In-Home Monitoring of Postural Sway and Cognitive Loading in Older Adults with and without Mild Cognitive Impairment

By

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For Tamara,

Who saw potential in me,

Who embraced me as her own,

Who will forever remain in my heart,

And who will for always serve as my inspiration.

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ABBREVIATIONS

Cognitive Status

MCI	Mild Cognitive Impairment
aMCI	Amnestic MCI
naMCI	Non-amnestic MCI
AD	Alzheimer disease

Other Disease-Related Status

PD	Parkinson's disease

Cognitive Exams

MMSE	Mini-Mental State Examination
MoCA	Montreal Cognitive Assessment

Anatomical Directions

AP	anteroposterior
ML	mediolateral

Biomechanics / Sway Signal Terminology

CoM	center of mass
CoP	center of pressure
Acc	acceleration

Statistics

SD	standard deviation
SE	standard error
CoV	coefficient of variation
ANOVA	analysis of variance

Postural Sway Measurement Devices

WBB	Wii balance board
AFP	AMTI force plate

Quiet Stance Conditions

EO	eyes open
EC	eyes closed
FEO	foam eyes open
FEC	foam eyes closed

Associated Research Groups, Studies, Departments, Laboratories, etc.

OHSU	Oregon Health & Science University
LAADC	NIA – Layton Aging and Alzheimer's Disease Center
ORCATECH	Oregon Center for Aging and Technology
OLL	ORCATECH's Living Laboratory
ISAAC	Intelligent Systems for Assessing Aging Changes
ADNI	Alzheimer's Disease Neuroimaging Initiative
CES	Dr. Hiroko Dodge's Conversational Engagement Study
BD	Dr. Fay Horak's Balance Disorder's Laboratory

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ABSTRACT

Postural instability is one of the most common causes of dependence, reduced quality of life, and falls, the leading cause of injury and subsequent death for older adults. Older adults with cognitive impairment are at an increased risk of postural instability and falls due to decreased neural control. Although quantitative postural sway measures have been used to assess postural instability, postural sway in older adults with mild cognitive impairment (MCI) has yet to be measured frequently across time. Inspired by other longitudinal studies conducted within the framework of OHSU's Oregon Center for Aging and Technology (ORCATECH), we integrated a Nintendo Wii balance board and a tablet into ORCATECH's current in-home technological platform to extract daily measures of postural sway with and without cognitive loading in older adults with and without MCI. This dissertation reveals associations between frequent postural sway measures and cognitive functioning, assesses the feasibility of in-home monitoring of postural sway in older adults with MCI, and lays the foundation for large-scale, long-term implementation. Tracking longitudinal changes in postural sway may further our understanding of early-stage postural decline and its association with cognitive decline and may aid in preclinical detection of dementia and fall risk.

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CONFLICT OF INTEREST

Dr. Fay Horak has a significant financial interest in APDM, Inc., a company that may have a commercial interest in the results from *Chapter 3* of this PhD research (where APDM's Opal sensor was used to quantify postural sway). This potential conflict of interest has been reviewed and managed by OHSU.

CHAPTER 1: *Introduction*

1.1 Background

1.1.1. Postural Control, Falls, & Cognitive Impairment

Postural instability is one of the most common causes of dependence, reduced quality of life and falls, a leading cause of injury and subsequent death for older adults [1]. Postural instability is the result of abnormal neural regulation of the body's center of mass (CoM) position relative to the base of foot support. Achieving postural control, an essential daily life motor control function, is a complex motor skill derived from the integration of several neural components including cognitive processing, which plays a central role in balance maintenance and fall prevention [2]. Cognitive impairment compromises postural control and, in turn, increases fall risk [3]. Cognitively impaired older adults are at least twice as likely to fall (annual incidence of 60-80%) and endure more severe fall consequences compared to cognitively intact older adults [4,5]. Because both direct and indirect costs of falls are significant, rising and increasingly unsustainable for our healthcare system and because cognitive impairments and postural instabilities are both independent predictors of falls, there is a pressing need to further elucidate the relationship between cognitive status and postural control and to monitor, manage, and help improve postural stability in our aging population [3,5,6].

The relationship between cognitive impairment and postural control has elicited great interest since motor function changes/decline have been evidenced in older adults with cognitive decline [7-9] and cognitive impairment has been identified as an independent fall risk factor in older adults [1,4,10-15]. Cognitively impaired older adults often have less postural control compared to cognitively intact older adults, as shown in studies comparing older adults with no cognitive impairment to those with significant cognitive impairment (*e.g.*, manifest dementia) [16-20]. However the specific cause of postural instability in cognitively impaired older adults remains unknown because isolating the specific cognitive deficits that decrease postural stability in older adults who are significantly impaired is challenging due to the global nature of the cognitive deficits [21]. In turn, individuals with mild cognitive deficits, such as those with mild cognitive impairment (MCI), are ideal

candidates when studying the relationship between cognitive impairment and postural control since domain specificity of cognitive deficits may make it easier to quantify associations between specific types of cognitive deficits and postural control/decline.

1.1.2. Mild Cognitive Impairment (MCI)

Mild cognitive impairment (MCI) is the transitional state between healthy aging and early dementia, characterized by decline in one or more cognitive domains (*e.g.*, memory, executive function, attention, language, visuospatial, *etc.*) without significant impairment to daily life function. More specifically, MCI is cognitive impairment greater than what is normal for one's age but less than what is clinically diagnosed as dementia, affecting an estimated 19% of all older adults, and 29% of individuals over the age of 85 [22]. Older adults with MCI are 10- to 15-times more likely to develop Alzheimer's disease (AD) compared to cognitively intact older adults [23] – within a three year period about 41-64% of individuals with MCI converted to AD [24] – making MCI an ideal sample population when working to develop early markers of disease progression and functional decline.

Although the term "MCI" is a clinically fluid construct, MCI is widely recognized as a potentially heterogeneous condition consisting of cognitive domain-specific subtypes: amnestic MCI (aMCI) pertains to memory-based MCI and non-amnestic MCI (naMCI) pertains to non-memory-based MCI [25]. Because recent studies suggest that older adults with aMCI are more susceptible to AD conversion than older adults with naMCI, and because aMCI pertains to mild memory-based cognitive impairment, many consider aMCI to be the prodromal stage of AD – preserved general intellect, an intact ability to function in daily life and no clinically diagnosable AD symptoms, yet mild symptoms are present that suggest AD pathology [24]. The time course of disease progression (*i.e.*, rate of decline) and overall outcome appears to differ between MCI subtypes – older adults with naMCI are less likely to convert to AD or other forms of dementia – suggesting that the underlying disease pathology associated with naMCI may be completely different than that associated with aMCI (prodromal AD). Due to our limited access to MCI subjects (challenges with subject selection/recruitment is discussed in *Chapter 4*), we did not differentiate based on MCI subtype in this PhD research. However it is important to note that for future research where a larger MCI cohort is accessible, it may be important to

differentiate between MCI subtypes since specific cognitive functions and deficits directly influence the postural control system.

Postural instability has been observed in older adults with MCI [8,12,26-28]. In general, the way in which both postural control and MCI are defined varies from study to study and differs in precision. MCI definitions range from course (*e.g.*, below a given threshold on the Mini-Mental State Exam (MMSE) [29] or the Montreal Cognitive Assessment (MoCA) [30]) to fine (*e.g.*, either the Petersen/Winblad [25] or Jak/Bondi criteria [31], which both depend on thorough clinical and neuropsychological examinations) measurements. Postural control can either be measured quantitatively or qualitatively, but it is most often measured qualitatively in the clinic (*e.g.*, Tinetti Balance and Gait Assessment [32], Berg Balance Scale [33]), yielding subjective measures that are susceptible to measurement bias. Postural control is best measured quantitatively and objectively to increase the validity and reliability of observations linking MCI with postural instability.

1.1.3. Postural Sway & MCI

Postural control is often measured by characterizing postural sway (the small postural shifts in both the anteroposterior (AP) and mediolateral (ML) directions during quiet stance (*i.e.*, standing in place with a fixed foot position)). Postural sway has been shown to be related to age, postural stability and falls [27,34-43] and has been used to measure postural control in older adults both with and without cognitive impairment [27,44,45]. Postural sway abnormalities have been detected in older adults with MCI however the number of studies relying on quantitative measurements is limited [12,20,27,46-49]. Like postural control in general, current clinical measures of postural sway are acquired via rating scales and/or timed trials and are coarse, qualitative, subjective, influenced by clinician bias, and insensitive to mild postural instability [50]. Quantitative, objective postural sway measures are necessary to be sensitive to mild pathology, express experimental and clinical validity, and have good test-retest reliability [50,51]. This PhD research will lay the foundation to develop quantitative, objective, clinical postural sway measures capable of detecting mild postural instability specific to (and/or present in) older adults with MCI.

1.1.4. Quantifying Postural Sway

Postural sway is quantified by either the movement of the body's center of pressure (CoP) or the acceleration (Acc) of the body's CoM. Both CoP- and Acc-based measurement devices are currently used to measure postural sway.

1.1.4.i. CoP-based Measurement Devices

The Force Plate

Static stabilometry is the "gold standard" instrumental technique used to quantify both static (*i.e.*, postural sway) and dynamic postural control: a laboratory-grade force plate is used to measure the movement of the body's CoP within the limits of stability (which is bounded within the base of foot support during quiet stance). Prior research has shown force plate-based postural sway measures to be sensitive to mild postural instability in older adults with mild neurodegenerative diseases [52-54] and/or a high fall risk [55,56]. But because force plates are expensive and require proper installation, they are not feasible for quantifying postural sway in the home or small clinic environments.

The Nintendo Wii Balance Board

The Nintendo Wii balance board (WBB) (**Figure 1.1**) has recently generated significant interest in its application as a postural control measurement device in both the clinical and (basic, clinical, and rehabilitation) research domains. Because the WBB is incredibly affordable, portable, and easily-accessible, it has been proposed as an alternative to the "gold standard" laboratory-grade force plate. However, it is important to note that the WBB is an inferior CoP measurement device. It was designed and manufactured for entertainment purposes and does not come close to meeting the specifications required of a laboratory-grade measurement device. (The WBB's technological limitations are detailed in *Chapter 2, Part 1*). Nonetheless, the WBB may be used to derive CoP estimates once the WBB's measurement error is sufficiently characterized in the laboratory.

Figure 1.1: The Nintendo Wii balance board (WBB) as an alternative to the "gold standard" force plate to provide CoP estimates. The WBB is an affordable, portable, and easily-accessible alternative that may be used to estimate CoP-based postural sway measures once the WBB's CoP measurement error is fully characterized in the laboratory.

1.1.4.ii. Acc-based Measurement Device

The Body-Worn Inertial Sensor

Static posturography is an alternative instrumental technique that is affordable, portable and has been validated as a postural control measurement device: a wireless, body-worn inertial sensor (**Figure 1.2**) composed of a triaxial accelerometer and gyroscope is mounted to the approximate location of the body's CoM to measure the Acc of the body's CoM. Studies have shown that inertial sensor-based postural sway measures are valid and reliable and are also sensitive to postural sway features associated with age, mild neurodegenerative disease, and/or high fall risk [54,57-59].

Figure 1.2: Inertial sensors are validated as an alternative postural sway measurement device to the "gold standard" force plate. A wireless, body-worn inertial sensor (Opal sensor, APDM, Inc.) mounted to the approximate location of the body's CoM (*i.e.*, the trunk, or more specifically, near the L5 lumbar spine) is used to quantify Acc-based postural sway measures.

1.1.5. Objective Postural Sway Measures

Objective postural sway measures can be derived from both CoP- and Acc-based postural sway signals. Traditional, objective postural sway measures are based on the statistical mean or variance of the postural sway signal and are divided into two domains: time- and frequency-domain measures. Time-domain measures are based on the displacement, velocity, or acceleration of the CoP or Acc trajectory; frequency-domain measures characterize the area and shape of the power spectral density (obtained by a discrete Fourier transform of the time series) of the CoP or Acc trajectory [35,60]. Both traditional time- and frequency-domain postural sway measures have been shown to be sensitive to age [34,35,38-43], high fall risk [36], postural stability [37], neurodegenerative disorders (*e.g.,* cerebellar disorders [61], Parkinson's disease (PD) [37,62-69], and AD [44,70-72]), and even mild cognitive impairment as in MCI [27,44,46].

