCOP trajectory time series from the entire two minutes of available data. Data were downsampled from 12000 to 1200 data points as we had observed little physiological signal above 10Hz during our pilot studies. The SampEn algorithm is defined as the negative natural logarithm for conditional properties that a series of data points a certain distance apart, m, would repeat itself at $m + 1$[67]. SampEn takes the logarithm of the sum of conditional probabilities. Given the time series $g(n) = g(1), g(2), \ldots, g(N)$, where N is the total number of data points, a sequence of m-length vectors is formed. Vectors are considered alike if the tail and head of the vector are within the set tolerance level. The sum of the total number of like vectors is divided by $m+1$ and defined as A or by $N-m+1$ and defined as B. SampEn is then calculated as $-\ln(A/B)$. A time series with similar distances between data points would result in a lower SampEn value while large differences result in greater SampEn value with no upper limit. Thus, a perfectly repeatable time series has a SampEn value = 0 and a perfectly random time series has a SampEn value converging toward infinity. In the current study, the following parameters were selected and used in the determination of SampEn values: (a) a pattern length (m) of 2, (b) and error tolerance (r) of 0.2[67].

Statistical Analysis: Four two-way fully repeated measures ANOVAs (3 MV by 6 LSOT conditions/levels of analysis) were performed to determine statistical significance for the four dependent variables – mean netCOP sway area, coefficient of variation of the netCOP and the SampEn for the netCOP trajectory time series in the Anterior-Posterior and the Medial-Lateral directions. When significant main or interaction effects were determined, post-hoc comparisons were performed using the Tukey method. Statistical analysis was completed in SPSS 18.0 (IBM Corporation, Armond, NY).

RESULTS

Mean Sway area (Table 4-1):

A significant LSOT main effect (F = 2.88, p = 0.018) was found (Table 4-1). However, the post hoc analysis did not reveal any significant differences between conditions due to the pairwise comparisons being adjusted for multiple comparisons. There was no significant MV main effect or interaction effect.

Amount of sway variability (Figure 4-3):

A significant LSOT main effect (F = 1020.00, p < 0.0001) was found (Figure 4-3A). Post-hoc comparisons revealed that every LSOT condition was significantly different from all others. The largest value was present in condition 5, whilst the smallest was found for condition 1. In addition, a significant MV main effect (F = 200.58, p < 0.0001) was found (Figure 4-3B). Post-hoc comparisons showed that the amount of sway variability was significantly larger in the bilateral MV condition than in the other two conditions. No differences were found between the unilateral MV and no MV conditions. A significant interaction was also identified between MV and LSOT (F = 12.03, p < 0.0001) (Figure 4-3C). Post-hoc comparisons showed that for normal unperturbed walking (LSOT Condition 1), MV did not produce any significant effect on the amount of netCOP sway variability. For LSOT condition 2, only bilateral MV significantly increased the amount of netCOP sway variability in comparison with no MV and unilateral MV. For the rest of the LSOT conditions, all possible comparisons were found to be significant with bilateral MV always producing the largest effect.

Temporal structure of sway variability in the anterior-posterior (AP) direction (Figure 4-4):

A significant LSOT main effect (F = 3122.01, p < 0.0001) was found for SampEn in the AP direction (Figure 4-4A). The post-hoc tests revealed that all possible comparisons were significant with the exception of the comparison between conditions 2 and 4. Group mean values were found to be at the lowest for Condition 3 and at the highest for Condition 5. A significant MV main effect (F = 275.24, $p < 0.0001$) was also found (Figure 4-4B). Post-hoc comparisons showed that bilateral MV condition produced significantly larger values than the no MV condition, while unilateral MV did not produce any differences with the other two conditions. A significant interaction was also found (F = 54.72, $p < 0.0001$) (Figure 4-4C). All post-hoc comparisons were significant. Specifically and for five of the LSOT conditions, the unilateral MV produced significantly larger values than the no MV condition, while the bilateral MV produced significantly larger values than both the other two MV conditions. However, the opposite was the case for LSOT condition 3; bilateral MV produced the smallest value, while the no MV condition produced the largest.

Temporal structure of sway variability in the medial-lateral (ML) direction (Figure 4-5):

A significant LSOT main effect (F = 9.85, $p < 0.001$) was found (Figure 4-5A). Post hoc comparisons revealed that conditions 2 and 5 produced significantly larger values than conditions 1, 3, and 6. No significant differences were found between conditions 2 and 5. Condition 4 did not produce any significantly different results. No significant MV main effect or interaction was found (Figure 4-5B and 4-5C).

DISCUSSION

We investigated how mastoid vibration could affect dynamic postural control in walking during simultaneous manipulation of the visual and the somatosensory systems. To accomplish this task we used three levels of MV (none, unilateral, and bilateral) and combined them with our LSOT paradigm[11-12]. We used both amount and temporal structure measures of sway variability to investigate dynamic postural control[11-12]. We hypothesized that the MV will affect both the amount and temporal structure measures of sway variability during walking and in combination with manipulations of the visual and the somatosensory inputs will further augment the results observed in our previous research work.

Our hypotheses were partially supported. MV produced significant increases for both measures of the amount and temporal structure of sway variability during walking. Regarding the temporal structure of sway variability, however, this was only the case for the AP direction but not the ML direction. Furthermore, for all conditions that involved visual and/or somatosensory manipulation, MV augmented the effect. This was the case regardless of whether MV was presented unilaterally or bilaterally. However, the bilateral MV stimulation produced larger effects than the unilateral. A notable exception to the above was LSOT condition 3 (the visual input is perturbed with no somatosensory manipulation being present) where MV resulted in decreased effects. Interestingly, MV affected only sway variability and not the mean sway area.

The overall lack of significant differences for the mean sway area could be due to the continuous adjustments the subjects made to step length and step width as they walked on the treadmill. Algorithmically, sway area highly depends on step length and step width. In our previous study we found that LSOT manipulations did not significantly affect step width[11]. Specifically, we observed an increasing trend from LSOT condition 1 to 6 with the largest difference between conditions to be about 0.09 meters. On the other hand, step length significantly decreased and the largest difference between conditions was 0.12 meters. Thus, it is possible that when we consider calculating sway area, the changes in step length and step width cancel each other out with our LSOT manipulations. In addition, MV produces no effect regarding this variable, however, MV did affect the variability of this variable.

Our results showed that MV further increased amount of sway variability during walking and this was the case for all LSOT conditions. Bilateral MV had a larger effect than unilateral MV, and MV effect increased with increased difficulty of the LSOT condition presented (Figure 4-3C). Practically, these increases in variability reflect a significant positional drift towards the front and the back of the treadmill; as sensory input is affected, positional information during locomotion is compromised. These results lead us to suggest that MV, due to the affected vestibular input, causes confusion of the egocentric body-centered coordination system used during walking[89-90]. The increase in the amount of sway variability may be related to a response to correct the location of the netCOP to compensate for this confusion.

We found that that manipulation of the vestibular input through MV does not produce a significant effect for amount of sway variability as we see in LSOT condition 1 (Figure 4-2C) unless combined with changes in another sensory input. Further, the size of the change produced by MV when just one other sensory input is manipulated (vision or somatosensory; LSOT conditions 2, 3, and 4) is quite similar. However, when both vision and somatosensory input are manipulated (LSOT conditions 5 and 6) and there is a greater reliance on vestibular input, MV produces much larger changes. Theoretically, sensory ambiguity could lead to a broader probability curve of sway estimation and uncertainty regarding necessary corrections compared to when a single modality is involved. When even less sensory input is available, the signal leads to a less accurate estimation of our position in space[15-16].

Similar results to those observed for the amount of sway variability were produced in the AP direction for the temporal structure of sway variability, with few notable exceptions. MV further increased sample entropy values during walking. This was the case for five LSOT conditions. Overall, these changes in variability reflect significant alterations in the way positional drift towards the front and the back of the treadmill is temporally organized. Larger values of sample entropy reflect more uncertainty in the temporal structure and more irregular netCOP trajectory patterns. As sensory input is affected, positional information during locomotion becomes more convoluted and uncertainty is evident in the walking patterns as they evolve over time. With visual input perturbed but no somatosensory manipulation (LSOT condition 3), however, MV resulted in decreased effects demonstrated by more regular netCOP trajectories. This serendipitous finding should be validated via rigorous replication; however, it is supported by Chien et al who found that this LSOT condition produces more regular trajectories even when is compared with LSOT condition 1 (where no sensory input is manipulated)[12]. The question is then, why MV had an opposite effect in this condition in comparison with all others. It is likely that it is related to the manipulation used in this condition; perturbed visual input via a change in optic flow speed. Given that simply reducing vision as is the case in LSOT condition 2 does not have such an effect, we hypothesize that this finding is related to the intricate relationships between optic flow manipulation and MV through visual and vestibular input interactions. Manipulating optic flow affects the visual signal of self-motion[95], which could evoke the well-known vection sensations of self-motion[96] and after-rotation when walking[97]. This is combined here with MV that, as has been suggested, may affect space reference and thus locomotion[97]. This hypothesis should be tested experimentally to further understand the mechanisms involved in the interaction of sensory inputs during locomotion.

Another interesting result that is different for the temporal structure of sway variability in comparison with the amount of sway variability, is that MV has an effect even when other sensory inputs are not being manipulated as is the case with LSOT Condition 1. Thus, it seems that MV, regardless of whether it is provided unilaterally or bilaterally, can affect the way the netCOP trajectories are organized in time producing more irregularity. This result suggests that vestibular input may be important for timing related movement decisions. Interestingly, unilateral local anesthesia of the upper dorsal cervical roots causes ataxia in humans, while ataxia and unsteadiness of gait characterize cervical vertigo[89]. Vestibular signals are frequency encoded around a central firing rate, but how they maintain a stable sense over time is not yet understood[95]. Our results support the notion that there is a closer relationship between vestibular inputs and timing of movements, regardless of whether we are dealing with unilateral or bilateral inputs.

Our results from both the amount and temporal structure of sway variability measures agree that bilateral MV produces a larger effect than the unilateral. Literature supports that bilateral and unilateral MV may produce different locomotor outcomes. Research has shown that continuous bilateral vibration of the dorsal neck muscles produces a reactive response in the sagittal plane and the AP direction resulting in a forward inclination of the body[95, 99-100]. Ivanenko et al suggested that, since the vestibular input is constant, such bilateral vibration could produce an illusion of the body's center of mass being located forward, "pressing for forward" propulsion of the body[100]. On the other hand, unilateral mastoid vibration, as used in the present study, results in body turns to the side opposite to the vibration[101-102]. In the context of treadmill walking, the lesser effects we observed with unilateral MV may be a result of the presence of external directional references provided by the experimental set up (e.g. fall harness, corridor, orientation of the moving belt) that allow the participant to recalibrate towards the anterior direction[103], thus countering the effect of the stimulation. This mechanism, similarly, may explain both the lack of a main effect of MV on the temporal structure of ML sway variability, and the modest differences between LSOT conditions in this direction. Conversely, the “pressing for forward” effect associated with bilateral MV would produce much larger results since AP is also the direction of motion.