To the best of our knowledge, only five studies to date have used CoP-based measurement devices to quantify (time-domain) postural sway in older adults with MCI (and we have no knowledge of any studies using Acc-based measurement devices to quantify postural sway in MCI). Both Shin *et al.* [27] (using the WBB) and Young Jeon *et al.* [47] (using a force plate) derived postural sway distance and speed from the CoP-based signals. Both groups found higher measures of both distance and speed to be associated with MCI status. Deschamps *et al.* [46] (using a force plate) derived both the means and standard deviations (SD) of position, velocity, and the average absolute maximal velocity (AAMV) from the CoP-based signals and found higher SD velocity and AAMV to be associated with MCI status. Mignardot *et al.* [48] (using a force plate) derived AAMV from the CoP-based signals and found higher measures of AAMV to be associated with MCI status. And Sidorovich *et al.* [73] (using a force plate) derived confidence ellipse area from the CoP-based signals and found higher sway areas to be associated with MCI status. In sum, increasing distance and velocity-based measures appear to be a hallmark feature of MCI. To the best of our knowledge, no studies to date have assessed the relationship between frequency-domain postural sway measures and cognitive status. This PhD research will further the investigation of distinct postural sway features in MCI and will be the first to include frequency-domain measures as part of the analysis.

1.1.6. Cognitive-Postural Dual-Tasking

The attentional demand for regulating postural sway is typically examined with the dual-task paradigm, which presumes that cognitive and postural control compete for limited attentional capacity [74]. Cognitive loading during the postural task (dual-tasking) is thought to increase the difficulty level of the postural task by redirecting neural resources away from the postural task (*e.g.*, quiet stance) and to the cognitive task, however the effect of cognitive task on posture has been found to depend on the specific task type [74-76]. The amount of cognitive processing required for the dual-task condition depends on both the complexity of the postural and cognitive tasks and the capacity of the older adult's cognitive and postural control systems [2]. An individual's ability to maintain postural stability during cognitive loading decreases with age, with a decline in cognitive reserve, and further, with cognitive impairment [21,77-79]. Because cognitively impaired older adults often do not have sufficient neural resources to adequately regulate both tasks [80], the differences in postural sway between cognitively intact and impaired older adults will likely be more pronounced under dual-task conditions. Postural instability under dual-task conditions has been shown to predict both falls and cognitive decline [3] and may reveal mild cognitive and/or sensorimotor pathology affecting postural control. Thus in principle, postural instability in MCI may be too mild to detect under the single-task condition (quiet stance without cognitive loading), so the dual-task condition (quiet stance with cognitive loading) may be necessary to reveal mild pathology that would otherwise remain undetected [81].

For a healthy older adult, maintaining postural stability during quiet stance while tending to a cognitive dual-task requires minimal attention. Nonetheless, the primary postural task (*i.e.*, quiet stance) is compromised in the presence of a secondary task (*i.e.*, the added cognitive load), often quantified by an increase in postural sway from the single- to dual-task condition (*i.e.*, a positive postural dual-task cost) [82]. However some studies have observed the opposite – an increases in postural sway with the addition of a cognitive load (*i.e.*, a negative postural dual-task cost) [61,65] – leading us to believe that cognitive dual-task effect on postural likely depends on many different features (*e.g.*, sample population, primary postural task type, and secondary cognitive task type). Although the

specific neurophysiological mechanisms responsible for this postural dual-task cost are not yet fully understood [83], many hypothesize that the cognitive load interferes with postural control by competing for the same collection of neural resources [65]. Because of this, the specific type of cognitive load (taxing a specific cognitive domain, such as memory, executive function, attention, visuospatial, *etc.*) and task response (*e.g.*, verbal *vs.* nonverbal) may be critical and may dictate the type and/or severity of cognitive interference [74,75,84,85].

1.1.7. The Fundamental Insufficiencies of Infrequent Measures

There are fundamental insufficiencies in the current paradigm of infrequent measures [86]. Both cognitive and postural performance are inherently variable and become increasingly more variable during the initial stages of functional decline [87]. In existing longitudinal studies of cognition and/or motor (*e.g.*, postural) control, neurocognitive and postural control measures are acquired only once or twice a year. These infrequent measures reflect one instance of performance, do not measure changes in performance variability over time, and in turn may mask true status and decline in cognition and postural control. Therefore, current measures may not sufficiently represent the underlying longitudinal trends associated with the cognitive and postural control systems (**Figure 1.3**, modified from Hayes *et al.* [9]).

Frequent measures are often only attainable via in-home monitoring methods. In-home monitoring is an important assessment tool when working to infer true functional status since quantifying postural performance in the natural environment of one's home is likely more telling of true postural (dis)ability than that assessed in the unnatural environment of a clinic or laboratory. Additionally, by conducting postural assessments out of the clinic and in the absence of a task administer/rater, the potential influence of the white coat effect on postural performance is avoided. Physiological stress, indexed by elevated blood pressure, is often inherent to a doctor's visit and likely influences one's ability to perform in his/her natural state (*i.e.*, the white coat effect) [88]. In-home monitoring methods remove this artifact and preserve the integrity of the biomedical (postural control) signals.

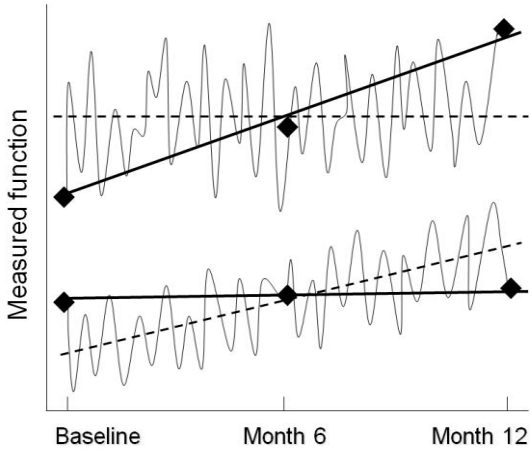

Figure 1.3: Infrequent measures are fundamentally insufficient when inferring true functional status. The solid lines represent the trends inferred by infrequent (semi-annual) measures of an unspecified (cognitive or motor) function. The dotted lines represent the underlying trends that are revealed due to frequent measures. The disconnect between infrequent and frequent measures applies to the function of postural control.

1.1.8. Pathophysiological Association between Cognitive & Postural Control

Prior research has identified pathophysiological associations between cognition and postural control [32], revealing cognition and postural control as interdependent processes. Although both cognitive and postural decline relate to old age, neither process is an imminent result of normal aging; functional decline is often coupled with age-related disease [89]. Models of aging with neurological disease assign variable behaviors to declining systems; instead of abrupt failure, both cognitive and postural control systems often demonstrate an initial period of increased variability during the depreciation of physiologic reserve [90]. Detecting variability in postural sway over time may result in the early detection of postural decline among elders (**Figure 1.4**, modified from ORCATECH). And because changes in postural control have been shown to far precede changes in cognition [91,92], such detection may predict cognitive decline, identify elevated risk of disease progression and other disease-related events such as falls, and yield the development and implementation of therapeutic interventions [49]. Early detection and intervention is integral when promoting independent living and increased quality of life because treatment during the initial stages of pathological processes may prevent subsequent neurodegeneration and progressive cognitive and/or motor decline.

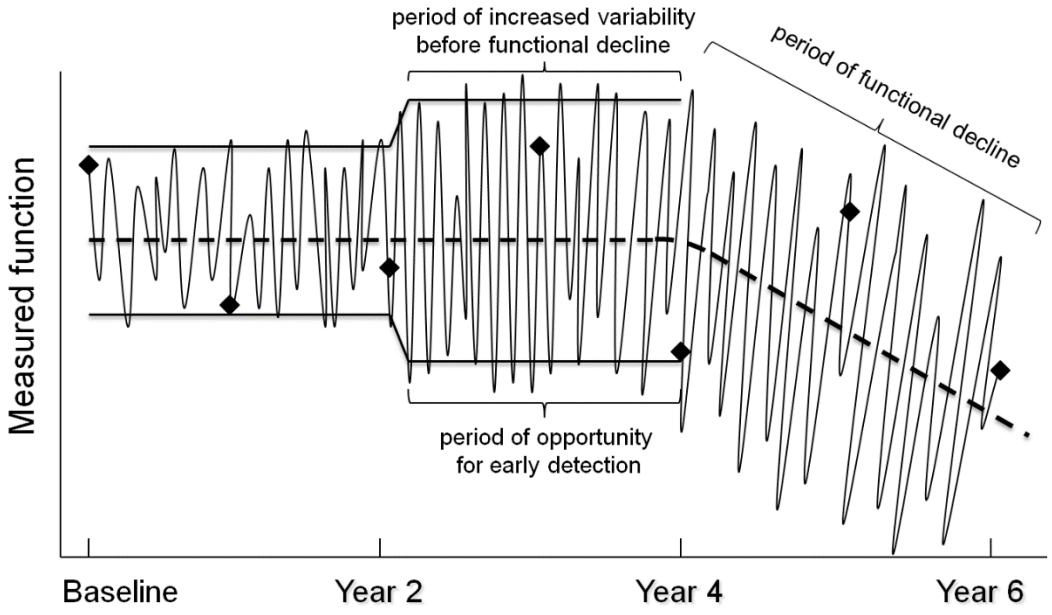

Figure 1.4: Importance of detecting variability in a measured function. The period of increased variability that precedes functional decline provides a critical opportunity for early detection. Infrequent (annual) measures of an unspecified (cognitive or motor) function do not sufficiently represent behavior. Frequent (semi-daily) measures of postural sway will enable early detection of both cognitive and motor decline.

1.2. Motivation & Impact

1.2.1. The Social & Economic Impact of Falls

Postural instability often results in falls, creating significant costs for the United States healthcare system. Falls are the leading cause of injury and subsequent death in the older adult population [5]. Approximately one third of all older adults fall each year [5] and 20-30% of all falls cause moderate to severe injuries that result in disability, loss of independence, and an increased risk of early death [6]. The frequency of falls and fall-related injuries rise in parallel with the increasing population of older adults; consequently, the costs associated with falls are projected to be over $240 billion by 2020 [93]. Both direct (emergency, acute, rehabilitation, and long-term care expenditures) and indirect (disability, dependence, and reduced quality of life) [6] fall costs are significant, rising, and increasingly unsustainable for our healthcare system [5].

1.2.2. The Social & Economic Impact of Aging & Age-Related Disease

Preserving independence, increasing quality of life, and providing proper medical care for older adults has become a multifaceted challenge. Extended life does not necessarily imply high quality of life. Because older adults now live longer, our elderly population, and healthcare costs associated with this population, continues to rise. Frequent, longitudinal, objective measures of postural sway may enable early detection of motor decline (*e.g.*, postural instability). Early detection of motor decline will likely predict future cognitive decline, identify elevated risk of disease progression and other disease-related events such as falls, and enable early healthcare planning which allows time for both the older adult and the care provider (family or professional) to make proper arrangements/adjustments. Early detection may also yield the development and implementation of therapeutic interventions [49]. Timely intervention is integral because treatment during the initial stages of disease state (*e.g.*, MCI) may prevent subsequent neurodegeneration and progressive motor and/or cognitive decline (*e.g.*, progression to dementia). This PhD research will lay the foundation for an integrated postural sway assessment system capable of extracting frequent, longitudinal, objective measures of postural sway in the natural environment of one's home. In turn, the proposed research will create potential for a future decrease in healthcare costs and an increase in quality of life and care for our older adults.

1.3. Chapter Overview

1.3.1. Chapter 1: Introduction

In this chapter, *Chapter 1*, we introduce the work carried out within the framework of this PhD research. We provide the reader with sufficient background to understand the basis of this work. We also detail the motivation and potential impact of this PhD research.

1.3.2. Chapter 2: Validation Study for the Postural Sway Measurement Device

In *Chapter 2*, we conduct two validation studies in effort to fully characterize the WBB's CoP measurement error and prepare for the use of the WBB as the sole CoP measurement device in our longitudinal, in-home study (*Chapter 4*). The "gold standard" laboratory-grade force plate is used as our ground truth in both validation studies. In

Chapter 2, Part 1, we validate the WBB against the force plate using simulated, one-dimensional postural sway signals produced by an inverted pendulum mechanical model. We observe a significant effect of sway amplitude, frequency, and direction on the WBB's measurement error and propose a linear signal adjustment to calibrate the WBB-based CoP (CoP_{WBB}) signals and help reduce CoP measurement error. A version of *Chapter 2, Part 1* was published in the *Sensors* on September 29, 2014 (ISSN 1424-8220). In *Chapter 2, Part 2*, we validate the WBB against the force plate using real, two-dimensional postural sway signals produced by healthy young adults. We observe far less CoP measurement error with real, biomedical signals. We propose an alternative linear signal adjustment based on human postural sway to better fit the CoP_{WBB} signals. We compare our calibrated CoP_{WBB} signals produced by our two linear calibration procedures to the uncalibrated CoP_{WBB} signals and determine that, despite the effort invested in calibration, the uncalibrated CoP_{WBB} signals contain less measurement error and best represent human postural sway.

1.3.3. Chapter 3: Cross-Sectional Study of Postural Sway in MCI

In *Chapter 3*, we conduct a cross-sectional study on postural sway, postural dual-task cost, and MCI. We use a body-worn inertial sensor to characterize the associations between cognitive status (intact *vs.* MCI) and postural control in older adults during quiet stance both with (dual-task) and without (single-task) cognitive loading. We find objective Acc-based measures of postural sway to differentiate between cognitive status groups. Both measures of postural sway (extracted from the single-task condition) and postural dual-task costs (extracted from the dual-task conditions) separate the MCI from the intact group. Our cross-sectional findings suggest that quantifying postural sway under the dual-task condition may help differentiate postural sway in older adults with MCI from cognitively intact older adults.

1.3.4. Chapter 4: Longitudinal Study of Postural Sway in MCI

In *Chapter 4,* we conduct a longitudinal, in-home study of postural sway in MCI within the ORCATECH framework. We integrate a WBB and a tablet into ORCATECH's current technological platform to administer cognitive tasks and extract measures of postural sway and postural dual-task cost. We monitor both cognitively intact and mildly cognitively

impaired older adults daily for 30 days. We use the uncalibrated CoP_{WBB} signals to provide daily estimates of postural control. We determine the feasibility of daily, in-home monitoring of postural sway and cognitive dual-tasking in an older adult population with MCI. We assess the reliability of objective postural sway measures across time. And, we characterize the association between mean and variability measures of postural sway and cognitive functioning. We find time-domain postural sway variability to be lower and frequency-domain postural sway to be higher in older adults who tested higher in cognitive functioning. Our findings suggest that changes in postural sway variability across time may serve as a sensitive biomarker for early cognitive decline.

1.3.5. Chapter 5: Conclusions & Future Direction

In *Chapter 5*, we summarize the studies conducted within the framework of this PhD research and discuss our overall findings. We conclude that our significant findings from our small (longitudinal) pilot study conducted on a small time scale motivate the large-scale implementation of this research over a more extended period of time (*e.g.*, months, years, and even decades). Tracking longitudinal changes in postural sway may further our understanding of early-stage motor decline and its association with cognitive decline and may aid in the early detection of dementia during the preclinical stages.

1.4. PhD Dissertation Contributions

This PhD dissertation presents contributions to three different fields: engineering, basic science, and applied/translational research. These contributions are detailed below:

1.4.1. Engineering Contributions

In *Chapter 2* we carry out a novel validation study to quantify the Nintendo WBB's CoP measurement error for controlled, dynamic input/output signals. The WBB has generated significant interest in its application as a postural control measurement device in both the clinical and (basic, clinical, and rehabilitation) research domains. Although the WBB has been proposed as an alternative to the "gold standard" laboratory-grade force plate, its CoP measurement error has not yet been fully characterized and therefore cannot yet be considered a valid and reliable CoP measurement device. Although previous

research has clearly specified the WBB's limitations when quantifying CoP under controlled static conditions, the WBB's CoP measurement error under controlled dynamic conditions remains unknown. Characterizing the WBB's performance under controlled dynamic conditions is imperative since most, if not all, potential WBB applications call for measuring biomedical signals which are dynamic by nature. The WBB has been used to measure CoP in many different human populations and under a variety of postural sway conditions in effort to test the WBB across varying sway profiles. Nonetheless, human sway remains an uncontrolled input signal, rendering the experimenter unable to systematically test the WBB's CoP measurement error with respect to specific postural sway features (e.g., sway amplitude, frequency, velocity, *etc*.). Because quantifying the WBB's CoP measurement error with controlled, dynamic input/output signals is fundamental in the effort to fully characterize the WBB's limitations as a CoP measurement device, *Chapter 2* of this dissertation serves as a significant contribution to the field of engineering.

In *Chapter 4*, we present a novel method to measure postural sway frequently over time from the comfort and ease of the home environment. Two off-the-shelf technologies (the Nintendo WBB and the Barnes & Noble Nook tablet) are integrated with ORCATECH's current in-home technological platform to quantify postural sway daily across time. A custom-written application is designed and built to continuously run on the tablet, providing both a user interface for the subject as well as means to acquire, store, and transfer both postural sway and cognitive performance data automatically and immediately once data is received. This PhD research determined that longitudinal, in-home monitoring of postural sway is feasible within the in-home environment and lays the foundation for large-scale implementation. Because activity and behavioral health monitoring systems have generated significant interest in recent years and because postural sway is considered a sensitive health outcome measure, the technological development accomplished within the framework of this dissertation serves as a significant contribution to the field of engineering.

1.4.2. Basic Science Contribution

In *Chapter 3*, we present the results of our novel cross-sectional study on postural sway and domain-specific cognitive loading in older adults with and without MCI. First we find more postural sway to be associated with MCI during quiet stance, a finding that is supported by the literature. Then we find added cognitive loads to have less of an effect on postural sway (quantified by lower postural dual-task costs) in the MCI group compared to the intact group, a finding that is not substantially supported by the literature but may be of interest since we are the first study to use our specific cognitive load-types as cognitive dual-tasks during quiet stance in an older adult (MCI) population. The significance of this finding and how it compares to previous findings is discussed in greater detail in *Chapter 3, Section 3.4.1.* Both the experimental methods and findings from our cross-sectional study in *Chapter 3* are novel and serve as contributions to the field of basic science.

In *Chapter 4*, we present the results of our novel longitudinal study on postural sway and cognitive loading in older adults with and without MCI. The natural variability of postural sway across time remains unknown. We are the second (small pilot) study to quantify postural sway daily across weeks in older adults. We are the first study to add a secondary cognitive load to the primary postural task as well as the first to include older adults with MCI in our sample population. The most promising results from our small pilot study pertain to the relationship between postural sway variability (quantified by the variance in postural sway across the 30-day monitoring period) and cognitive functioning (quantified by cognitive global z-scores). We find more day-to-day variability in time-domain postural sway and less day-to-day variability in frequency-domain postural sway to be related to lower cognitive functioning. Our time-domain (*i.e.,* distance and area-based postural sway measures) findings are consistent with the literature (discussed previously in *Chapter 1, Section 1.1.8*) and couple well with findings from other ORCATECH studies: increased variability in motor function is related to (and may be found to precede) a decrease in cognitive function over time. We are the first to assess the variability of the frequency content of a motor/postural control signal and relate it to cognitive status/decline. Our frequency-domain results are the inverse of our time-domain results and may prove to be of significance if our findings are reproduced with a larger sample population and on a

larger time-scale. Both the experimental methods and findings from our longitudinal study in *Chapter 4* are novel and serve as contributions to the field of basic science.

1.4.3. Applied/Translational Research Contribution

Our in-home technological setup from our longitudinal study has potential to contribute greatly to the field of applied/translational research. In *Chapter 4*, we determine longitudinal monitoring of postural sway feasible within the in-home environment and lay the foundation for large-scale implementation. Our in-home technological setup may be applied for the purpose of therapeutic intervention: to help an individual maintain and/or improve his/her dual-tasking ability, a necessary skillset for independent living and the safe execution of activities of daily living. Studies have shown that dual-task training reduces the impact of cognitive distractions on postural sway in older adults [94], and substantial gains after dual-task training are sustained even with new task combinations involving new stimuli [95]: these findings suggest that dual-task skills can be substantially improved in older adults and that cognitive plasticity in attentional control is attainable even in old age [95]. So by simply installing our system (after making the necessary technological improvements detailed in *Chapter 5*, Section 5.1.2.vi), we could easily implement a dual-task training program to help improve and/or sustain dual-task skills in older adults, which in turn may directly aid in fall prevention. Relatively little time, effort, and resources would be required to implement this system in all homes outfitted with ORCATECH equipment and supported by ORCATECH researchers and staff. A significant amount of gain could be acquired with little additional work and financial support.

As discussed in *Chapters 4 & 5*, large-scale research deployment of in-home monitoring is an impressive feat with great potential to facilitate the study of both healthy aging and disease-related processes. Our longitudinal study also contributes to the field of applied/translational research by laying the foundation for longitudinal tracking of postural sway from the comfort of one's home. Tracking longitudinal changes in postural sway across a larger time-scale may further our understanding of early-stage postural decline and its association with cognitive decline and may aid in the early detection of dementia during the preclinical stages. Early detection may also yield the development and implementation of therapeutic interventions [49,96]. Timely intervention is integral because treatment

during the initial stages of disease state (*e.g.*, MCI) may prevent subsequent neurodegeneration and progressive motor and/or cognitive decline (*e.g.*, progression to dementia).

CHAPTER 2, Part 1: *Validation Study for the Postural Sway Measurement Device**:** Validating and Calibrating the Nintendo WBB to Derive Reliable Measures of Postural Sway Based on Simulated One-Dimensional Postural Sway Signals Acquired from an Inverted Pendulum*

Summary

Objective: To characterize the Nintendo Wii balance board's (WBB) CoP measurement error, using the "gold standard" laboratory-grade force plate as ground truth, in preparation to use the WBB as the sole CoP measurement device in our in-home study (*Chapter 4*).

Methods: The WBB and a laboratory-grade AMTI force plate (AFP) were used to simultaneously measure the CoP displacement of a controlled dynamic load, which has not been done before. A one-dimensional inverted pendulum was displaced at several different displacement angles and load heights to simulate a variety of postural sway amplitudes and frequencies (< 1 Hz). Twelve WBBs were tested to address the issue of inter-device variability.

Results: There was a significant effect of sway amplitude, frequency, and direction on the WBB's CoP measurement error, with an increase in error as both sway amplitude and frequency increased and a significantly greater error in the mediolateral (ML) (compared to the anteroposterior (AP)) sway direction. There was no difference in error across the 12 WBB's, supporting low inter-device variability. A linear calibration procedure was then implemented to correct the WBB's CoP signals and reduce measurement error. There was a significant effect of calibration on the WBB's CoP signal accuracy, with a significant reduction in CoP measurement error (quantified by root-mean-squared error) from 2–6 mm (before calibration) to 0.5–2 mm (after calibration). WBB-based CoP signal calibration also significantly reduced the percent error in derived (time-domain) CoP sway measures, from −10.5% (before calibration) to −0.05% (after calibration) (percent errors averaged across all sway measures and in both sway directions).

Conclusions: In this study, we characterized the WBB's CoP measurement error under controlled, dynamic conditions and implemented a linear calibration procedure for WBB CoP signals that is recommended to reduce CoP measurement error and provide more reliable estimates of time-domain CoP measures. Despite our promising results, additional work is necessary to understand how our findings translate to the clinical and rehabilitation research domains. Once the WBB's CoP measurement error is fully characterized in human postural sway (which differs from our simulated postural sway in both amplitude and frequency content), it may be used to measure CoP displacement in situations where lower accuracy and precision is acceptable, such as in our in-home study.

*A version of **CHAPTER 2, Part 1** was published in Sensors on 29 September 2014: Sensors 2014, 14, 18244-18267; doi:10.3390/s141018244*
***ISSN 1424-8220**, www.mdpi.com/journal/sensors*

2.1.1. Introduction

The Nintendo WBB has generated significant interest beyond the public domain, particularly in its application as a postural sway measurement device in both the clinical and (basic, clinical, and rehabilitation) research domains. Posturography is the traditional instrumental technique used to objectively quantify postural sway. This technique uses one or two laboratory-grade force plates to measure two-dimensional center of pressure (CoP) displacement. Prior research has shown force plate-based CoP measures to be sensitive to mild postural instability in older adults with mild neurodegenerative diseases and/or a high fall risk [27,37,39,40,42,52,53,55,97]. However, because force plates are expensive, not easily portable, and require proper installation, they are not feasible for quantifying postural sway in the small clinic or home on a frequent basis. Although, frequently quantifying postural sway in the laboratory is neither reasonable nor economical. The WBB has been recently proposed as an affordable, portable, and easily accessible alternative to the force plate [98-103], however additional research is necessary before the WBB can be considered a valid and reliable CoP measurement device.

Both the WBB and laboratory-grade force plate measure force distribution and the resultant CoP displacement. However, there are significant differences between devices, pertaining to both material composition and technical capacity, which result in functional limitations of the WBB. Force plates are composed of metal while the WBB is composed of plastic. Due to the WBB's material properties, it is susceptible to elastic deformation when a significant load is applied to the WBB's usable surface. If the usable surface deforms during data acquisition, the WBB's ability to acquire accurate CoP measurements may be hindered. Also, both devices rely on four force sensors located near each of the four corners of the plate or board to measure force distribution. Force plates measure tri-axial forces and moments while the WBB only measures uni-axial (vertical) forces. Because the WBB is unable to measure moments and horizontal forces, its ability to acquire

accurate CoP measurements may be hindered when the input signal has significant horizontal and shear components. The WBB's accuracy is further restricted by several mechanical and electronic limitations, characterized in a 2011 publication on the differences between the WBB and a force plate. Pagnacco *et al.* [104] clearly substantiated the WBB's low resolution (0.5 mm), low and inconsistent sample rate (time jitter), low signal to noise ratio, and occasional glitches in the WBB data (discussed further in *Section 2.1.4*). According to the authors, a significant amount of noise in the WBB data can be attributed to the unshielded cables, under-designed electronics (incapable of noise minimization), and unsynchronized sampling across the four force sensors. These limitations, along with the uncertain validity and reliability of WBB-based CoP measures derived from a dynamic input signal, currently restrict our utilization of the WBB for clinical or research purposes.