In sum, our major conclusions were that MV produced significant increases for both measures of the amount and temporal structure of sway variability during walking. Regarding the temporal structure of sway variability, however, this was only the case for the AP direction but not the ML direction. Furthermore, for all conditions where visual and/or somatosensory manipulations were also introduced, MV presented both unilaterally and bilaterally augmented the effect. These conclusions should be tested if our experiments will be replicated with: (i) walking overground using technology that allows visual, somatosensory, and vestibular manipulations to be performed without the restrictions of the treadmill and safety harness; (ii) using a different direction of motion such as lateral stepping which will reverse the role of the AP and the ML directions for locomotion[104-105]; (iii) using galvanic vestibular stimulation[106], dorsal neck muscles vibrations[101-102], or changing head posture which affects balance and orientation responses[107-109]. These experiments will allow us to eliminate alternative explanations of our results that were described above that arise from the proprioceptive contributions of the apparatus and the contribution of the mastoid vibration to vestibular inputs versus other stimulations.

Table 4-1. Group condition means for netCOP sway area for 85 gait cycles per subject (m^2). A significant main effect was found only for LSOT. No interaction effect was present. Post-hoc analysis using pairwise Tukey comparisons revealed no significant differences between conditions.

Conditions	LSOT 1	LSOT 2	LSOT 3	LSOT 4	LSOT 5	LSOT 6
No MV	0.0493±0.007	0.0493±0.008	0.0498±0.005	0.0515±0.007	0.0495±0.008	0.0503±0.009
Unilateral MV	0.0497±0.007	0.0486±0.008	0.0482±0.008	0.0511±0.011	0.0480±0.007	0.0506±0.010
Bilateral MV	0.0493±0.008	0.0488±0.006	0.0486±0.008	0.0497±0.009	0.0468±0.010	0.0508±0.009

LSOT: Locomotor Sensory Organization Test; MV: Mastoid Vibration

Figure 4-1. A) The tactors were secured in a cap and placed on the mastoid process on each side. B) The tactor controller unit: for communication with the computer through Bluetooth and transmission of stimulus control signals to the tactors.

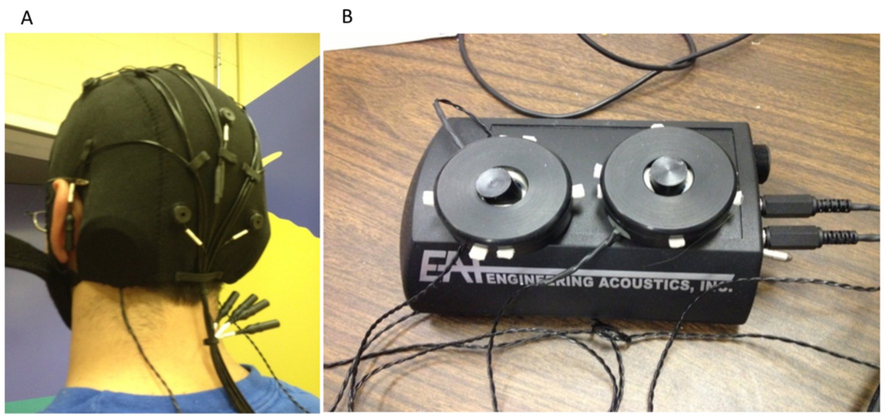


Figure 4-2. The netCOP sway area was composed by two-triangle areas that are represented as the areas with solid lines. Five points was used to generate these two-triangle areas as following: intersection point (IP), right heel-strike (RHS), right toe-off (RTO), left heel-strike (LHS), left toe-off (LTO).

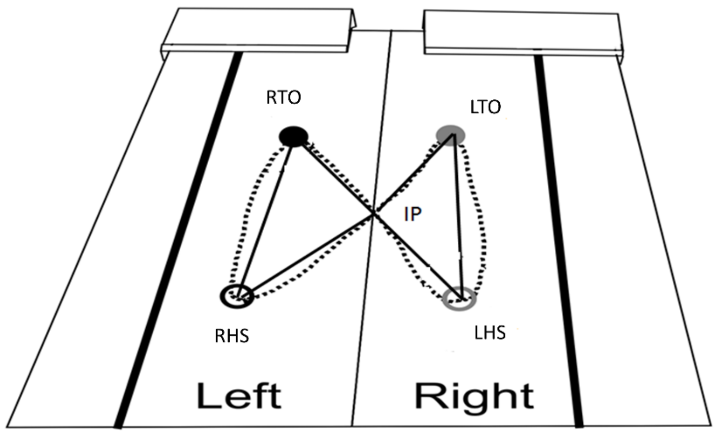


Figure 4-3. A) Bar charts showing the margin means (averaging the three MV conditions) for the coefficient of variation of the six LSOT conditions. Error bars are standard deviations. The post hoc differences are indicated over the bars with the number of the condition with which differences were found. B) Bar charts showing the margin means (averaging the six LSOT conditions) of the coefficient of variation of the three MV conditions. Error bars are standard deviations. The post hoc differences are indicated over the bars with the type of the condition with which differences were found. C) Bar charts for the group means (cell means in terms of the two-way ANOVA) for all conditions with brackets over the bars to identify significant differences between conditions. **: < 0.01; ***: < 0.0001.

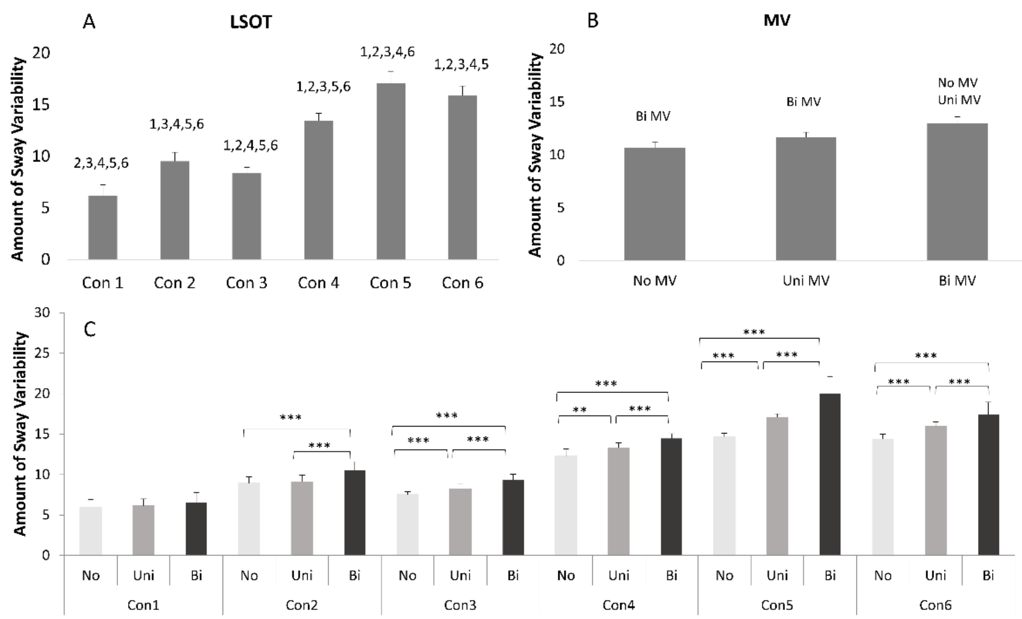


Figure 4-4. Bar charts showing the margin means (averaging the three MV conditions) for the Sample Entropy in the AP direction for the six LSOT conditions. Error bars are standard deviations. The post hoc differences are indicated over the bars with the number of the condition with which differences were found. B) Bar charts showing the margin means (averaging the six LSOT condition) for the Sample Entropy in the AP direction for the three MV conditions. Error bars are standard deviations. The post hoc differences are indicated over the bars with the type of the condition with which differences were found. C) Bar charts for the group means (cell means in terms of the two-way ANOVA) for all conditions with brackets over the bars to identify significant differences between conditions. **: < 0.01; ***: < 0.0001.

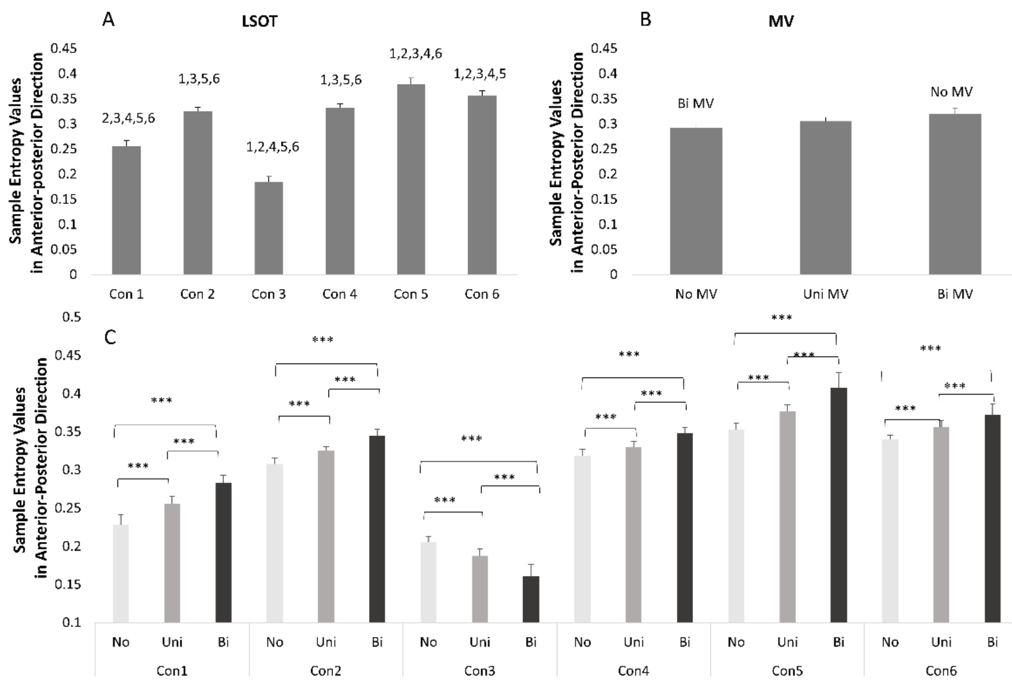
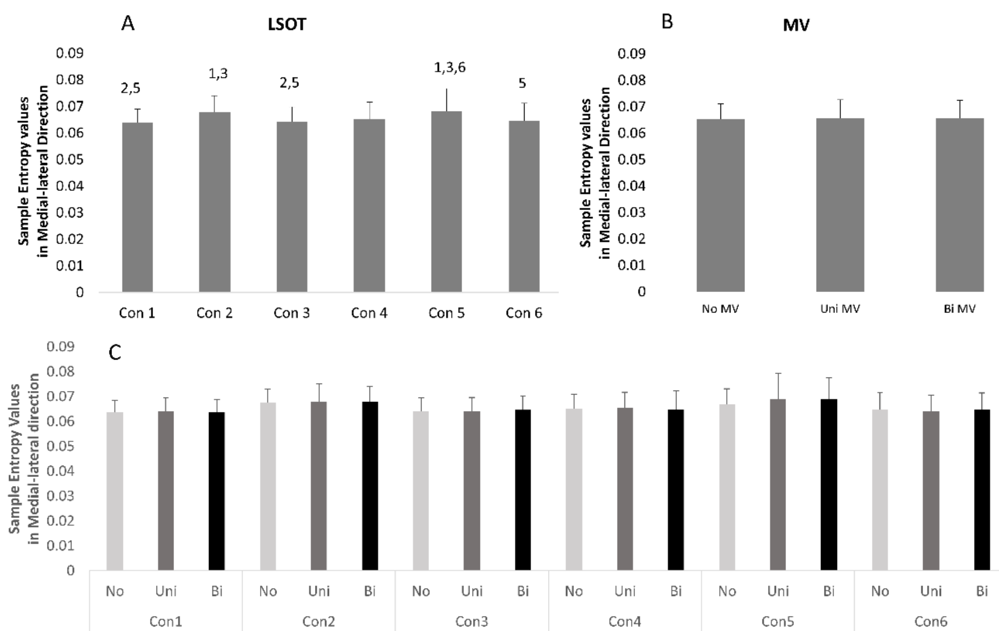


Figure 4-5. Bar charts showing the margin means (averaging the three MV conditions) for the Sample Entropy in the ML direction for the six LSOT conditions. Error bars are standard deviations. The post hoc differences are indicated over the bars with the number of the condition with which differences were found. B) Bar charts showing the margin means (averaging the six LSOT condition) for the Sample Entropy in the ML direction for the three MV conditions. Error bars are standard deviations. No significant main effect was found. C) Bar charts for the group means (cell means in terms of the two-way ANOVA) for all conditions. No significant interaction was found.