Many studies have used the WBB to quantify postural sway in varying populations (*e.g.*, healthy young, healthy old, and impaired old) and under varying sway conditions (*e.g.*, eyes open *vs.* eyes closed, single- *vs.* double-leg stance, *etc.*) [98-102]. In all but two prior studies [99,104], the WBB and force plate were used to measure CoP displacement during separate trials. Although WBB- and force plate-based CoP measures were found to be highly correlated, CoP measurement error could not be determined since CoP displacement was not measured simultaneously by the WBB and force plate. In 2011, Pagnacco *et al.* [104] were the first to simultaneously measure CoP displacement with the WBB and force plate, eliminating within-subject variability and increasing the validity of their between-device comparison. Unlike in previous work [98], Pagnacco and colleagues chose to not calibrate the WBB data using a custom calibration method and used the manufacturer's internally-stored values instead. The authors relied on the WBB's internal calibration values *vs.* those determined empirically because a custom calibration method is expensive, time intensive, and neither affordable nor feasible for most users. Also, according to Pagnacco *et al.*, custom calibration detailed in Clark *et al.* [98] has minimal effect on the noise inherent in the WBB data. For data acquisition, the authors quantified the WBB's CoP measurement error for two "subjects"—A 50 kg dead weight and a 48 kg, 1600 mm tall human—During 60 s of quiet stance. In doing so, Pagnacco and colleagues characterized

the WBB's mechanical and electronic limitations as a CoP measurement device (discussed above). Despite the aforementioned limitations and Pagnacco's strong recommendation to not use the WBB for anything other than its intended use (*i.e.,* as a toy) [104,105], the WBB continued to generate significant interest in both the clinical and research domains.

In 2013, Huurnink *et al.* [99] were the second to measure CoP displacement with the WBB and force plate simultaneously. The authors investigated postural sway in 14 healthy, young adults under three different sway conditions (single-leg stance with eyes open, with eyes closed, and after a short sideways hop). Although Huurnink and colleagues determined the WBB as "sufficiently accurate" when measuring CoP displacement, they only investigated a narrow CoP displacement range (*i.e.,* which was restricted to the area of the standing footprint during their single-leg stance conditions) and quantified CoP using only two, two-dimensional time-domain measures (mean sway amplitude and velocity). Because Huurnink *et al.* did not assess one-dimensional (AP *vs.* ML) CoP measures, they were unable to quantify the WBB's dimension-specific performance error (*e.g.,* the WBB may be more accurate in measuring sway in the AP direction compared to that in the ML direction). Additionally, the authors did not assess the WBB's ability to measure frequency content, nor did they assess the inter-device variability across multiple WBBs [99].

Information typically available for laboratory-grade force plates, such as measurement uncertainty and reliability across varying sway conditions and measurement variability across multiple devices, was unavailable for the WBB until a recent 2014 publication by Bartlett *et al.* [103]. Bartlett and colleagues conducted a standard measurement uncertainty analysis to quantify the repeatability and accuracy of WBB CoP measurements. They also assessed the effect of wear (lightly used *vs.* heavily used WBBs) on CoP measurement performance. Two different static loads (14.3 kg and 45.8 kg) were systematically applied to five specified locations on the WBB's usable surface (center and four corner positions located approximately halfway from the WBB's center to the corner edges). Nine WBBs (three lightly used, six heavily used) were tested. The authors found the total uncertainty of CoP measurement to be within ±4.1 mm across the nine WBBs, which is much higher than that recommended for posturography (0.1 mm). They found repeatability within a single WBB to be better (1.5 mm), suggesting that the WBB be applied as a relative (*vs.*

absolute) CoP measurement device (*i.e.*, comparing measurements within, as opposed to across, WBBs). Consistent with previous findings [106], Bartlett *et al.* found the WBB to behave linearly, with a statistically significant increase in error from the center to the corner locations and from the light to heavy static loads. There was no significant effect of wear on mean CoP measurement error. Additionally, the authors found the WBB's internal calibration values to be comparable to those determined empirically. According to Bartlett *et al.*, although the WBB lacks the accuracy recommended for posturography and should not be used as a replacement for the "gold standard" laboratory grade force-plate, it may be used to estimate force and CoP measurements when lower accuracy and precision is acceptable [103]. In static analyses, the WBB may be sensitive to postural sway differences greater than 10 mm, which could differentiate between healthy and impaired populations [103,107].

Although Bartlett *et al.* clearly specified the WBB's limitations when measuring CoP under controlled static conditions, the WBB's CoP measurement error under controlled dynamic conditions remains unknown. Characterizing the WBB's performance under controlled dynamic conditions is imperative since most, if not all, potential WBB applications call for measuring biomedical signals which are dynamic by nature. As mentioned above, the WBB has been used to measure CoP in many different human populations and under a variety of postural sway conditions in an effort to test the WBB across varying sway profiles. Nonetheless, human sway remains an uncontrolled input signal, rendering the experimenter unable to systematically test the WBB's CoP measurement error with respect to specific postural sway features (*e.g.*, sway amplitude, frequency, velocity, *etc.*). Quantifying the WBB's CoP measurement error with controlled, dynamic input/output signals is fundamental in our effort to fully characterize the WBB's limitations as a CoP measurement device.

In this study, we used the WBB and a laboratory-grade force plate (AFP) (AMTI OR6-6, Watertown, MA, USA) to simultaneously measure one-dimensional CoP displacement of controlled, dynamic input/output signals. An inverted pendulum mechanical system was employed as our dynamic load so we could systematically modulate CoP displacement (*via* adjustments made to the inverted pendulum's displacement angle and load height). The

WBB's CoP measurement error was quantified and analyzed with respect to sway amplitude, frequency, and direction (AP *vs.* ML). Twelve WBBs were tested to address the issue of inter-device variability. Our two research aims were: Aim I, to validate the WBB against the "gold standard" AFP by quantifying the WBB's CoP measurement error under controlled dynamic conditions; and, Aim II, to determine the WBB's inter-device variability across 12 different WBBs.

2.1.2. Experimental Methods

Our experiment was conducted under controlled laboratory conditions using an inverted pendulum mechanical system (described in *Section 2.1.2.1* and illustrated in **Figure 2.1.1**) to simulate one-dimensional postural sway. We carried out one laboratory experiment to address our two research aims. For Aim I, we tested a variety of sway amplitudes and frequencies in both sway directions to validate the WBB against the AFP. For Aim II, we repeated our Aim I testing protocol (detailed in *Section 2.1.2.2*) with 12 different WBBs to determine the WBB's inter-device variability. All data were collected at the Oregon Health & Science University using resources and materials from the Balance Disorder's Laboratory and the Human Spatial Orientation Laboratory.

2.1.2.1. Description of Mechanical System

A single inverted pendulum mechanical system (**Figure 2.1.1C**) was constructed to simulate one-dimensional postural sway. Springs (**Figure 2.1.1C**) were employed to counteract gravitational forces and stabilize the pendulum at equilibrium (perpendicular to the ground). The inverted pendulum weighed 15.1 kg, with most of its weight concentrated at the base. The pendulum was loaded to the maximum tolerable weight (16.0 kg) at the approximate height of a human body's center of mass (CoM) [108,109]. Four lead blocks, each weighing ~6.8 kg, were then positioned symmetrically on the pendulum's base (**Figure 2.1.1B**) to stabilize the loaded pendulum as it oscillated. Therefore, the total mass of the mechanical system was $15.1 + 16.0 + 4 \times 6.8 = 58.3$ kg. To simulate one-dimensional postural sway, the inverted pendulum was displaced at a specified angle and then released. The pendulum oscillated, following a dampened oscillation pattern due to internal friction

and air resistance. To test a variety of sway amplitudes and frequencies (for Aim I), we systematically adjusted both the displacement angle and load height prior to each trial.

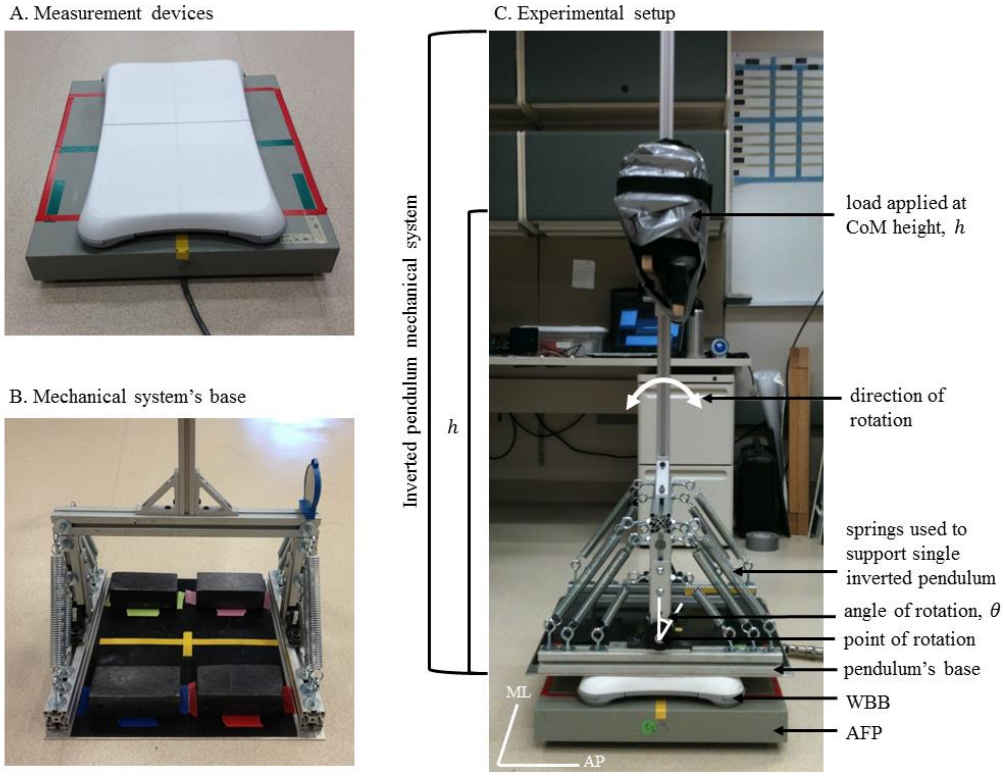

Figure 2.1.1: Experimental setup to measure simulated one-dimensional postural sway. (**A**) The Nintendo Wii balance board (WBB) mounted and centered on the AMTI force plate (AFP). (**B**) Four (6.8 kg) lead blocks positioned symmetrically on the mechanical system's base to stabilize the inverted pendulum during oscillation. (**C**) The experimental setup: the mechanical system was mounted and centered on the WBB, which was mounted and centered on the AFP. The mechanical system consisted of a single inverted pendulum supported by springs (15.1 kg), a (16.0 kg) load applied at the CoM height, *h*, and four lead blocks positioned on the base to stabilize the inverted pendulum during oscillation. The inverted pendulum was displaced at a specified angle, θ_i, and then released to oscillate in the AP direction. The mechanical system was rotated 90º to acquire one-dimensional sway in the ML direction.

2.1.2.2. Procedures

Aim I: to validate the WBB against the AFP. The mechanical system was mounted and centered on the WBB (**Figure 2.1.1C**), which was mounted and centered on the AFP (**Figure 2.1.1A**). Our testing protocol consisted of nine 30-second trials to test a variety of sway amplitudes and frequencies: three initial displacement angles (θ_i = 2, 4 and 6°) at three

different load heights ($h = 900$, 1000 and 1100 mm, corresponding to three different oscillation frequencies (ω) 0.6, 0.5, and 0.4 Hz, respectively). Because the pendulum oscillated in one-dimension, the testing protocol was repeated twice to acquire sway data in both the AP and ML directions, for a total of 18 30-second trials for each WBB. (NOTE: the mechanical system was rotated 90º to acquire sway data in the ML direction (**Figure 2.1.1C**)).

Aim II: to determine the WBB's inter-device variability. The Aim I testing protocol detailed above was repeated 12 times with 12 different WBBs. Two WBBs had been lightly used and the remaining 10 were new.