CHAPTER 5

Mastoid vibration affects dynamic postural control during gait in healthy older adults

ABSTRACT

Our objective of this study investigated how manipulating sensory input through mastoid vibration (MV) could affect dynamic postural control during walking in healthy older adults, with and without simultaneous manipulation of the visual and the somatosensory systems. We used three levels of MV (none, unilateral, and bilateral) via vibrating elements placed on the mastoid processes. We combined this with the six conditions of the Locomotor Sensory Organization Test (LSOT) paradigm to challenge the visual and somatosensory systems. We assessed postural control during walking using both amount and temporal structure measures of sway variability. We hypothesized that the MV will affect both the amount and temporal structure of sway variability during walking in older adults and, when applied in combination with manipulations of the visual and the somatosensory inputs, would produce similar observations as found in our previous work with young adults. Our results revealed that MV significantly increased the amount of sway variability during walking in older adults. However, MV significantly decreased the measure of the temporal structure of sway variability. Regarding the temporal structure of sway variability, MV produced significant results only for the AP direction but not the ML. Furthermore, for all conditions where visual and/or somatosensory manipulations were also introduced, MV augmented the effect. The bilateral MV stimulation produced usually larger effects than the unilateral. When these results are compared with our previous study with young adults, similar findings are observed with one notable exception. The MV effect on the measure of the temporal structure of variability is opposite where MV produced an increasing effect in young adults. This is a very important finding as vestibular disorders has been difficult to diagnose lacking a systematic assessment leading to speculations that more than 1/3 of adults in the US that are 40 and older may experience vestibular problems that have never been

diagnosed. Our experimental design and the results produced could guide a more reliable screening of vestibular system deterioration.

INTRODUCTION

Falls are a major focus of geriatric medicine because they are common among older adults, and often have serious consequences, including mortality, morbidity and disability. Because falls often occur while walking, and poor gait performance is associated with falling, efforts are needed to address the increased gait unsteadiness in community-dwelling elderly fallers. During the last thirty years much effort has been devoted to identifying sensitive measures of gait instability (i.e. gait speed, stride time variability)[110-111]. Less effort has been made towards identifying the mechanisms that could contribute to this gait instability. Specifically, how aging affects the contributions of the sensory systems that are involved in the control of gait remains relatively unknown[112-114]. Recently, we have developed an experimental paradigm the Locomotor Sensory Organization Test (LSOT) to study these contributions with more precision[11-12]. The LSOT allows manipulation of the visual and somatosensory inputs to study their effects on postural control during walking, paralleling the Sensory Organization Test (SOT) which is a widely used clinical test for examining such effects on standing posture.

Our previous work with the LSOT has shown that dynamic balance control during walking is affected by the systematic manipulation of multisensory inputs[11-12]. The amount of sway variability observed during walking reflects similar balance performance with standing posture, indicating that similar feedback processes may be involved. However, the contribution of visual input is significantly increased during walking in comparison to standing[11]. Our results with respect to the temporal structure of sway variability also revealed that as sensory conflict increases, more rigid and regular sway patterns are found during standing, while the opposite is the case with walking where more exploratory and adaptive movement patterns are present[12]. However, these studies have been performed with healthy young adults and thus the effect of aging has not investigated. An additional unknown from these experiments was the involvement of any type of input from vestibular signals, as such contributions are not manipulated systematically with the LSOT (or the SOT).

However, the contribution of the vestibular system is important to be assessed especially for older adults. Previous work has found that the density of the labyrinthine hair cell receptors gradually decreases beginning as early as 30 years old, followed by a steep decline in the number of vestibular receptor ganglion cells beginning around 55 to 60[115]. At 70, only 60% of the hair and nerve cells in the vestibular system remain[116]. The deteriorated vestibular system produces impaired balance and dizziness. Particularly, it has been shown that older adults demonstrate significantly increased postural sway during standing and feel dizziness while visual and somatosensory systems are conflicted simultaneously[117]. A deteriorated vestibular system could result in self-orientation that is less reliable and could impair the ability to integrate sensory information reducing the capacity to compensate for discordant input[118]. Therefore, it is important to incorporate a manipulation of vestibular input to investigate this system's contribution to walking performance especially when the focus is older adults. Recently, we have incorporated Mastoid Vibration (MV) to our LSOT experimental paradigm to address this issue[13].

Our results indicated that MV produces significant increases for both measures of the amount and temporal structure of sway variability during walking. Regarding the temporal structure of sway variability, however, this was only the case for the anterior posterior direction but not the mediolateral direction. Bilateral MV produced larger effects than unilateral stimulation. Furthermore, for all conditions where visual and/or somatosensory manipulations were also introduced, MV augmented the effect regardless if it was presented unilaterally or bilaterally. However, this study was performed only with healthy young adults and thus the effect of aging has not investigated.

Therefore, the purpose of the present study was to combine MV with the LSOT paradigm to determine the contributions of the vestibular system to dynamic postural control during walking in healthy older adults. Sway variability measures were used to investigate dynamic postural control as described in our previous studies[11-12]. We hypothesized that the MV will affect both the amount and temporal structure of sway variability during walking in older adults and, when applied in combination with manipulations of the visual and the somatosensory inputs, would produce similar observations as found in our previous work with young adults[13].

METHODS

Subjects: Ten healthy older adults (five males and five females; age 66.50±4.32 years, height 1.72±0.10 m and weight, 72.42±20.93 kg) participated in this study. The average of preferred walking speed (PWS) was 0.93±0.09 m/s. They were free from any neural or musculoskeletal problems and had no recent history of lower extremity injures that might have affected their gait. Subjects were excluded from the study if they had a history of visual or vestibular deficits and scored above zero on the dizziness handicap inventory for a vestibular deficit[33]. Prior to the experiment, each subject gave informed consent as approved by our university's Institutional Review Board.

Instrumentation:

The Locomotor Sensory Organization Test (LSOT) consists of two components: a virtual reality (VR) environment with a virtual corridor, and an instrumented treadmill (Bertec Corp., Columbus, OH, USA) (Chien et al, 2014). The LSOT contains six conditions similar to the Sensory Organization Test to manipulate sensory information during walking:

1) Normal walking condition: both the speed of the virtual corridor and the treadmill speed are matched with the PWS.

2) Reduced visual condition: no VR is presented, the treadmill speed is matched with the PWS, and the subjects wear vision-reduced goggles.

3) Perturbed visual condition: achieved by manipulating the optic flow speed. The speed of the virtual corridor is pseudo-randomly varied between 80% and 120% (restricted randomization between 80% and 120% in steps of 1%) of the selected PWS. Furthermore, these variations occur in pseudo-randomly assigned time intervals within 1 to 10 seconds (restricted randomization between 1 and 10 seconds in steps of 1 second)[11-12, 37-38] in order to reduce likelihood of adaptation of walking in the perturbed environment. The treadmill speed is matched with the PWS.

4) Perturbed somatosensory condition: achieved by manipulating the treadmill speed. The speed of the virtual corridor is matched with the PWS. The treadmill speed is varied between 80% and 120% of the PWS in pseudo-randomly assigned time intervals within 1 to 10 seconds. This experimental design is justified as walking speed is highly associated with the sensitivity of the somatosensory system and is crucial during stance-to-swing transition[39-40].

5) Perturbed visual and somatosensory condition: achieved by reducing vision and manipulating the treadmill speed. No VR is presented. The treadmill speed is varied between 80% and 120% of PWS in pseudo-randomly assigned time intervals within 1 to 10 seconds, and the subjects wear vision-reduced goggles.

6) Perturbed visual and somatosensory condition: achieved by manipulating optic flow and treadmill speed. Both the speed of the virtual corridor and the treadmill speed are varied between 80% and 120% of the selected PWS in pseudo-randomly assigned time intervals of 1 to 10 seconds duration. In this condition the velocity of the virtual corridor and treadmill are synchronized with a unitary gain relationship.

The Mastoid Vibration (MV) used in the present study contained two vibrating elements, called EMS tactors (Engineering Acoustics, FL, USA.), that were placed on the mastoid process bilaterally to perturb the vestibular feedback signals (Figure 5-1). The frequency and magnitude of the stimulation were communicated wirelessly to the tactor controller unit, which transmitted these signals through cables to the tactors. The frequency of MV was set to 100 Hz and the amplitude was set to 17.5 db. This specific combination of frequency and magnitude was based on our pilot studies and previous literatures[92, 95] as were found to be large enough to induce changes in eye movement and in postural control during standing. A pulsed firing pattern was used where the duration of the firing period was 0.3 s and the duration of the resting period was 0.6 s in order to prevent saturating the sensation of the vestibular system. Three conditions of

MV were presented to the participants: bilateral, unilateral or none (control). For unilateral stimulation, one side was randomly selected for each subject at the beginning of experiment and this side was consistent for all the unilateral trials.

Subjects wore a safety harness attached to a LiteGait system (Mobility Research, AZ, USA) in order to increase safety whilst on the treadmill.

Procedures: Participants were required to complete 18 randomly presented conditions (3 MV conditions by 6 LSOT conditions) on the same visit. Prior to the data collection each subject walked for five minutes on the treadmill to determine their PWS. This commenced with the subject standing on the sides of the treadmill without touching the belts. The belt velocity was incremented from 0 to 0.8 m/s and the subject was asked to step onto the treadmill whilst holding the handrail. After the subject had started walking on the treadmill, experimenters asked the subject to evaluate the speed: “Is this walking speed comfortable, like walking around the grocery store?” The treadmill velocity was increased or decreased, based on subject directions. After a comfortable walking velocity had been attained, the subject walked continuously for 5 minutes. After the PWS had been determined, all subjects walked on the treadmill at their PWS for two minutes for each condition while data were captured. Between conditions, the subjects were asked to rest with closed eyes for one minute.

Data Reduction: The ground reaction force data acquired from the instrumented treadmill were low-pass filtered at 10Hz (with a 4th order Butterworth filter). The net center of pressure sway variability metric was calculated using the filtered data. The net center of pressure (netCOP) is the point at which the total sum of a pressure field acts on a body during walking[43]. The netCOP variable requires the identification of four specific netCOP points: right heel strike (RHS), left heel strike (LHS), right toe-off (RTO), and left toe-off (LTO). These four points were defined by using the data from the instrumented treadmill. In order to estimate the postural sway during walking, we calculated the netCOP area by calculating the two area triangles created. One triangle consisted of the LHS, LTO, and intersection point. The other consisted of the RHS, RTO, and intersection point. We then added these two triangles to find the total area of netCOP for one gait cycle (Figure 5-2). The mean and the standard deviation for each subject were calculated by averaging all available gait cycles. Then, the netCOP sway variability was calculated as the coefficient of variation of netCOP sway area for each subject and was used as a metric of the amount of variability. In the current study, 85 gait cycles, which was the lowest number of gait cycles performed by these twenty participants in two minutes, was used to calculate the netCOP sway variability.

Sample Entropy (SampEn): The temporal structure of sway variability was quantified using Sample Entropy (SampEn), calculated using a customized script in MatLab R2011a (Mathworks, Natick, MA). The SampEn was computed from the netCOP trajectory time series from the entire two minutes of available data. Data were downsampled from 12000 to 1200 data points as we had observed little physiological signal above 10Hz during our pilot studies. The SampEn algorithm is defined as the negative natural logarithm for conditional properties that a series of data points a certain distance apart, m, would repeat itself at $m + 1$[67]. SampEn takes the logarithm of the sum of conditional probabilities. Given the time series $g(n) = g(1), g(2), \ldots, g(N)$, where N is the total number of data points, a sequence of m-length vectors is formed. Vectors are considered alike if the tail and head of the vector are within the set tolerance level. The sum of the total number of like vectors is divided by $m+1$ and defined as A or by $N-m+1$ and defined as B. SampEn is then calculated as $-\ln(A/B)$. A time series with similar distances between data points would result in a lower SampEn value while large differences result in greater SampEn value with no upper limit. Thus, a perfectly repeatable time series has a SampEn value equal to zero and a perfectly random time series has a SampEn value converging toward infinity. In the current study, the following parameters were selected and used in the determination of SampEn values: (a) a pattern length (m) of 2, (b) and error tolerance (r) of 0.2[67].

Statistical Analysis: Four two-way fully repeated measures ANOVAs (3 MV by 6 LSOT conditions/levels of analysis) were performed to determine statistical significance for the four dependent variables – mean netCOP sway area, coefficient of variation of the netCOP and the SampEn for the netCOP trajectory time series in the Anterior-Posterior and the Medial-Lateral directions. When significant main or interaction effects were determined, post-hoc comparisons were performed using the Tukey method. Statistical analysis was completed in SPSS 18.0 (IBM Corporation, Armond, NY).

RESULTS

Mean Sway area (Table 5-1): A significant LSOT main effect (F = 5.68, $p < 0.0001$) was found (Table 5-1). The post hoc analysis revealed LSOT condition 5 had significantly smaller values than LSOT condition 1. There was no significant MV main effect or interaction effect.

Amount of sway variability (Figure 5-3): A significant LSOT main effect (F = 219.90, $p < 0.0001$) was found (Figure 5-3A). Post-hoc analysis revealed that only the comparisons between conditions 2 and 4 and conditions 3 and 4 were not significantly different; all others were found to be significant. The largest value was present in condition 5, whilst the smallest was found for condition 1. In addition, a significant MV main effect (F = 162.39, $p < 0.0001$) was found (Figure 5-3B). Post-hoc comparisons showed that the amount of sway variability was significantly larger in the bilateral MV condition than the no MV condition. This was also the case with the unilateral MV condition. No differences were found between the bilateral MV and unilateral MV condition. A significant interaction was also identified between MV and LSOT (F = 4.22, $p < 0.0001$) (Figure 5-3C). Post-hoc comparisons showed that for normal unperturbed walking (LSOT Condition 1), MV did not produce any significant effect on the amount of netCOP sway variability. For all other LSOT conditions, both unilateral and bilateral MV significantly increased the amount of netCOP sway variability in comparison with no MV. However, for LSOT conditions 3, 4, and 5, bilateral and unilateral MV were not different from each other, while for LSOT conditions 2 and 6, bilateral MV produced a larger effect than the unilateral MV.

Structure of sway variability in anterior-posterior (AP) direction (Figure 5-4): A significant LSOT main effect (F = 1632.99, $p < 0.0001$) was found for SampEn in the AP direction (Figure 5-4A). Post-hoc analysis revealed that only the comparison between conditions 4 and 6 was not significantly different; all others were found to be significant.

Group mean values were found to be at the lowest for Condition 3 and at the highest for Condition 5. A significant MV main effect (F = 288.72, p < 0.0001) was also found and all post-hoc comparisons were significant (Figure 5-4B). Group mean values were found to be at the lowest for the bilateral MV condition and at the highest for the no NV condition. A significant interaction was also found (F = 36.05, p < 0.0001) (Figure 5-4C). All post-hoc comparisons were significant except the comparison between no MV and unilateral MV for LSOT condition 1. For the other five LSOT conditions, the unilateral MV produced significantly smaller values than the no MV condition. The bilateral MV produced significantly smaller values than both the other two MV conditions for all LSOT conditions.

Structure of sway variability in medial-lateral (ML) direction (Figure 5-5): A significant LSOT main effect (F = 21.87, p < 0.001) was found (Figure 5-5A). Several post hoc comparisons were found to be significant (Figure 5-5A). In general, group mean values were found to be at the highest for condition 1 and at the lowest for condition 6, revealing a decreasing trend across the LSOT conditions. No significant MV main effect or interaction was found (Figure 5-5B and 5-5C).

DISCUSSION

We investigated how mastoid vibration (MV) could affect dynamic postural control in walking during simultaneous manipulation of the visual and the somatosensory systems in healthy older adults. To accomplish this task, we used three conditions of MV (none, unilateral, and bilateral) and combined them with our LSOT paradigm[11-12]. We used both amount and temporal structure measures of sway variability to study dynamic postural control[11-12]. We hypothesized that the MV will affect both the amount and temporal structure of sway variability during walking in older adults and, when applied in combination with manipulations of the visual and the somatosensory inputs, would produce similar observations as found in our previous work[13] with young adults.

Our hypotheses were partially supported. MV significantly increases the measure of the amount of sway variability in healthy older adults. However, MV significantly decreases the measure of the temporal structure of sway variability. Regarding the temporal structure of sway variability, MV produces significant results only for the AP direction but not the ML. Furthermore, for all conditions that involve visual and/or somatosensory manipulation, MV augments the effect. This was the case regardless of whether MV is presented unilaterally or bilaterally. The bilateral MV stimulation produces usually larger effects than the unilateral. MV affects only sway variability and not the mean sway area. When comparing all these results with our previous study with young adults, we observe similar findings with one notable exception. The MV effect on the measure of the temporal structure of variability is opposite for all LSOT conditions except LSOT condition 3 where MV produced a decreasing effect in both young and older adults.

Mean sway area was not affected by MV, however was affected by the LSOT where a decreasing trend is present as the older adults are progressively challenged more through the visual and somatosensory manipulations presented. The largest decrease is present in LSOT condition 5, where vision is reduced and somatosensory input is manipulated at the same time. This result could be attributed to the fact that sway area highly depends mathematically on step length and has been found that older adults decrease their stride under reduced lighting conditions[120]. This conclusion is reinforced by our earlier study with the young adults where no differences were found between the LSOT conditions.

Our results showed that MV further increased amount of sway variability during walking and this was the case for all LSOT conditions. In addition, the MV effect was more pronounced in LSOT condition 2 and 5 which are both associated with reduced vision. This result emphasizes the enhanced importance of vision for locomotion as compared to standing[11], and possibly more so for older adults. Another interestingly result is that bilateral MV had a larger effect than unilateral MV in LSOT conditions 2 (reduced vision) and 6 (vision and somatosensory are both manipulated). This is not the same with young adults where bilateral MV had always a significantly larger effect for all LSOT conditions where manipulations are present. We believe that this is a statistical power effect for these conditions in the older adults because even in these conditions we have larger means for the bilateral MV. The increase in sample size would have probably resulted in all comparisons to be significant as was the case in our previous study with young adults. Another worth mentioning comparison between the present study and our previous study with the young adults is that here we have much larger values for this measure, in some cases even doubled, indicating that the older adults are much more challenged by our overall experimental design. These large increases in variability reflect a significant positional drift towards the front and the back of the treadmill; as sensory input is affected, positional information during locomotion is compromised. These results lead us to believe that MV, due to the affected vestibular input, causes confusion of the egocentric body-centered coordination system used during walking[88-89]. The increase in the amount of sway variability may be related to a response to correct the location of the netCOP to compensate for this confusion which is larger in older adults. Deshpande and Patla (2007) further supports this claim as they have shown that vestibular input reweighting is less effective in older individuals[112].

Another interesting result is that manipulation of the vestibular input through MV does not produce a significant effect for amount of sway variability as we see in LSOT condition 1 unless combined with changes in another sensory input. This was also the case with young adults as we found in our previous study[13]. It is then possible that MV by itself does not produce a significant sensory input problem for this variable; at least not so big that other sensory systems could not compensate. This could also be the result of treadmill walking as used in the present study as we explain below.

Regarding the temporal structure of sway variability in the AP direction, our results showed that MV decreased sample entropy values during walking. This was the case for all LSOT conditions and was even present in LSOT condition 1 when bilateral MV was present. These changes in variability reflect significant alterations in the way positional drift towards the front and the back of the treadmill is temporally organized. Smaller values of sample entropy reflect more rigidity in the temporal structure and more regular netCOP trajectory patterns. Importantly, this result is opposite to what we observed before with young adults where sample entropy values increased due to MV, except for LSOT condition 3 where they also decreased[13]. The explanation we provided before for LSOT condition 3, was based on the relationship between optic flow and MV through visual and vestibular input interactions. It is known that manipulating optic flow affects the visual signal of self-motion[95], which could evoke the well-known vection sensations of self-motion[96] and after-rotation when walking[97]. When this is combined with MV, it may affect space reference and thus locomotion[120].

However, this explanation was given what we observed with LSOT condition 3. In the present study, the decreasing effect is uniform across all conditions and thus requires a more general explanation which we believe is related with aging. Perception of the postural vertical that provides an indicator measure of vestibular function in the absence of visual input and diminished somatosensory feedback, is affected in older adults[121]. There is also a strong indication that aging results in deterioration of reciprocal cortico-cortical inhibition and decreases in the ability for multimodal vestibular integration of sensory inputs[122]. Therefore, MV could have an opposite effect as we observe here with older adults in comparison with young adults, regardless of LSOT condition. In the context of this experimental design, is possible that young adults produce more temporally variable netCOP trajectory patterns as a compensation mechanism to adapt to the challenges presented to them by exploring more movement patterns. They do so whenever they can, except for LSOT condition 3 where the intricate relationship between optic flow and MV through visual and vestibular input interactions is just too difficult of a system constraint to overcome. In this condition instead, they decide to become more rigid as a protective mechanism because the situation now is truly serious. The older adults have this problem in all conditions and utilize this protective strategy everywhere due to the neural problems described above. However, this explanation should be tested experimentally to further understand the mechanisms involved in the interaction of sensory inputs during locomotion and how aging affects this interaction. Importantly though our results support the notion that there is a closer relationship between vestibular inputs and timing of movements.

Our results from both the amount and temporal structure of sway variability measures generally agree that bilateral MV produces a larger effect than the unilateral. Research has shown that bilateral and unilateral MV can produce different locomotor outcomes[98-102]. In the context of our experimental design, the lesser effects observed with unilateral MV may be a result of the presence of external directional references provided by the set up (e.g. harness, corridor, orientation of the moving belt). These references could help the subject to readjust towards the AP direction[103]. This may also explain both the absence of a main effect of MV on the temporal structure of ML sway variability, and the small differences in the actual SampEn values between LSOT conditions in this direction. On the contrary, the bilateral MV due to the production of a "pressing for forward" effect[100], could produce much larger results since AP is the direction of motion.

The above discussion with respect to aging differences between the present study and our previous publication is subject to a limitation of the study. It is possible that there is an a priori difference in the preferred walking speed between the two age groups which may have affected the outcomes of all the variables. Thus, we statistically compared the preferred walking speed between the young adults from our previous study and the older adults from the present study. We found no significant differences ($t = 1.587$, $p = 0.133$).