CoP displacement was measured by both an AFP and a WBB. The WBB functions with four force sensors housed in the foot-pegs located under each of the four corners of the WBB (**Figure 2.2.2B**). The force sensors act as uni-axial force transducers, each consisting of a metal beam and strain gauge, and measure vertical forces [103]. The WBB was interfaced with a laptop computer (operating on Microsoft Windows Vista) using custom-written software (C++) and a Bluetooth connection. The initial (vertical) offset was recorded by each of the four force transducers when the WBB was first connected, before the mechanical system was positioned atop the WBB's usable surface (**Figure 2.1.2A**). During data acquisition, both raw sensor values and internal calibration values (issued at three different calibration points) were reported for each of the four force transducers. The raw sensors values were converted into calibrated mass measurements (in kg) using the internal calibration values and the initial (vertical) offset and were then converted into force units (N). (The use of the manufacturer's internally-stored calibration values to calibrate WBB data is justified in by Pagnacco *et al.* [104]). The calibrated sensor values were then stored as our WBB data. The AFP was calibrated in accordance with the manufacturer's recommendations. The initial (tri-axial) offset was recorded by the AFP prior to data acquisition, when the WBB was mounted and centered on the AFP, but before the mechanical system was positioned atop both measurement devices. The weight of the WBB was subtracted from the vertical force channel of the AFP's initial offset. This adjusted offset, excluding the vertical force applied by the weight of the WBB, was then used to

calibrate the AFP measurements. Calibrated tri-axial forces and moments were stored as our AFP data.

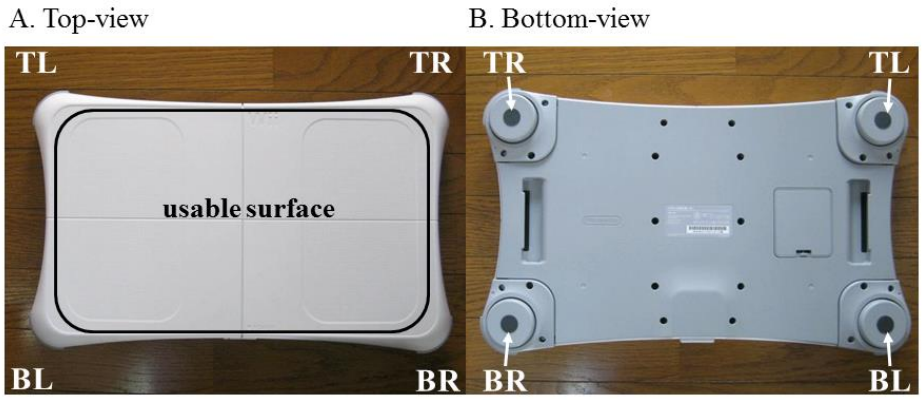

Figure 2.1.2: The WBB's usable surface and sensor location. (**A**) Top-view of the WBB shows the usable surface. (**B**) Bottom-view of the WBB shows the four foot-pegs, located under each of the four corners of the WBB: top right (TR), top left (TL), bottom left (BL), and bottom right (BR). The four force sensors are housed in the four foot-pegs.

2.1.2.3. Data Acquisition

To determine an appropriate sampling rate, the spectral characteristics of our simulated postural sway were first examined. During pilot testing, the inverted pendulum's maximum oscillation frequency (induced by the shortest load height) was found to be 0.6 Hz. All frequency content within the power spectrum lay below 1.0 Hz for all tested displacement angles and load heights.

The WBB sampled at approximately 50 Hz when interfaced with our laptop computer. Because the WBB samples at an inconsistent rate, a data averaging method was employed to create time series with samples at equal time intervals (t_{DA}). During data acquisition, our custom-written software averaged across (approximately 3–6) samples every 93.75 ms (t_{DA} = 0.09375 s; data averaging frequency, $f_{DA} = 1/t_{DA}$ = ~10.7 Hz). Although a rate of ~10.7 Hz is low compared to what is clinically recommended for posturography [110], it was high enough to capture the spectral characteristics of our simulated postural sway since all frequency content lay below 1.0 Hz.

The AFP sampled at 100 Hz, and a 10.5 Hz low-pass filter was applied during data acquisition.

2.1.2.4. Data Analysis

All data were analyzed in Matlab R2014a (The MathWorks, Natick, MA, USA).

2.1.2.4.i. CoP Signals

To account for the inherent (yet small) positioning errors during the experimental setup (described in *Section 2.1.2.1*: The mechanical system was mounted and centered atop the WBB, which was mounted and centered atop the AFP), a Principal Component Analysis [111] was used to transform the (x- and y-) axes of both the WBB and AFP data sets. CoP displacement (in both the AP (y-axis) and ML (x-axis) directions) was then calculated from the transformed axes of both WBB and AFP data.

WBB-Based CoP Signals

The WBB measures vertical (z-axis) ground reaction forces but is unable to measure horizontal (x- or y-axis) forces and (x-, y-, and z-axis) moments (**Figure 2.1.3**). Specifically, the CoP calculations used for the WBB data do not take horizontal and shear components into account. The WBB's calibrated sensor values were expressed in force units (N). The vertical forces (F_{TR}, F_{BR}, F_{TL}, F_{BL}) measured by each of the four force transducers were then used to calculate CoP for the WBB (CoP_{WBB}):

$$CoP_{WBB_x} = \frac{X}{2}\frac{(F_{TR} + F_{BR}) - (F_{TL} + F_{BL})}{F_{TR} + F_{BR} + F_{TL} + F_{BL}};$$
$$CoP_{WBB_y} = \frac{Y}{2}\frac{(F_{TR} + F_{TL}) - (F_{BR} + F_{BL})}{F_{TR} + F_{BR} + F_{TL} + F_{BL}} \quad (2.1.1)$$

where X and Y represent the distance (in mm) between each force transducer assuming that each transducer is positioned in the center of each foot-peg, and CoP_{WBB_x} and CoP_{WBB_y} represent the CoP displacement (in mm) calculated in the ML and AP directions, respectively [112].

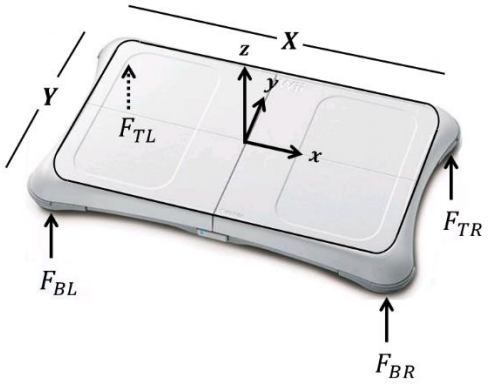

Figure 2.1.3: Diagram of the WBB. Accurate X and Y dimensions are essential for accurate CoP calculations: X = 433 mm, Y = 238 mm.

AFP-based CoP signals

The AFP measures tri-axial (x-, y-, and z-axis) forces (F) and moments (M) (F_x, F_y, F_z, M_x, M_y, and M_z), providing the "gold standard" measurement of CoP. For our experimental setup, a given motion of the inverted pendulum produced a different CoP displacement at the surface of the WBB compared to the surface of the AFP due to: 1. the additional height of the WBB (h_{WBB}), and 2. the additional (static) force applied to the surface of the AFP from the weight of the WBB (F_{WBB}) (**Figure 2.1.4**). In order to compare CoP measured by the AFP to that measured by the WBB (CoP_{WBB}), a CoP prediction (CoP_{AFP}' and in **Figure 2.1.4**) of the CoP at the surface of the WBB was derived from AFP data and known parameters of the experimental setup.

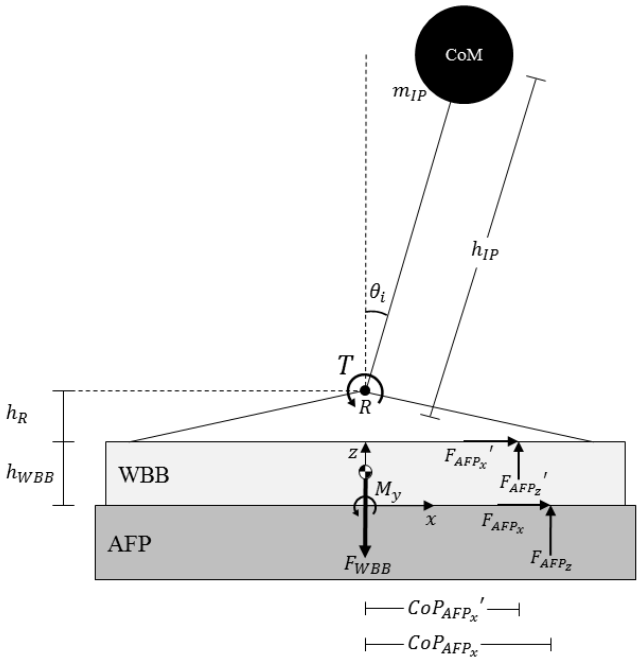

Figure 2.1.4: Simplified diagram of the experimental setup for x-direction CoP displacement. (NOTE: $F_{AFP_x}' = F_{AFP_x}$ since these values reflect the acceleration of the CoM, which is the same for both the WBB and AFP).

First, x-direction CoP displacement was calculated (CoP_{AFP_x}) in accordance with AMTI Biomechanics Platform Instructions Manual. Then, the predicted CoP at the WBB surface (CoP_{AFP_x}') was calculated using the following procedure:

1. With known CoP_{AFP_x}, moments were summed about the point of rotation, R to calculate T:

$$T = CoP_{AFP_x}F_{AFP_z} + (h_R + h_{WBB})F_{AFP_x} \tag{2.1.2}$$

2. With known T, the AFP's prediction of the WBB's CoP measurement was calculated:

$$CoP_{AFP_x}' = [T - h_R F_{AFP_x}']/F_{AFP_z}' \tag{2.1.3}$$

where, $F_{AFP_x}' = F_{AFP_x}$, $F_{AFP_z}' = F_{AFP_z} - F_{WBB}$, $F_{WBB} = m_{WBB}g$, m_{WBB} = the mass of the WBB, and

g = acceleration due to gravity.

A similar calculation was made for CoP displacement in the y-direction. The AFP-derived signals CoP_{AFP_x}' and CoP_{AFP_y}' were then compared to the WBB-based CoP (CoP_{WBB_x} and CoP_{WBB_y}) obtained using Equation (2.1.1).

Influence of displacement angle and load height on CoP displacement

As expressed in Equation (2.1.3) and illustrated in **Figure 2.1.4**, the AFP's prediction of the WBB's CoP displacement = = $CoP_{AFP_x}' = [T - h_R F_{AFP_x}'] / F_{AFP_z}'$. The distance from *R* to the surface of the WBB (h_R) is a constant and the vertical force (F_{AFP_z}') is unaffected by changes in both displacement angle (θ) and load height (h). So, CoP displacement is dependent on both T and the horizontal force (F_{AFP_x}'), which are both functions of θ_i and h:

$$T(t) = (k - m_{IP}gh)\theta(t) \tag{2.1.4}$$

where k = the spring constant of springs supporting the inverted pendulum, m_{IP} = the mass of the inverted pendulum mechanical system, h = the height of m_{IP} above the rotation axis, and t = time. Ignoring any damping, the angular motion of the inverted pendulum is given by:

$$\theta(t) = \theta_i \sin(\omega t) \tag{2.1.5}$$

where ω is the oscillation frequency of the inverted pendulum, and θ_i = the initial angular displacement of the pendulum. From torsion pendulum mechanics, the oscillation frequency is given by:

$$\omega = \sqrt{(k - m_{IP}gh)/m_{IP}h^2} \tag{2.1.6}$$

Thus as h increases ω decreases.

The horizontal shear is proportional to the horizontal acceleration of the pendulum mass:

$$F_{AFP_x}{}' = -m_{IP}\ddot{x} \approx -m_{IP}h\ddot{\theta}(t) = m_{IP}h\theta_i\omega^2 sin(\omega t) \tag{2.1.7}$$

So,

$$CoP_{AFP_x}{}'(t) = [(k - m_{IP}gh - h_R m_{IP}h\omega^2)\theta_i \sin(\omega t)]/F_{AFP_z}{}' \tag{2.1.8}$$

Therefore, the main effect is that larger θ_i produces larger CoP_{AFP_x}' but a secondary effect is that a shorter load height h also produces a larger CoP_{AFP_x}'.

CoP Signal Processing

All CoP signals were low-pass filtered with a fourth-order, zero-phase Butterworth filter with a cutoff frequency of 5 Hz [35]. Because the WBB sampled at a different rate than the AFP, the CoP_{WBB} signals were resampled at 100 Hz to match the CoP_{AFP}' sampling rate. Additionally, because the WBB and AFP were not time-aligned during data acquisition, offline signal synchronization was necessary. To synchronize offline, the CoP_{WBB} and CoP_{AFP}' signals were zero-meaned, cross-correlated using a Hanning window, and time-aligned.