In sum, our major conclusions were that MV significantly increased the amount of sway variability during walking in older adults. However, MV significantly decreased the measure of the temporal structure of sway variability. Regarding the temporal structure of sway variability, MV produced significant results only for the AP direction but not the ML. Furthermore, for all conditions where visual and/or somatosensory manipulations were also introduced, MV augmented the effect. This was the case regardless of whether MV was presented unilaterally or bilaterally. The bilateral MV stimulation produced usually larger effects than the unilateral. When these results are compared with our previous study with young adults, similar findings are observed with one notable exception. The MV effect on the measure of the temporal structure of variability is opposite for all LSOT conditions except LSOT condition 3 where MV produced a decreasing effect in both young and older adults. This is a very important finding as vestibular disorders has been difficult to diagnose lacking a systematic assessment[123]. This is why Agrawal et al has speculated that more than 1/3 of adults in the US that are 40 and older may experience vestibular problems that have never been diagnosed[1]. Our experimental design and the results produced could guide a more reliable screening of vestibular system deterioration. However and before such clinical translational efforts are made, the above conclusions should be tested by replication of our experiments with: (i) over ground walking where visual, somatosensory, and vestibular manipulations are introduced without the restrictions of the treadmill; (ii) lateral stepping walking where the roles of the AP and the ML directions in locomotion are reversed[104-105]; (iii) galvanic vestibular stimulation[106], dorsal neck muscles vibrations[101-102], or changing head posture which affects balance and orientation responses[107-109]. These experiments will allow us to eliminate alternative explanations of our conclusions that arise from the effect of the apparatus and the differences that exist between mastoid vibration and other stimulations to vestibular inputs.

Table 5-1. Group condition means for netCOP sway area for 85 gait cycles per subject (m^2). A significant main effect was found only for LSOT. No interaction effect was present. Post-hoc analysis using pairwise Tukey comparisons revealed significant differences between conditions LSOT 1 and LSOT 5.

Conditions	LSOT 1#	LSOT 2	LSOT 3	LSOT 4	LSOT 5!	LSOT 6
No MV	0.0444±0.006	0.0434±0.005	0.0451±0.004	0.0445±0.005	0.0416±0.006	0.0427±0.004
Unilateral MV	0.0459±0.005	0.0417±0.003	0.0436±0.005	0.0436±0.004	0.0399±0.005	0.0410±0.005
Bilateral MV	0.0443±0.005	0.0412±0.005	0.0423±0.005	0.0430±0.005	0.0400±0.005	0.0406±0.005

1. !: significant difference exhibited when compared to LSOT condition 1.
2. #: significant difference exhibited when compared to LSOT condition 5.
3. LSOT: Locomotor Sensory Organization Test; MV: Mastoid Vibration.

Figure 5-1. The tactor system contains two tactors and the tactor controller unit -- for communication with the computer through Bluetooth and transmission of stimulus control signals to the tactors.

Figure 5-2. The netCOP sway area was composed by two-triangle areas that are represented as the areas with solid lines. Five points was used to generate these two-triangle areas as following: intersection point (IP), right heel-strike (RHS), right toe-off (RTO), left heel-strike (LHS), left toe-off (LTO).

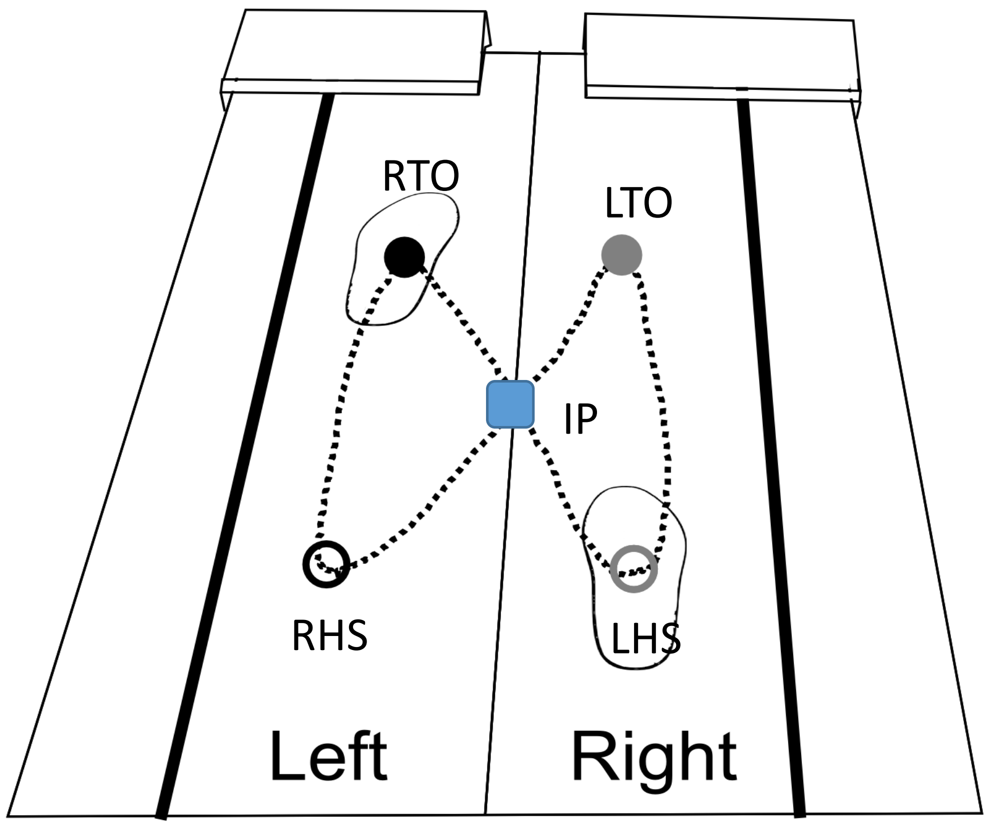


Figure 5-3. A) Bar charts showing the margin means (averaging the three MV conditions) for the coefficient of variation of the six LSOT conditions. Error bars are standard deviations. The post hoc differences are indicated over the bars with the number of the condition with which differences were found. B) Bar charts showing the margin means (averaging the six LSOT condition) of the coefficient of variation of the three MV conditions. Error bars are standard deviations. The post hoc differences are indicated over the bars with the type of the condition with which differences were found. C) Bar charts for the group means (cell means in terms of the two-way ANOVA) for all conditions with brackets over the bars to identify significant differences between conditions. **: < 0.01; ***: < 0.0001.

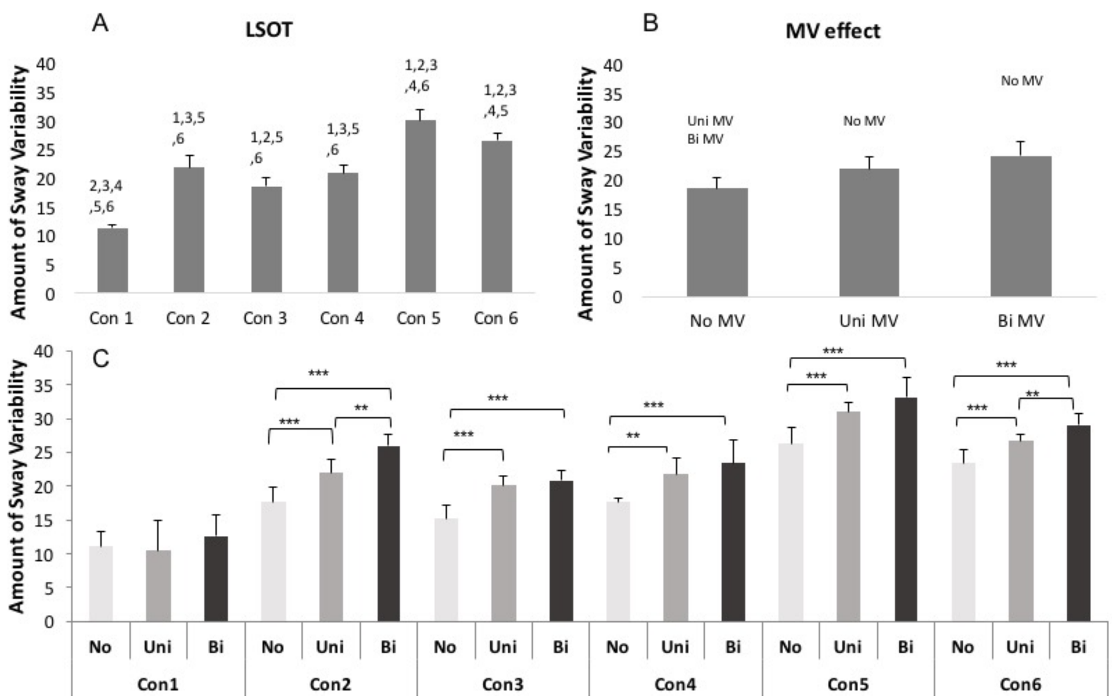


Figure 5-4. Bar charts showing the margin means (averaging the three MV conditions) for the Sample Entropy in the AP direction for the six LSOT conditions. Error bars are standard deviations. The post hoc differences are indicated over the bars with the number of the condition with which differences were found. B) Bar charts showing the margin means (averaging the six LSOT condition) for the Sample Entropy in the AP direction for the three MV conditions. Error bars are standard deviations. The post hoc differences are indicated over the bars with the type of the condition with which differences were found. C) Bar charts for the group means (cell means in terms of the two-way ANOVA) for all conditions with brackets over the bars to identify significant differences between conditions. **: < 0.01; ***: < 0.0001.

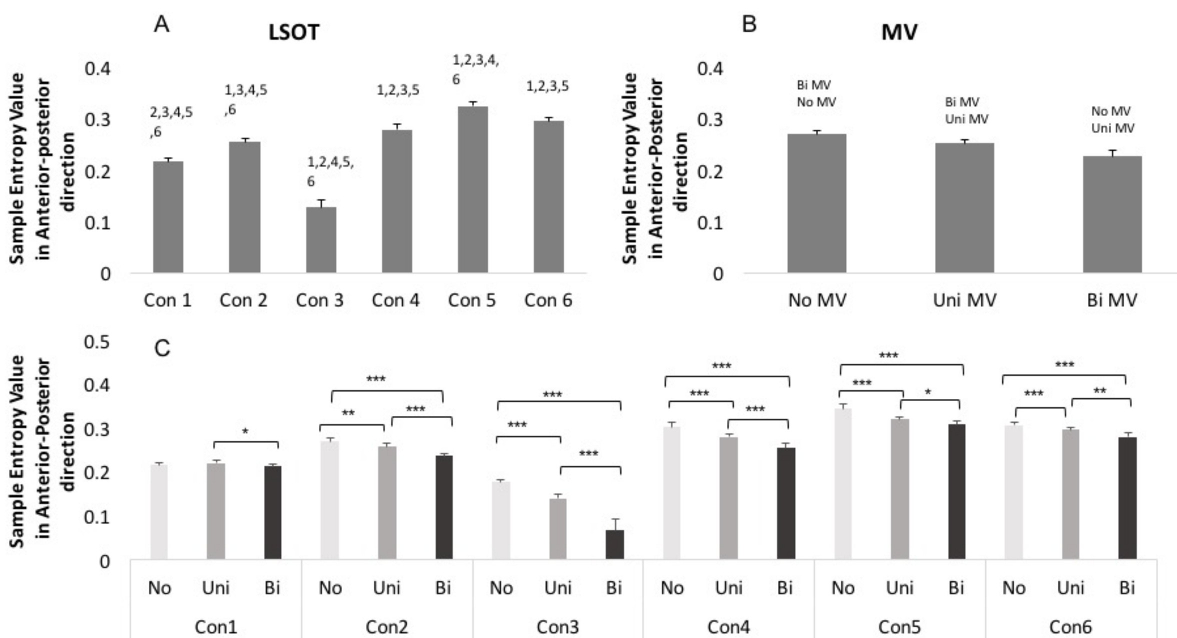
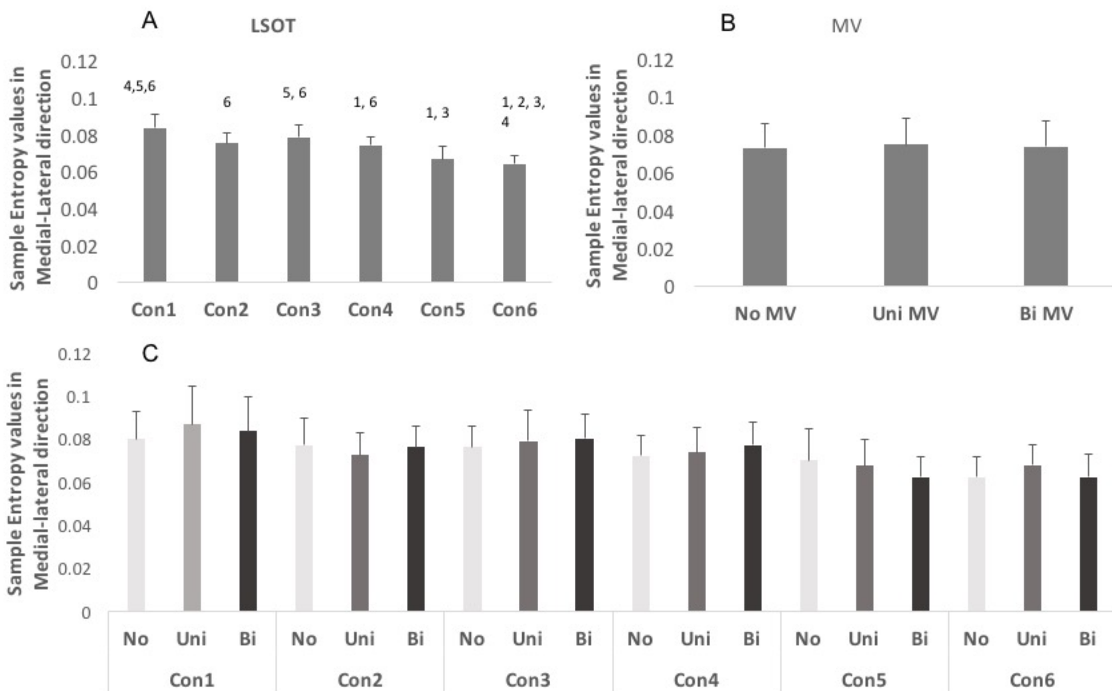


Figure 5-5. Bar charts showing the margin means (averaging the three MV conditions) for the Sample Entropy in the ML direction for the six LSOT conditions. Error bars are standard deviations. The post hoc differences are indicated over the bars with the number of the condition with which differences were found. B) Bar charts showing the margin means (averaging the six LSOT condition) for the Sample Entropy in the ML direction for the three MV conditions. Error bars are standard deviations. No significant main effect was found. C) Bar charts for the group means (cell means in terms of the two-way ANOVA) for all conditions. No significant interaction was found.



CHAPTER 6

CONCLUSION TO THE DISSERTATION

This dissertation was designed to gain insight into the contributions of different sensory systems to dynamic postural control during walking. It is hoped that this information may help scientists and clinicians to improve their understanding of visual, somatosensory, and vestibular contributions on the way we walk and to develop better diagnostic and prognostic tools for related diseases.

In order to quantify sensory contributions and the adaptive mechanisms involved in the control of posture during sensory conflict, the Sensory Organization Test (SOT) has been used in patients with vestibular disorder, concussion, stroke, and Parkinson’s disease. Through the systematic manipulation of sensory input, the SOT intends to perturb the system and induce adaptive sensory recalibration processes. This widely used clinical test can manipulate singly or in combination somatosensory and visual inputs to allow for the assessment of a patient’s ability for maintaining balance. However, a comprehensive study of how sensory information from the different systems is integrated to achieve dynamic postural control during walking has not been performed. It is possible that the reason for such a knowledge gap is the absence of an experimental apparatus like the SOT for walking. In this dissertation, we developed and implemented an experimental apparatus, consisting of an integrated instrumented multisensory virtual reality environment: the Locomotor Sensory Organization Test (LSOT). This allowed for the assessment of sensory contributions to the dynamic postural control during walking. We utilized this apparatus in all the experiments performed in this dissertation.

In the first manuscript (chapter 2) ten healthy young adults performed the six conditions of the traditional SOT to quantify standing postural control when exposed to sensory conflict. The same subjects performed these six conditions using the Locomotor SOT (LSOT), to study dynamic postural control during walking under similar types of sensory conflict. To quantify postural control during walking, the net Center of Pressure sway variability was used. This corresponds to the Performance Index of the center of pressure trajectory, which is used to quantify postural control during standing. Our results indicate that dynamic balance control during locomotion in healthy individuals is affected by the systematic manipulation of multisensory inputs. The sway variability patterns observed during locomotion reflect similar balance performance with standing posture, indicating that similar feedback processes may be involved. However, the contribution of visual input is significantly increased during locomotion, compared to standing in similar sensory conflict conditions. The increased visual gain in the LSOT conditions reflects the importance of visual input for the control of locomotion. Since balance perturbations tend to occur in dynamic tasks and in response to environmental constraints not present during the SOT, we suggested that the LSOT may provide additional information for clinical evaluation on healthy and deficient sensory processing.

In the second manuscript (chapter 3) we wanted to extend the above findings and investigate a phenomenon previously observed under increased sensory conflict during standing. Specifically, when maintaining postural stability temporally under increased sensory conflict, a more rigid response is observed where the available degrees of freedom are essentially frozen. We explored if such a strategy is also utilized during more dynamic situations of postural control as is the case with walking. Ten healthy young adults performed the six conditions of the traditional SOT and the corresponding six conditions on the LSOT. The temporal structure of sway variability was evaluated from all conditions. The results showed that in the anterior posterior direction somatosensory input is crucial for postural control for both walking and standing; visual input also had an effect but was not as prominent as the somatosensory input. In the medial lateral direction and with respect to walking, visual input has a much larger effect than somatosensory input. This is possibly due to the added contributions by peripheral vision during walking; in standing such contributions may not be as significant for postural control. In sum, as sensory conflict increases, more rigid and regular sway patterns are found during standing confirming the previous results presented in the literature, however the opposite was the case with walking where more exploratory and adaptive movement patterns are present.

The above two studies produced very important results, but they also identified a possible limitation. The LSOT (and the SOT) allows the manipulation of visual and somatosensory inputs; when both inputs are manipulated then the contribution of the vestibular system can be studied. However, the vestibular system is not manipulated directly. Therefore in a third manuscript (chapter 4), we investigated how manipulating sensory input through mastoid vibration (MV) could affect dynamic postural control during walking, with and without simultaneous manipulation of the visual and the somatosensory systems. We used three levels of MV (none, unilateral, and bilateral) via vibrating elements placed on the mastoid processes. We combined this with the six conditions of the LSOT paradigm to challenge the visual and somatosensory systems. We assessed postural control during walking using both amount and temporal structure measures of sway variability. Our results showed that MV produced a significant increase in the amount of sway variability in both anterior-posterior and medial-lateral directions. Significant changes in the temporal structure of sway variability were only observed in the anterior-posterior direction. When MV was applied either unilaterally or bilaterally was found to augment the effect of all visual and somatosensory manipulations of the LSOT. Bilateral MV produced larger effects than unilateral stimulation. We concluded that sensory input while walking could be affected through MV and such changes are in the direction of motion. Combining MV with manipulations of visual and somatosensory input could allow us to better understand sensory system contributions during locomotion.

Subsequently, we wanted to extend the results of the third manuscript and explore how older adults will respond to a similar type of an experimental protocol.

Therefore, in the fourth and final manuscript of this dissertation, we investigated how manipulating sensory input through mastoid vibration (MV) could affect dynamic postural control during walking in older adults, with and without simultaneous manipulation of the visual and the somatosensory systems. We used again three levels of MV (none, unilateral, and bilateral) via vibrating elements placed on the mastoid processes. We combined this with the six conditions of the LSOT paradigm to challenge the visual and somatosensory systems. We assessed postural control during walking using both amount and temporal structure measures of sway variability. Our results revealed that MV significantly increased the amount of sway variability during walking in older adults. However, MV significantly decreased the measure of the temporal structure of sway variability. Regarding the temporal structure of sway variability, MV produced significant results only for the AP direction but not the ML. Furthermore, for all conditions where visual and/or somatosensory manipulations were also introduced, MV augmented the effect. The bilateral MV stimulation produced usually larger effects than the unilateral. When these results are compared with our previous study with young adults, similar findings are observed with one notable exception. The MV effect on the measure of the temporal structure of variability is opposite where MV produced an increasing effect in young adults. This is a very important finding as vestibular disorders has been difficult to diagnose lacking a systematic assessment leading to speculations that more than 1/3 of adults in the US that are 40 and older may experience vestibular problems that have never been diagnosed. Our experimental design and the results produced could guide a more reliable screening of vestibular system deterioration.

The results of this dissertation however, should be considered with respect to certain general limitations. These limitations are also pointing towards some intriguing future studies. Thus, we believe that our conclusions should be tested by replication of our experiments with: (i) over ground walking where visual, somatosensory, and vestibular manipulations are introduced without the restrictions of the treadmill; (ii) lateral stepping walking where the roles of the AP and the ML directions in locomotion are reversed; and (iii) galvanic vestibular stimulation, dorsal neck muscles vibrations, or changing head posture which affects balance and orientation responses. These experiments will allow us to eliminate alternative explanations of our conclusions that arise from the effect of the apparatus and the differences that exist between mastoid vibration and other stimulations to vestibular inputs. Only then we can move forward with clinically translating our results.