2.1.2.4.ii. CoP Measures

Time- and frequency-domain CoP measures (**Table 2.1.1**) were derived from the last 25 s of both the CoP_{WBB} and CoP_{AFP}' signals. The calculations of the time-domain measures are detailed in Prieto *et al.* [35]. The single frequency-domain measure, peak frequency, was determined by finding the frequency index of the power spectrum at which the maximum power lies. The power spectrum was estimated using Welch's method [111].

Table 2.1.1: CoP-based measures. Time- and frequency-domain CoP measures derived from both the WBB- and AFP-based one-dimensional CoP signals.

Measure	Abbr.	Description	Units
Time-Domain Measures			
Mean distance, or sway amplitude	*MD*	Average distance from the center of the CoP time series	*mm*
Root-mean-squared distance	*RMS*	The standard deviation (SD) of the zero-meaned CoP time series	*mm*
Sway range	*RANGE*	Peak-to-peak range, or maximum distance, of the CoP values	*mm*
Mean velocity	*MV*	Average velocity of the CoP time series	$mm \cdot s^{-1}$
Frequency-Domain Measure			
Peak frequency	*PFREQ*	Peak frequency of the power spectrum	*Hz*

2.1.2.4.iii. Quantifying the WBB's Performance by Determining CoP Measurement Error

The CoP measurement error was differentiated into two parts: CoP signal error and CoP measure error. The CoP signal error (defined below) pertains to the difference between the CoP_{WBB} and CoP_{AFP}' signals. The CoP measure error (defined below) pertains to the difference between the WBB- and AFP-based CoP measures defined in **Table 2.1.1**.

The WBB's performance was first quantified by comparing the CoP signals (CoP_{WBB} *vs.* CoP_{AFP}'). The CoP signal error was defined as the difference (in mm) between the WBB CoP measurement and the AFP CoP measurement ($CoP_{WBB} - CoP_{AFP}'$). This error value was calculated for each data point in every trial (across all sway amplitudes and in both directions) for each WBB. Agreement between measurement devices (AFP *vs.* WBB) was visually represented by plotting the CoP signal error against the "gold standard" AFP CoP measurement (CoP_{AFP}'). Simple linear regression was used to fit a straight trend line to the CoP signal error plotted against the CoP_{AFP}' signals: $CoP_{WBB} - CoP_{AFP}' = \beta * CoP_{AFP}' + \alpha$. The slope of the trend line (β coefficient) was then used to quantify CoP signal error as a function of both sway amplitude and direction.

The WBB's performance was then quantified by comparing the CoP measures (**Table 2.1.1**) derived from both the CoP_{WBB} and CoP_{AFP}' signals ($measure_{WBB}$ *vs.* $measure_{AFP}$). The CoP measure error was defined as the percent difference between AFP- and WBB-based CoP measures. This error was calculated for each CoP measure, treating the measures derived from the CoP_{AFP}' signals as theground truth:

$$CoP\ measure\ error = \frac{100 * (\ measure_{AFP} - measure_{WBB})}{measure_{AFP}} \qquad (2.1.9)$$

Bland-Altman plots were used to visually represent the WBB's CoP measure error.

2.1.2.4.iv. Linear Calibration of the CoP_{WBB} Signals to Reduce the CoP Measurement Error

After characterizing the CoP signal error, simple linear regression was implemented to linearly correct the CoP_{WBB} signals and reduce measurement error. Simple linear regression was used to fit a straight trend line to the CoP_{WBB} signals plotted against the CoP_{AFP}' signals ($CoP_{WBB} = m * CoP_{AFP}' + b$). The linear regression coefficients (m_{AP}, b_{AP}, m_{ML}, b_{ML}) in **Table 2.1.2** represent the statistical means averaged across all sway amplitudes, in both sway directions, for each of the 12 WBBs. These WBB-specific coefficients were then used to linearly calibrate all one-dimensional CoP_{WBB} signals acquired from each WBB ($CoP_{WBB}^{calib} = 1/m * (CoP_{WBB} - b)$). The linear regression coefficients stored in the last row of **Table 2.1.2** represent the statistical means averaged across all 12 WBBs There was a statistical difference across directions: the slope of the trend lines (m coefficients) were

significantly less in the ML direction ($p < 0.001$). However, there was no statistical difference between m coefficients across the 12 WBBs ($p = 1$ in both directions).

Table 2.1.2: Linear regression coefficients (m_{AP}, b_{AP}, m_{ML}, b_{ML}) used to calibrate all one-dimensional CoP_{WBB} signals for each of the 12 WBBs. Simple linear regression was used to fit a straight trend line to the CoP_{WBB} signals plotted against the CoP_{AFP}' signals ($CoP_{WBB}^{calib} = 1/m*(CoP_{WBB} - b)$) for each WBB.

WBB	AP		ML	
	m_{AP}	b_{AP}	m_{ML}	b_{ML}
WBB_1	1.087	−0.002	1.111	0.001
WBB_2	1.086	0.020	1.097	0.010
WBB_3	1.086	0.006	1.098	−0.020
WBB_4	1.084	−0.011	1.094	−0.040
WBB_5	1.085	−0.001	1.095	0.014
WBB_6	1.088	−0.019	1.096	0.029
WBB_7	1.091	0.002	1.097	0.020
WBB_8	1.093	−0.015	1.102	−0.010
WBB_9	1.086	0.020	1.094	0.012
WBB_10	1.090	−0.008	1.101	−0.005
WBB_11	1.085	0.005	1.093	−0.017
WBB_12	1.099	0.025	1.097	−0.008
mean	1.088	0.002	1.098	−0.001
±std	±0.004	±0.014	±0.005	±0.019

Because all CoP signals were zero-meaned, the trend line y-intercepts (b_{AP} and b_{ML}) should equal zero. The y-intercepts reported in **Table 2.1.2** are not significantly different from zero and therefore should not influence the calibration procedure we recommend to use for any WBB. Only the mean trend line slopes (m_{AP} and m_{ML} in the last row of **Table 2.1.2**) should be used to linearly calibrate CoP_{WBB} signals acquired from any WBB (($CoP_{WBB}^{calib} = 1/m*(CoP_{WBB})$).

2.1.2.4.v. Statistical Analysis

First, the CoP signals were analyzed. For Aim I (validation), Pearson's linear correlation coefficients were calculated to assess CoP signal agreement (CoP_{WBB} *vs.* CoP_{AFP}'). Then, root-mean-squared errors (RMSE) (in mm) were calculated to quantify the difference between the CoP_{WBB} and CoP_{AFP}' signals. A t-test was performed to confirm that the RMSEs were significantly different from zero before calibration. To investigate the effect of direction on CoP signal error, one-way, fixed effect (sway direction) ANOVAs were performed on

both the RMSEs and β coefficients. Then, to investigate the effect of calibration on signal error, one-way, fixed effect (calibration) ANOVAs were performed on the RMSEs in both sway directions. We then performed a one-way, fixed effect (sway direction) ANOVA on the RMSEs after calibration to investigate the effect of direction on signal error after linear calibration of the CoP_{WBB} signals. For Aim II (inter-device variability), one-way, fixed effect (WBB) ANOVAs were performed on both the RMSEs and the β coefficients to assess the effect of the 12 WBBs on CoP signal error in both directions, before calibration. To assess inter-device variability after calibration, one-way, fixed effect (WBB) ANOVAs were performed on the RMSEs in both directions.

As a secondary analysis, we investigated the effect of sway amplitude and frequency on CoP signal error. Two-way, repeated measures, fixed effects (displacement angle, load height) ANOVAs were performed on the RMSEs to assess both the main and interaction effects of displacement angle and load height on signal error in both directions, both before and after calibration. A Bonferroni correction was applied to account for multiple comparisons (3 displacement angles × 3 load heights = 9 comparisons).

Second, the CoP measures were analyzed. For Aim I (validation), one-way, fixed effect (device) ANOVAs were first performed on all one-dimensional CoP measures (defined in **Table 2.1.1**) to assess the difference between AFP- and WBB-based CoP measures in both directions. To investigate the effect of direction on CoP measure error, one-way, fixed effect (sway direction) ANOVAs were performed on all CoP measure errors before calibration. Then, to investigate the effect of calibration on measure error, one-way, fixed effect (calibration) ANOVAs were performed on the CoP measure errors in both sway directions. We then performed one-way, fixed effect (sway direction) ANOVAs on all CoP measure errors after calibration to investigate the effect of direction after linear calibration of the CoP_{WBB} signals. For Aim II (inter-device variability), a one-way fixed effect (WBB) ANOVA was performed for each measure to assess the effect of the 12 WBBs on CoP measure error in both directions, both before and after calibration.

2.1.3. Results & Discussion

2.1.3.1. CoP Signal Error

2.1.3.1.i. CoP Signal Error before Linear Calibration of the CoP_{WBB} Signals

The CoP_{WBB} signals were significantly correlated with the CoP_{AFP} signals across all sway amplitudes and frequencies and in both sway directions for all 12 WBBs ($r > 0.99$) (**Figure 2.1.5**).

The CoP signal error was a function of CoP magnitude. As the sway amplitude increased the CoP signal error increased, indicated by positive slopes ($\beta_{AP,}$ β_{ML}) of the linear trend lines (in red) in **Figure 2.1.6**. In other words, the WBB's accuracy appears to decrease as horizontal and shear sway components increase. As shown below in **Figure 2.1.6**, agreement between CoP signals was not only a function of sway amplitude but also a function of sway direction. The CoP signal error was larger in the ML direction, indicated by a steeper slope (β_{ML}) in **Figure 2.1.6B**.

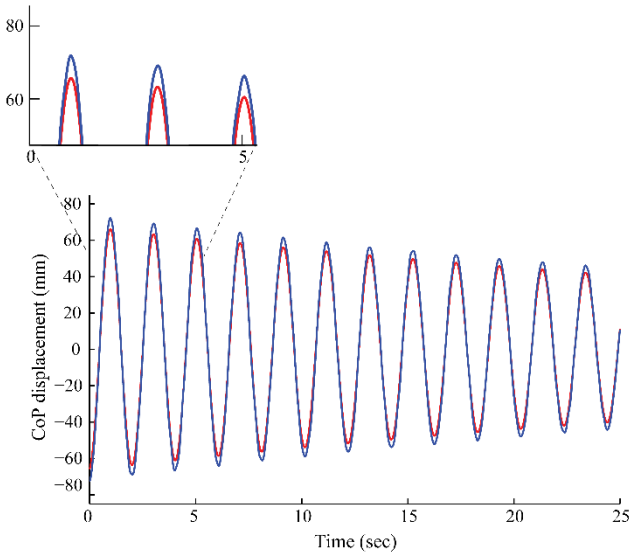

Figure 2.1.5: The WBB's CoP signal error. The CoP_{WBB} (in blue) and CoP_{AFP}' (in red) signals for the condition invoking the lowest frequency response and highest sway amplitude. The zoomed-in templates illustrate the WBB's CoP signal error: the difference (in mm) in CoP displacement ($CoP_{WBB} - CoP_{AFP}$').

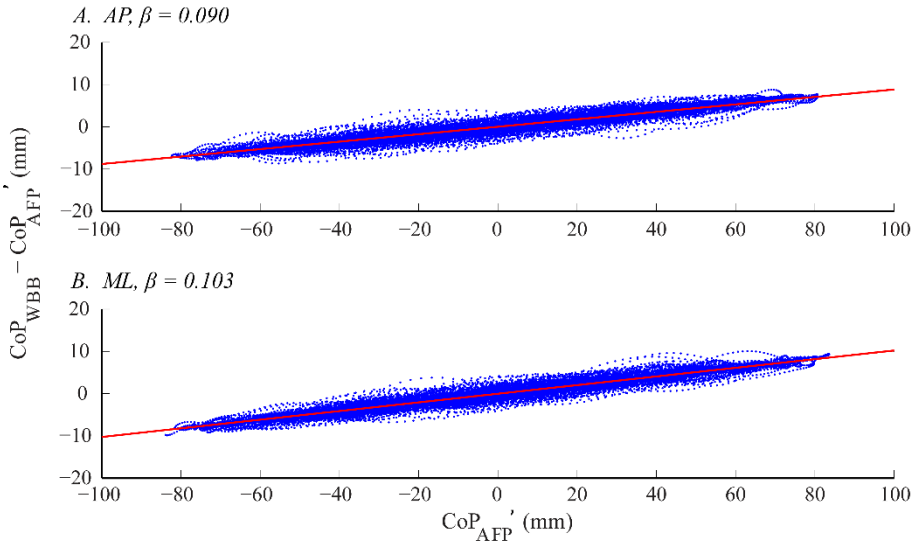

Figure 2.1.6: Linearity of the WBB's CoP signal error. An individual WBB's (WBB_4) CoP signal error ($CoP_{WBB} - CoP_{AFP}$') is plotted for all sway amplitudes and in both the AP (**A**) and ML (**B**) directions.