{it will be nice to have some cross analysis between chapters 4 and 5 to gain better understand about the aging effect on the topic! }

References

1. Agrawal Y, Carey JP, Della Santina CC, Schubert MC, Minor LB. Disorders of balance and vestibular function in US adults. Arch Intern Med. 169(10):938-944, 2009.
2. Ko C, Hoffman HJ, Sklare DA. Chronic Imbalance or Dizziness and Falling: Results from the 1994 Disability supplement to the national health interview survey and the second supplement on aging study. Paper presented at: Annual Meeting of the Association for Research in Otolaryngology. February 6, 2006; Baltimore, MD.
3. Colledge N, Lewis S, et al. Magnetic resonance brain imaging in people with dizziness: a comparison with non-dizzy people. J Neurol Neurosurg Psych. 72(5):587-589, 2002.
4. Vestibular Disorders Association. http://www.vestibular.org/ Sep. 2015.
5. Nashner L.M, Black F.O, Wall C 3rd. Adaptation to altered support and visual condition during stance: patients with vestibular deficits. 2(5): 536-544, 1982.
6. Black F.O, Shupert C.L, Peterka R.J, Nashner L.M. Effects of unilateral loss of vestibular function on the vestibule-ocular reflex and postural control. Ann Otol Rhinol Laryngol. 98(11): 884-889, 1989.
7. Black F.O, Nashner L. Vestibulospinal control differs in patients with reduced and distorted vestiblar function. Acta Otolarynol. 406:110, 1984.
8. Cavanaugh JT, Guskiewicz KM, Gluliani C, Marshell S, Mercer VS, Stergiou N. Recovery of postural control after cerebral concussion: new insights using approximate entropy. J Athl Train. 41(3): 305-313, 2006.
9. Cavanaugh J.T, Mercer V.S, Stergiou N. Approximate entropy detects the effect of a secondary cognitive task on postural control in healthy young: a methodological report. J Neuroeng Rehabil,4:42, 2007.
10. Turnock M.J, Layne C.S. Variations in linear and nonlinear postural measurements under Achilles tendon vibration and unstable support-surface condition. J Mot Behav. 42(1): 61-69, 2010.
11. Chien JH, Eikema DJ, Mukherjee M, Stergiou N. Locomotor sensory organization test: a novel paradigm for the assessment of sensory contributions in gait. Ann Biomed Eng. 42(12): 2512-23, 2014.
12. Chien JH, Mukherjee M, Siu KC, Stergiou N. Locomotor sensory organization test: how sensory conflict affects the temporal structure of sway variability during gait. Ann Biomed Eng. [Epub ahead of print].
13. Chien JH, Mukherjee M, Stergiou N. Mastoid vibration affects dynamic postural control during gait. Ann Biomed Eng. [Under Review].
14. Day, BL. and Cole J. Vestibular-evoked postural responses in the absence of somatosensory information. Brain. 125(Pt 9): 2081-8, 2002.
15. Ernst, MO, Banks, MS. Humans integrate visual and haptic information in a statistically optimal fashion. Nature, 415(6870):429-33, 2002.
16. Fetsch, CR, Turner, AH, DeAngelis, GC, Angelaki, DE, Dynamic reweighting of visual and vestibular cues during self-motion perception. J Neurosci, 29(49):15601-12, 2009.

17. Black, F.O., Shupert C.L., Horak F.B., Nashner L.M. Abnormal postural control associated with peripheral vestibular disorders. Prog Brain Res 76:263-75, 1988.
18. Gruhn M., Zehl L., Buschges A. Straight walking and turning on a slippery surface. J Exp Biol. 212:194-209, 2009.
19. Rossi-Izquierdo M., Santos-Pérez S., Soto-Varela A. What is the most effective vestibular rehabilitation technique in patients with unilateral peripheral vestibular disorders? Eur Arch Otorhinolaryngol. 268(11): 1569-74, 2011.
20. Donaldson CJ, Hoffer ME, Balough BJ, Gottshall KR. Prognostic assessments of medical therapy and vestibular testing in post-traumatic migraine-associated dizziness patients. Otolaryngol Head Neck Surg. 143(6): 820-5, 2010.
21. Parietti-Winkler C, Gauchard GC, Simon C, Perrin PP. Pre-operative vestibular pattern and balance compensation after vestibular schwannoma surgery. *Neuroscience*. 72: 285-92, 2011.
22. Cavanaugh J.T., Guskiewicz K.M., Giuliani C., Marshall S., Mercer V., Stergiou N. Detecting altered postural control after cerebral concussion in athletes with normal postural stability. Br J Sports Med. 9(11): 805-11, 2005.
23. Smania N., Picelli A., Gandolfi M., Fiaschi A., Tinazzi M. Rehabilitation of sensorimotor integration deficits in balance impairment of patients with stroke hemiparesis: a before/after pilot study. Neurol Sci. 29(5): 313-9, 2008.
24. Nocera J., Horvat M., Ray C.T. Effects of home-based exercise on postural control and sensory organization in individuals with Parkinson disease. Parkinsonism Relat Disord. 15(10): 742-5, 2009.
25. Peterka RJ. Sensorimotor integration in human postural control. J Neurophysiol. 88(3): 1097-118, 2002.
26. Patla A.E, Tomescu S.S, Ishac M.G. What visual information is used for navigation around obstacles in a cluttered environment? Can J Physiol Pharmacol. 82(8-9): 682-92, 2004.
27. Alexander M.S., Flodin B.W., Marigold D.S. Prism adaptation and generalization during visually guided locomotor tasks. J Neurophysiol. 106(2): 860-71, 2011.
28. Thies S.B., Richardson J.K., Ashton-Miller J.A. Effects of surface irregularity and lighting on step variability during gait: a study in healthy young and older women. Gait Posture. 22(1): 26-31, 2005.
29. Ishikawa K., Edo M., Yokomizo M., Terada N., Okamoto Y., Togawa K. (1994). Analysis of gait in patients with peripheral vestibular disorders. ORL J Otorhinolaryngol Relat Spec. 56(6): 325-30.
30. Ishikawa K., Edo M., Yokomizo M., Togawa K. Characteristics of human gait related variables in association with vestibular system disorders. Acta Otolaryngol Suppl. 520 Pt 1:199-201, 1995.
31. Deshpande N, Metter E.J, Ferrucci L. Validity of clinically derived cumulative somatosensory impairment index. Arch Phys Med Rehabil. 91(2): 226-32. 2010.
32. Patla A.E., Prentice S.D., Rietdyk S., Allard F., Martin C. What guides the selection of alternate foot placement during locomotion in humans? *Exp Brain Res*. 128(4): 441-50, 1999.
33. Jacobson G.P, Newman C. W. The development of the Dizziness Handicap Inventory. Arch Otolanryngol Head Surg. 116: 424-427, 1990.

34. Kiss RM. Comparison between kinematic and ground reaction force techniques for determining gait events during treadmill walking at different speeds. Med Eng Phys. 32(6): 662-7. 2010.
35. Zeni JA Jr, Richards JG, Higginson JS. Two simple methods for determining gait events during treadmill and overground walking using kinematic data. Gait Posture. 27(4): 710-4. 2008.
36. Mickelborough J, van der Linden ML, Richards J, Ennos AR. Validity and reliability of a kinematic protocol for determining foot contact events. Gait Posture. 11(1): 32-7. 2000.
37. Jordan K., Challis J.H., Newell K.M. Walking speed influences on gait cycle variability. Gait Posture. 26(1): 128-34, 2007.
38. Jordan K., Newell K.M. The structure of variability in human walking and running is speed-dependent. Exerc Sport Sci Rev. 36(4): 200-4, 2008.
39. Deshpande N, Metter E.J, Ferrucci L. Validity of clinically derived cumulative somatosensory impairment index. Arch Phys Med Rehabil. 91(2): 226-32. 2010.
40. Deshpande N, Ferrucci L, Metter J. Faulkner KA, Strotmeyer E, Satterfield S, Schwartz A, Simonsick E. Association of lower limb cutaneous sensitivity with gait speed in the elderly: the health ABC study. Am J Phys Med Rehabil. 87(11): 921-8, 2008.
41. Pearson KG. Proprioceptive regulation of locomotion. Current Opinion in Neurobiology. 5:786-791, 1995.
42. Chung, MJ, Wang, MJ. The change of gait parameters during walking at different percentage of preferred waling speed for healthy adults aged 20-60 years. Gait Posture. 31(1):131-5. 2010.
43. Mawase F., Haizler T., Bar-Haim S., and Karniel A. Kinetic adaptation during locomotion on a split-belt treadmill. J Neurophysiol. 109: 2216-2227, 2013.
44. Thies S.B., Richardson J.K., Demott T., Ashton-Miller J.A. Influence of an irregular surface and low light on the step variability of patients with peripheral neuropathy during level gait. Gait Posture. 22(1): 40-5, 2005.
45. Callisaya M. L., Blizzard L., McGinley J. L., Schmidt M. D., Srikanth V. K. Sensorimotor factors affecting gait variability in older people – a population-based study. J Gerontol A Biol Sci Med Sci. 65(4): 386-92, 2010.
46. Wardman D. L., Taylor J. L., Fitzpatrick R. C. Effect of galvanic vestibular stimulation on human posture and perception while standing. J Physiol. 551(Pt 3): 1033-42, 2003.
47. Berard J. R., Fung J., Lamontagne A. Evidence for the use of rotational optic flow cues for locomotor steering in healthy older adults. J Neurophysiol. 106(3): 1089-96, 2011.
48. O' Conner S., Kuo A.D., Direction-Dependent control of balance during walking and standing. J Neurophysiol. 102: 1411-1419, 2009.
49. Altman A.R., Reisman D.S., Higginson J.S., Davis I.S. Kinematic comparison of split-belt and single-belt treadmill walking and the effects of accommodation. Gait and posture. 35: 287-291, 2012.
50. Mergner T, Schweigart G, Fennell L, and Maurer. Posture control in vestibular-loss patients. Ann N Y acad Sci. 1164:206-15. 2009.

51. Riccio G.E. Information in movement variability about qualitative dynamics of posture and orientation in: K. M. Newell, D. Corcos, Variability and Motor Control, Human Kinetics, Champaign, Il., 1993, 317-357.
52. Riley M.A., Clark S. Recurrence analysis of human postural sway during the sensory organization test. Neuro let. 342: 45-48, 2003.
53. Goldberger AL, Peng CK, Lipsitz LA. What is physiologic complexity and how does it change with aging and disease? Neurobiology of Aging, 23(1):23-26, 2002.
54. Vaillancourt D.E., Newell K.M. Complexity in aging and disease: response to commentaries. Neurobiol Aging, 23(1): 27-29, 2002.
55. Vaillancourt D.E., Newell K.M. Changing complexity in human behavior and physiology through aging and disease. Neurobiol Aging, 23(1):1-11, 2002.
56. Abasolo, D., James, C.J., & Hornero, R. Non-linear analysis of intracranial electroencephalogram recordings with approximate entropy and Lempel-Ziv complexity for epileptic seizure detection. Conference Proceedings: Annual International Conference of the IEEE Engineering in Medicine and Biology Society, 2007, 1953-6.
57. Glenn, T., Whybrow, P.C., Rasgon, N., Grof, P., Alda, M., Baethge, C., & Bauer, M. Approximate entropy of self-reported mood prior to episodes in bipolar disorder. Bipolar Disorders, 8(5 Pt 1), 424-9, 2006.
58. Yeragani, V.K., Pohl, R., Mallavarapu, M., & Balon, R. Approximate entropy of symptoms of mood: an effective technique to quantify regularity of mood. Bipolar Disorders, 5(4), 279-86, 2003.
59. Glenn, T., Whybrow, P.C., Rasgon, N., Grof, P., Alda, M., Baethge, C., & Bauer, M. Approximate entropy of self-reported mood prior to episodes in bipolar disorder. Bipolar Disorders, 8(5 Pt 1), 424-9, 2006.
60. Decker L.M., Moraiti C, Stergiou N, Georgoulis A.D. New insight into anterior cruciate ligament deficiency and reconstruction through the assessment of knee kinematic variability in terms of nonlinear dynamics. Knee Surg Sports Traumatol Arthrosc. 19(10): 1620-33, 2011.
61. Harbourne RT, Stergiou N. Movement variability and the use of nonlinear tools: principles to guide physical therapist practice. Phy Ther. 89(3):267-82, 2009.
62. Dettmer M, Pourmoghaddam A, O'Connor DP, Layne CS. Interaction of support surface stability and Achilles tendon vibration during a postural adaptation task. Hum Mov Sci. 32(1):214-27, 2013.
63. Newell, KM (1997). Degrees of freedom and the development of postural center of pressure profiles. In Newell, K.M. and Molenaar, P.C.M. (Eds.), Applications of nonlinear dynamics to developmental process modeling, (pp. 63-84). Mahwah, NJ: Lawrence Erlbaum Associates.
64. Guskiewicz K.M., Riemann B.L., Perrin D. H., Nashner L.M. Alternative approaches to the assessment of mild head injury in athletes. Med Sci Sports Exerc. 29(7 Suppl):s213-21, 1997.
65. Newell, KM and Vaillancourt DE. Dimensional change in motor learning. Human Movement Science. 20: 695-715, 2001.
66. Borg FG, Laxaback G. Entropy of balance – some recent results. J Neuroeng Rehabil. 7:38, 2010.