The β coefficients in **Table 2.1.3** characterize the direction-specific slope of the linear trends for each WBB. The linear regression coefficients (β_{AP}, α_{AP}, β_{ML}, α_{ML}) were derived

from the CoP signal error across all sway amplitudes, in both directions, for each of the 12 WBBs. There was a significant difference in signal error across directions: the β coefficients are significantly greater in the ML direction ($F_{1,22}$= 24.30, p < 0.001). However, there was no statistical difference between β coefficients across the 12 WBBs, indicating low inter-device variability (p = 1 in both directions).

Table 2.1.3: Linear regression coefficients for the 12 WBBs. The linear regression coefficients (β_{AP}, α_{AP}, β_{ML}, α_{ML}) were derived from the CoP signal error across all sway amplitudes and frequencies, in both directions, for each of the 12 WBBs. Simple linear regression was used to fit a straight trend line to the CoP signal error plotted against the CoP_{AFP}' signals: $CoP_{WBB} - CoP_{AFP}' = \beta * CoP_{AFP}' + \alpha$.

WBB	AP		ML	
	β_{AP}	α_{AP}	β_{ML}	α_{ML}
WBB_1	0.094	−0.002	0.125	0.001
WBB_2	0.094	0.021	0.107	0.011
WBB_3	0.093	0.007	0.108	−0.022
WBB_4	0.090	−0.012	0.103	−0.044
WBB_5	0.092	−0.001	0.104	0.015
WBB_6	0.096	−0.021	0.105	0.032
WBB_7	0.099	0.003	0.107	0.022
WBB_8	0.102	−0.017	0.112	−0.011
WBB_9	0.094	0.022	0.103	0.013
WBB_10	0.098	−0.009	0.111	−0.006
WBB_11	0.092	0.006	0.101	−0.019
WBB_12	0.109	0.028	0.107	−0.009
mean	**0.096**	**0.002**	**0.108**	**−0.001**
± std	**±0.005**	**±0.016**	**±0.006**	**±0.022**

These findings were statistically supported by our analysis of RMSEs. The RMSEs quantify residuals and represent the difference between the CoP_{WBB} and CoP_{AFP}' signals. The means and standard deviations of the RMSEs were 3.5 ± 0.9 mm and 4.0 ± 1.1 mm for the AP and ML directions, respectively. The RMSEs were significantly greater than zero (p < 0.001 in both directions), and the ML RMSEs were significantly greater than the AP RMSEs ($F_{1,214}$ = 15.19, p < 0.001). There was no statistically significant difference in RMSEs across the 12 WBBs, indicating low inter-device variability (AP: $F_{11,96}$ = 0.53, p = 0.881; ML: $F_{11,96}$ = 0.28, p < 0.988).

Additionally, there was a significant effect of displacement angle (θ_i = 2, 4, and 6°) on RMSE, with a significant increase in RMSE as displacement angle increased (AP: $F_{2,2,4}$ = 234.46, $p < 0.001$; ML: $F_{2,2,4}$ = 232.79, $p < 0.001$). There was a significant effect of load height (h = 900, 1000 and 1100 mm) on RMSE in the AP direction ($F_{2,2,4}$ = 5.86, $p < 0.004$), with a significant decrease in RMSE as load height increased. There was not a significant effect of load height in the ML direction $F_{2,2,4}$ = 0.05, p = 0.950) and there was no interaction between the two factors (displacement angle and load height). We hypothesize that there was no effect of load height on RMSE in the ML direction due to the larger magnitude and wider distribution of RMSE in the ML direction (see **Figure 2.1.8**, before calibration).

2.3.1.ii. CoP Signal Error after Linear Calibration of the CoP_{WBB} Signals

The difference between the CoP_{WBB} and CoP_{AFP}' signals, quantified by the RMSEs, was significantly reduced by the linear calibration of the CoP_{WBB} signals. **Figure 2.1.7** shows the effect of calibration on the CoP_{WBB} signals.

There was a significant reduction in RMSEs with calibration (AP: $F_{1,214}$ = 856.52, $p < 0.001$; ML: $F_{1,214}$ = 794.05, $p < 0.001$). After calibration, the RMSEs were no longer significantly greater in the ML direction ($F_{1,214}$ = 0.37, p = 0.5451). Similar to the results before calibration, there was no difference in RMSEs across the 12 WBBs (AP: $F_{11,96}$ = 0.11, p = 0.999; ML: $F_{11,96}$ = 0.24, $p < 0.993$). Linear calibration of the CoP_{WBB} signals reduced the inter-device variability, which in turn strengthened the WBB's inter-device reliability.

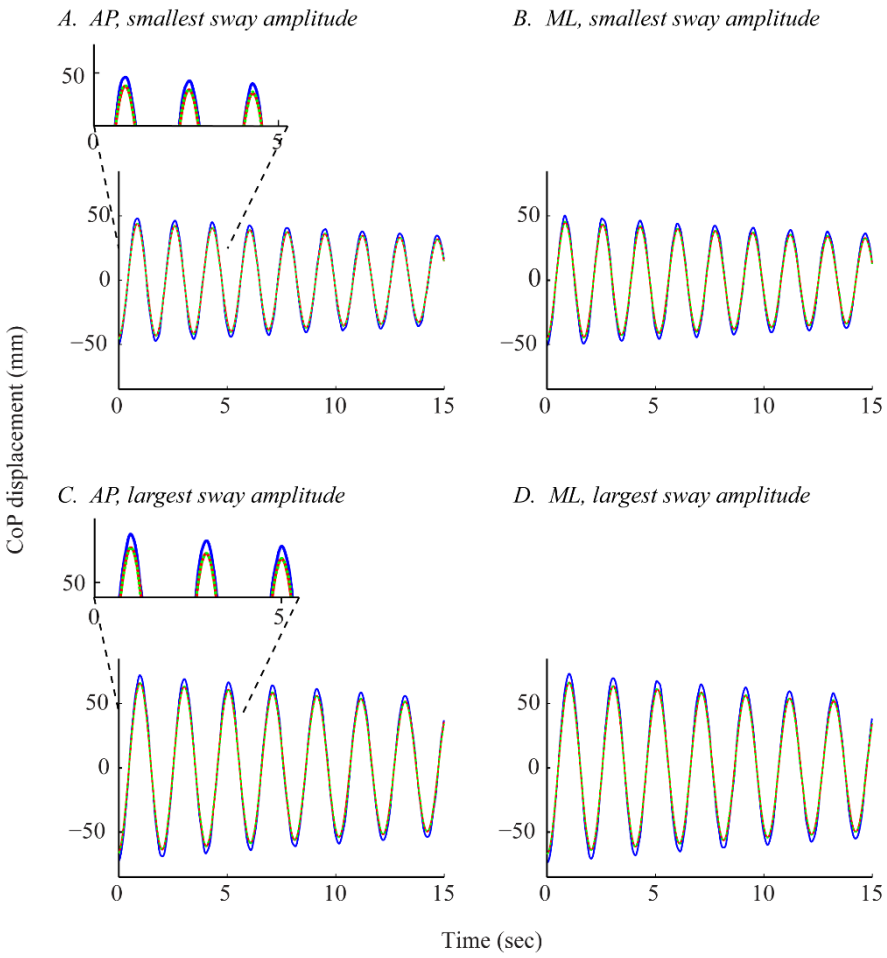

Figure 2.1.7: Effect of calibration on CoP_{WBB} signals. All four plots contain three signals: The CoP_{WBB} signal before calibration (in blue, solid line), the CoP_{WBB} signal after calibration (CoP_{WBB}^{calib}) (in green, dashed line), and the "gold standard" CoP_{AFP}' signal (in red, solid line).

The significant effect of displacement angle remained after calibration. Like before, the RMSE values increased as displacement angle increased (AP: $F_{2,2,4}$ = 204.71, $p < 0.001$; ML: $F_{2,2,4}$ = 170.82, $p < 0.001$). There was a significant effect of load height in the AP but not in the ML direction before calibration. Because the CoP signal error was significantly greater in the ML direction before calibration, and because our linear calibration procedure corrects the CoP measurement and reduces error, there was an effect of load height in the ML direction after calibration. After calibration, the RMSEs significantly decreased as load height increased in both sway directions (AP: $F_{2,2,4}$ = 55.27, $p < 0.001$; ML: $F_{2,2,4}$ = 20.75, $p < 0.001$). These results are consistent with what we expected to see since larger displacement angles and shorter load heights produce larger CoP amplitudes and, as we

saw in our primary analysis, RMSEs increase as sway amplitude increases. Like before, there was no interaction between the two factors (displacement angle and load height). The significant effect of calibration on CoP signal error is shown in **Figure 2.1.8**.

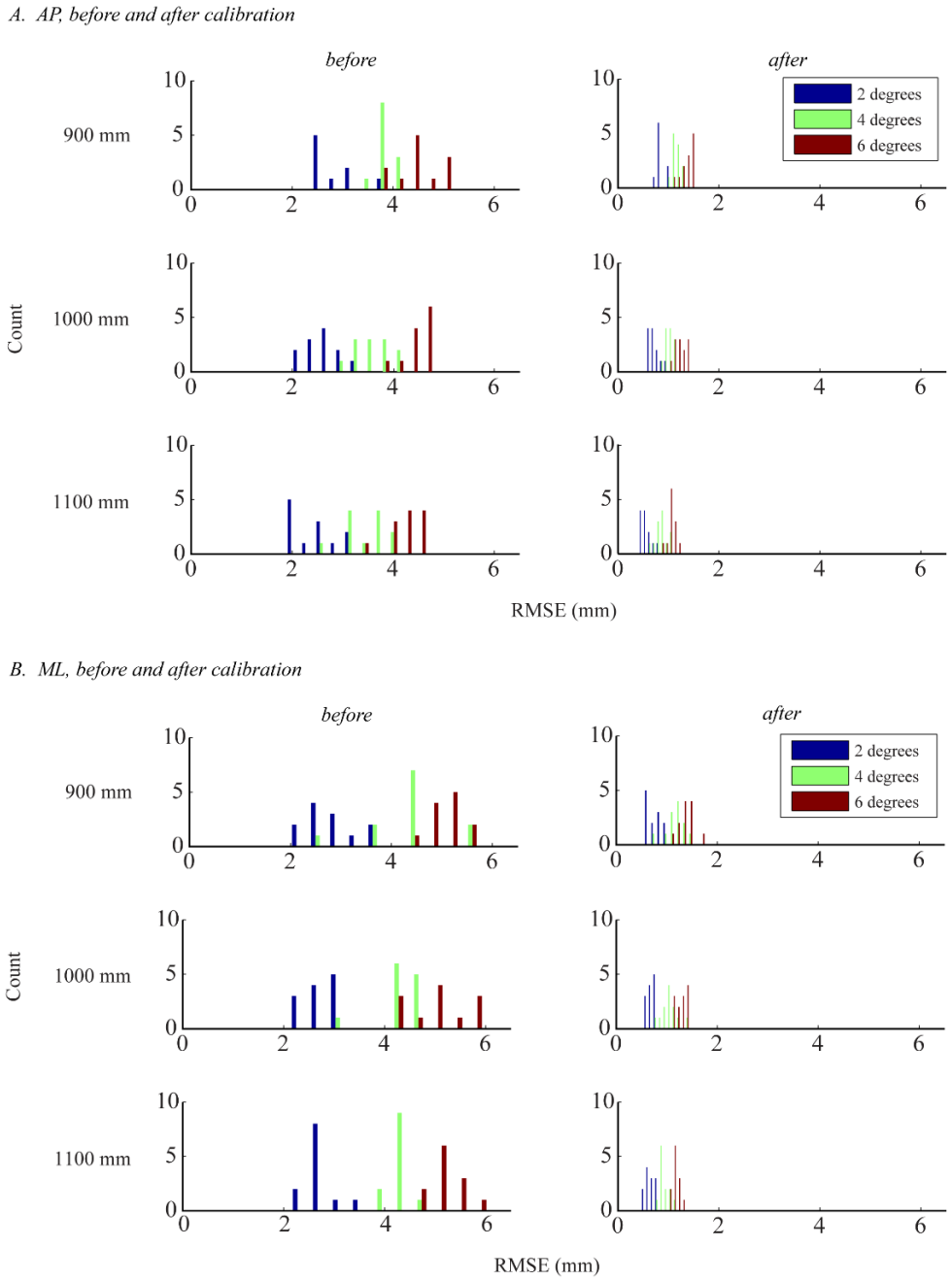

Figure 2.1.8: Effect of calibration on CoP_{WBB} signal error measured by RMSEs. This figure shows the distribution of the RMSEs across all sway amplitudes and WBBs, in both the AP (**A**) and ML (**B**) directions, both before and after linear calibration of the CoP_{WBB} signals. The three oscillation frequencies (ω) corresponding to the three load heights (h = 900, 1000 and 1100 mm) are 0.6, 0.5, and 0.4 Hz, respectively.