67. Yentes JM, Hunt N, Schmid KK, Kaipust JP, McGrath D. Stergiou N. The appropriate use of approximate entropy and sample entropy with short data sets. Ann Biomed Eng 41(2): 349-65, 2013.
68. Ramdani S, Seigle B, Lagarde J, Bouchara F, Bernard PL. One the use of sample entropy to analyze human postural sway data. Med Eng Phys. 31(8):1023-31, 2009.
69. Rigoldi C, Cimolin V, Camerota F, Celletti C, Albertini G, Mainardi L, Galli M. Measuring regularity of human postural sway using approximate entropy and sample entropy in patients with Ehlers-Danlos syndrome hypermobility type. Res Dev Disabli. 34(2): 840-6, 2013.
70. Perry SD, Santos LC, Patla AE. Contribution of vision and cutaneous sensation to the control of centre of mass (COM) during gait termination. Brain Res. 14; 913(1): 27-34, 2001.
71. Graci V, Elliott DB, Buckley JG. Utility of peripheral visual cues in planning and controlling adaptive gait. Optom Vis Sci. 87(1):21-7, 2010.
72. Katsavelis D., Mukherjee M., Decker L., Stergiou N. The effect of virtual reality on gait variability. Nonlinear Dynamics Psychol life Sci. 14(3): 239-56, 2010.
73. Clark DJ, Christou EA, Ring SA, Williamson JB, Doty L. Enhanced somatosensory feedback reduces prefrontal cortical activity during walking in older adults. J Gerontol A Biol Sci Med Sci, 69(11): 1422-8, 2014.
74. Woollacott M, Shumway-Cook A., Attention and the control of posture and gait: a review of an emerging area of research. Gait Posture. 16(1):1-14, 2002.
75. Graci V, Elliott DB, Buckley JG. Peripheral visual cue affect minimum-foot-clearance during overground locomotion. Gait Posture. 30(3): 370-4, 2009.
76. Turvey MT, Harrison SJ, Frank TD, Carello C. Human odometry verifies the symmetry perspective on bipedal gaits. J Exp Psychol Hum Percept Perform, 38(2): 1014-25, 2012.
77. Neuhauser HK, Radtke A, von Brevern M. Burden of dizziness and vertigo in the community. Arch Intern Med. 168(19): 2118-2124, 2008.
78. Cohen HS. Vestibular disorders and impaired path integration along a linear trajectory. J Vestib Res. 10(1): 7-15, 2000.
79. Brandt T, Strupp M, Benson J, Dieterich M. Vestibulopathic gait. Walking and running. Adv Neurol. 87: 165-72, 2001.
80. Fife TD, Tusa RJ, Furman JM, Zee DS, Frohman E, Baloh RW, Hain T, Goebel J, Demer J, Eviatar L. Assessment: vestibular testing techniques in adults and children: report of the Therapeutic and Technology Assessment Subcommittee of American Academy Neurology. Neurology, 55(10):1431-41, 2000.
81. Kubo T, Kumakura H, Hirokawa Y, Yamamoto K, Hirasaki E. Acta Otolaryngol. 3D analysis of human locomotion before and after caloric stimulation. 117(2): 143-8, 1997.
82. Goldberg JM, Smith CE, Fernandez C. Relation between discharge regularity and response to externally applied galvanic currents in vestibular nerve afferents of the squirrel monkey. J Neurophysiol. 51(6): 1236-56, 1984.
83. Jahn K, Strupp M, Schneider E, Dieterich M, Brandt T. Differential effects of vestibular stimulation on walking and running. Neuroreport. 11(8): 1745-8, 2000.

84. Dilda V, MacDougall HG, Moore ST. Tolerance to extended galvanic vestibular stimulation: optimal exposure for astronaut training. Aviat Space Environ Med. 82(8): 770-4, 2011.
85. Proctor LR. Clinical experience with a short-acting caloric test. Laryngoscope. 95(1):75-80, 1985.
86. Karlberg M, Aw S, Black R, Todd M, MacDougall H, Halamgyi M. Vibration-induced ocular torsion and nystagmus after unilateral vestibular deafferentation. Brain. 126: 956-64, 2003.
87. Strupp M, Arbusow V, Dieterich M, Brandt T. Perceptual and oculomotor effects of neck muscle vibration in vestibular neuritis: ipsilateral somatosensory substitution of vestibular function. Brain. 121: 677-85, 1998.
88. Brandt T, Bronstein AM. Cervical vertigo. J Neurol Neurosurg Psychiatry. 71(2):8-12, 2001.
89. Brandt T. Cervical vertigo – reality or fiction? Audiol Neurootol, 1: 187-96, 1996.
90. Biguer B, Donaldson IM, Hein A, Jeannerod M. Neck Muscle vibration modifies the representation of visual motion and direction in man. Brain. 111: 1405-24, 1988.
91. Bottini G, Karnath HO, Vallar G, Sterzi R, Frith CD, Frackowiak RS, Paulesu E. Cerebral representation for egocentric space: functional-anatomical evidence from caloric vestibular stimulation and neck vibration. Brain. 124; 1182-96, 2001.
92. Bove M, Brichetto G, Abbruzzese G, Marchese R, Schieppati M. Neck proprioception and spatial orientation in cervical dystonia. Brain. 127: 2764-78, 2004.
93. Chan YS, Kasper J, Wilson VJ. Dynamics and directional sensitivity of neck muscle spindle responses to head rotation. J Neurophysiol. 57, 1716-1729, 1987.
94. Nuti D, Mandala M. Sensitivity and specificity of mastoid vibration test in detection of effects of vestibular neuritis. Acta Otorhinolarynqol Ital. 25(5): 271-6, 2005.
95. St George RJ, Fitzpatrick RC. The sense of self-motion, orientation and balance explored by vestibular stimulation. J Physiol, 589(pt 4): 807-13, 2011.
96. Brandt T, Dichgans J, Buchle W. Motion habituation: inverted self-motion perception and optokinetic after-nystagmus. Exp Brain Res. 21(4): 337-52, 1974.
97. Gordon CR, Tal D, Gadoth N, Shupak A. Prolonged optokinetic stimulation generates podokinetic after rotation. Ann N Y Acad Sci. 1004: 297-302, 2003.
98. Lekhel H, Popov K, Bronstein A, Gresty M. Postural reponses to vibration of neck muscles in patients with uni- and bilateral vestibular loss. Gait and posture.7:228-236, 1998.
99. Kavounoudias A, Gilhodes JC, Roll R, Roll JP. From balance regulation to body orientation: two goals for muscle proprioceptive information processing? Exp Brain Res. 124(1): 80-8, 1999.
100. Ivanenko YP, Grasso R, Lacquaniti F. Neck muscle vibration makes walking humans accelerate in the direction gaze. J Physiol. 525(pt 3):803-14, 2000.
101. Bove M, Diverio M, Pozzo T, Schieppati M. Neck muscle vibration disrupts steering of locomotion. J Appl Physiol (1985). 91(2): 581-8, 2001.

102. Bove M, Courtine G, Schieppati M. Neck muscle vibration and spatial orientation during stepping in place in humans. J Neurophysiol. 88(5):2232-41, 2002.
103. Souman JL, Frissen I, Sreenivasa MN, Ernst MO. Walking straight into circles. Curr Biol. 19(18):1538-42, 2009.
104. Wurdeman SR, Huben NB, Stergiou N. Variability of gait is dependent on direction of progression: implication of active control. J Biomech. 45(4): 653-9, 2012.
105. Wurdeman SR, Stergiou N. Temporal structure of variability reveals similar control mechanisms during lateral stepping and forward walking. Gait Posture. 38(1):73-8, 2013.
106. Fitzpatrick RC, Wardman DL, Taylor JL. Effects of galvanic vestibular stimulation during human walking. J Physiol. 517, 931-939, 1999.
107. Fransson PA, Karlberg M, Sterner T, Maqnusson M. Direction of galvanically-induced vestibulo-postural responses during active and passive neck torsion. Acta Otolaryngol. 120(4): 500-3, 2000.
108. Deshpande N, Patla AE. Postural responses and spatial orientation to neck proprioceptive and vestibular inputs during locomotion in young and older adults. Exp Brain Res. 167(3): 468-74, 2005.
109. Fitzpatrick RC, Butler JE, Day BL. Resolving head rotation for human bipedalism. Curr Biol. 16(15): 1509-14, 2006.
110. Bruijn SM, Meijer OG, Beek PJ, van Dieen JH. Assessment the stability of human locomotion: a review of current measures. J R Soc Interfacce. 10(83):20120999, 2013.
111. Jerome GJ, Ko SU, Kauffman D, Studenski SA, Ferrucci L, Simonsick EM. Gait characteristics associated with walking speed decline in older adults: results from the Baltimore Longitudinal Study of Aging. Arch Gerontol Geriatr. 60(2):239-43, 2015.
112. Deshapnde N, Patla AE. Visual-vestibular interaction during goal directed locomotion: effects of aging and blurring vision. Exp Brain Res. 176(1):43-53, 2007.
113. Novak AC, Deshpande N. Effects of aging on whole body and segmental control while obstacle crossing under impaired sensory conditions. Hum Mov Sci. 35:121-130.
114. Brach JS, Vanswearingen JM. Interventions to improve walking in older adults. Curr Transl Geriatr Exp Gerontol Rep. 2(4), 2013.
115. Bergstrom B. Morphology of the vestibular nerve: II. The number of myelinated vestibular nerve fibers in man at various ages. Acta Otolaryngol. 76, 173-179, 1973.
116. Rosenhall U, Rubin W. Degenerative changes in the human vestibular sensory epithelia. Acta Otolaryngol. 79(1-2): 67- 80, 1975.
117. Woollacott MH, Shumway-Cook A, Nashner LM. Aging and posture control: changes in sensory organization and muscular coordination. Int J Aging Hum Dev. 23(2):97-114, 1986.

118. Hay L, Bard C, Fleury M, Teasdale N. Availability of visual and proprioceptive afferent messages and postural control in elderly adults. Exp Brain Res. 108(1):129-39, 1996.
119. Figueiro MG, Plitnick B, Rea MS, Gras LZ, Rea MS. Lighting and perceptual cues: effects on gait measures of older adults at high and low risk for falls. BMC Geriatr. 11:49, 2011.
120. Pettorossi VE, Schieppati M. Neck proprioception shapes body orientation and perception of motion. Front Hum Neurosci. 8:895, 2014.
121. Menant JC, St George RJ, Fitzpatrick RC, Lord SR. Lord SR. Perception of the postural vertical and falls in older people. Gerontology. 58(6): 497-503, 2012.
122. Cyran CA, Boegle R, Stephan T, Dieterich M, Glasauer S. Age-related decline in functional connectivity of the vestibular cortical network. Brain Struct Funct. 2015 [Epub ahead of print].
123. Sloane PD, Coeytaux RR, Beck RS, Dallara J. Dizziness: state of the science. Ann Intern Med. 134(9 pt 2): 823-32, 2001.