2.1.3.2. CoP Measure Error

2.1.3.2.i. CoP Measure Error before Linear Calibration of the CoP_{WBB} Signals

Before calibration, there was a significant difference between the AFP- and WBB-based time-domain measures, indicated by large *F* statistics and small *p*-values in **Table 2.1.4A**. However, there was no difference between the AFP- and WBB-based frequency-domain measure, peak frequency (*PFREQ*), in both directions (**Table 2.1.4A**).

The CoP measure error, averaged across all sway amplitudes and WBBs, was about −10% and −11% for all AP and ML time-domain measures, respectively (**Table 2.1.5A**). There was a significant difference in error between directions (AP *vs.* ML) for all CoP time-domain measures (*p*-values in **Table 2.1.5A**). Since the CoP measures were derived from the CoP signals, the error in CoP_{WBB} time-domain measures was a direct function of the CoP signal error, as seen in our Bland-Altman analysis. For example, the Bland-Altman plot for the CoP time-domain measure, mean velocity (*MV*), before calibration (**Figure 2.1.9A,C**) follows the same trend expressed by the CoP signal error **(Figure 2.1.6**). There was no CoP measure error for the frequency-domain measure, *PFREQ* (**Table 2.1.5A**), meaning the WBB accurately measured the frequency content of the CoP signals.

There was a significant effect of WBB on CoP measure error $p < 0.001$ for all CoP time-domain measure errors, with error from one WBB (WBB_12) being significantly greater than the error from the remaining 11 WBBs in the AP direction and error from a different WBB (WBB_1) being significantly greater than the error from the remaining 11 WBBs in the ML direction). Evidently, there is significant inter-device variability on CoP measure error (based on the performance of two out of 12 different WBBs) before calibration.

2.1.3.2.ii. CoP Measure Error after Linear Calibration of the CoP_{WBB} Signals

After calibration, there was no statistical difference between the AFP- and WBB-based time-domain measures, indicated by small *F* statistics and large *p*-values in **Table 2.1.4B**. Like before calibration, there was no difference between the AFP- and WBB-based *PFREQ* after calibration (**Table 2.1.4B**). Since our linear calibration simply corrects the CoP measurement (in mm) and reduces error, it has no effect on the frequency content of the CoP signal and in turn on the frequency-domain measure *PFREQ*.

The significant reduction of time-domain CoP measure errors (from **Table 2.1.5A–B**) shows the significant effect of calibration on CoP_{WBB} measure accuracy in the time-domain ($p < 0.001$ for all CoP time-domain measure errors, in both directions). This effect is clearly illustrated in **Figure 2.1.9**: before calibration there was a strong correlation between measure error and amplitude, with an increase in error as measure amplitude increases, but this effect was absent after calibration. After calibration, just one time-domain CoP measure remained sensitive to direction: the magnitude of error for *MV* was significantly greater in the AP direction (*p*-values in **Table 2.1.5B**). As expected, the CoP measure error for *PFREQ* did not change with calibration.

Dissimilar to the results before calibration, there was no effect of WBB on CoP measure error after calibration ($0.930 < p \leq 1.000$ for all time-domain CoP measure errors, in both directions). These findings suggest that our proposed calibration procedure is effective when comparing CoP measures acquired from different WBBs.

Table 2.1.4: Means and standard deviations of both AFP- and WBB-based CoP measures, both before and after linear calibration of the CoP_{WBB} signals. Results from the one-way, fixed effects (device) ANOVAs shows the difference between AFP- and WBB-based CoP measures before and after linear calibration.

***A. Before* Linear Calibration of CoP_{WBB} Signals:**

Measure	AP				ML			
	AFP: mean ± std	**WBB: mean ± std**	$F_{1,214}$	***p*- value**	**AFP: mean ± std**	**WBB: mean ± std**	$F_{1,214}$	***p*- value**
MD	31.0 ± 7.8	34.0 ± 8.5	7.23	0.008	32.2 ± 8.8	35.6 ± 9.7	7.64	0.006
RMS	34.9 ± 8.8	38.2 ± 9.6	7.32	0.007	36.1 ± 9.8	40.0 ± 10.8	7.71	0.006
RANGE	123.5 ± 30.4	135.6 ± 33.2	7.82	0.006	128.3 ± 34.4	142.2 ± 38.0	7.97	0.005
MV	97.2 ± 27.1	106.8 ± 29.9	6.16	0.014	100.0 ± 28.4	110.9 ± 31.6	7.14	0.008
PFREQ	0.5 ± 0.1	0.5 ± 0.1	0.00	1.000	0.5 ± 0.1	0.5 ± 0.1	0.00	1.000

***B. After* Linear Calibration of CoP_{WBB} Signals:**

Measure	AP				ML			
	AFP: mean ± std	**WBB: mean ± std**	$F_{1,214}$	***p*- value**	**AFP: mean ± std**	**WBB: mean ± std**	$F_{1,214}$	***p*- value**
MD	31.0 ± 7.8	31.0 ± 7.8	<0.001	0.993	32.2 ± 8.8	32.1 ± 8.8	<0.001	0.996
RMS	34.9 ± 8.8	34.9 ± 8.7	<0.001	0.998	36.1 ± 9.8	36.1 ± 9.8	<0.001	0.998
RANGE	123.5 ± 30.4	123.6 ± 30.3	<0.001	0.975	128.3 ± 34.4	128.3 ± 34.4	<0.001	0.994
MV	97.2 ± 27.1	97.4 ± 27.3	<0.001	0.957	100.0 ± 28.4	100.0 ± 28.5	<0.001	0.983
PFREQ	0.5 ± 0.1	0.5 ± 0.1	0.00	1.000	0.5 ± 0.1	0.5 ± 0.1	0.00	1.000

Table 2.1.5: Time-domain CoP measure (%) errors both before and after linear calibration of CoP_{WBB} signals. The p-values quantify the direction-specific difference in error (AP *vs.* ML) both before (A) and after (B) calibration. The (%) errors for the one frequency-domain CoP measure *PFREQ* is not reported here because there is no difference in *PFREQ* measured by both the WBB and AFP (see **Table 2.1.4**).

Measures	A. CoP Measure (%) Error *before* Linear Calibration of CoP_{WBB} Signals:			B. CoP Measure (%) Error *after* Linear Calibration CoP_{WBB} of Signals:		
	AP mean ± std	**ML mean ± std**	***p*-value**	**AP mean ± std**	**ML mean ± std**	***p*-value**
MD	−9.70 ± 0.67	−10.85 ± 0.88	<0.001	−0.01 ± 0.40	0.01 ± 0.57	0.805
RMS	−9.71 ± 0.64	−10.86 ± 0.88	<0.001	−0.02 ± 0.37	0.00 ± 0.56	0.744
RANGE	−9.83 ± 0.76	−10.90 ± 0.91	<0.001	−0.13 ± 0.57	−0.03 ± 0.64	0.251
MV	−9.89 ± 0.60	−10.90 ± 0.87	<0.001	−0.18 ± 0.34	−0.04 ± 0.56	0.021

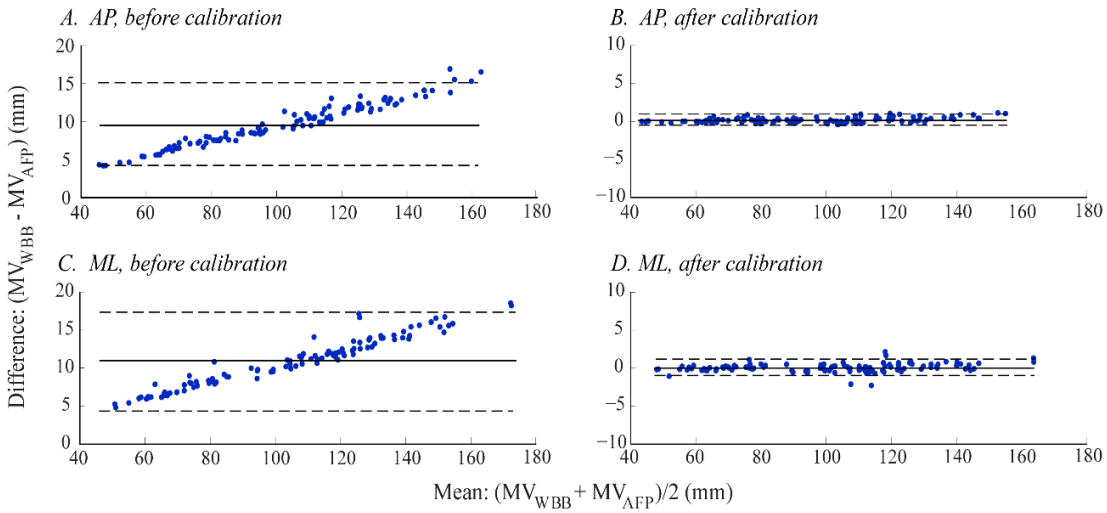

Figure 2.1.9: Bland-Altman plots of a time-domain CoP measure, mean velocity (*MV*), before and after linear calibration of the CoP_{WBB} signals. Comparison of *MV* derived from both the CoP_{WBB} and CoP_{AFP}' signals for every trial (12 WBBs, 3 load heights, 3 displacement angles per load height, per sway direction = 108 trials). The solid line represents the mean difference between measurements (MV_{WBB} *vs.* MV_{AFP}) and the dotted lines represent the 95% limits of agreement (± 1.96 times the standard deviation of the mean difference).

2.1.4. Conclusions

The WBB is an affordable, portable, and easily accessible device that may be used to measure ground reaction forces and CoP displacement in situations where lower accuracy and precision is acceptable. The WBB should not be used as a replacement for the "gold standard" laboratory grade force-plate when measuring CoP under both static and dynamic conditions, as it is a uni-axial device and lacks the accuracy recommended for posturography [110]. However, once the WBB's CoP measurement error is fully characterized and accounted for (under uncontrolled dynamics conditions – *e.g.*, real human postural sway), the WBB could substitute for a laboratory-grade force plate in situations where lower accuracy and precision is acceptable.

The WBB's time jitter poses a significant limitation, in general, for the use of the WBB as a CoP measurement device. Because the WBB samples at an inconsistent rate, we employed a data averaging method to create time series with samples at equal time intervals (t_{DA}). In this study, we averaged across samples every 93.75 ms (t_{DA}= 0.09375 s; f_{DA} = ~10.7 Hz). Because we found the WBB's mean sampling rate f_s to be ~50 Hz, we could

potentially increase CoP measurement accuracy and reduce error by decreasing the time interval t_{DA}, in which we averaged across samples. However, occasionally the WBB only acquired 1 or 2 samples worth of data during the specified t_{DA} (even though it usually acquired 3–6 samples). If our custom-written software was set to average across samples at a faster rate, f_{DA}, our data set could contain missing data. Because the WBB has been reported to sample at different mean rates (f_s = 35 [99], 40 [98], 64 [104], and even 100 Hz [103]), we conclude that the WBB's mean sampling rate depends on both the device and the operating system of the device used to connect to the WBB. The WBB's time jitter combined with an inappropriately fast f_{DA} (dependent upon the connected device) could explain the "occasional glitches in the data" reported in previous publications [99,104]. In sum, the device and operating system used to acquire data from the WBB, as well as the way in which the WBB's time jitter is treated, may affect the quality of CoP measures derived from WBB data.

The way in which we processed both the WBB- and AFP-based CoP signals poses another limitation of this study. We used PCA to synchronize the CoP_{WBB} and $CoP_{AFP}{}'$ signals in space (to account for the inherent yet small positioning errors) and we zero-meaned the signals when time-aligning offline. In doing so, we were unable to detect the WBB's initial (horizontal) offset error previously documented by Bartlett *et al.* [103]. Despite this limitation, our research findings remain significant with regards to purpose and implementation. Although we do not quantify the WBB's initial (horizontal) offset error, we do quantify the WBB's (horizontal) CoP measurement error once the CoP_{WBB} and $CoP_{AFP}{}'$ signals are synchronized in both space and time. Our future research aims motivated the signal processing methods carried out in this study. In future work, we plan to derive summary postural sway measures (such as the CoP time-domain measures reported in **Table 2.1.1**) from human postural sway measured by a single WBB on a frequent, longitudinal basis. We are more concerned with the relative accuracy and reliability of WBB-based CoP measures and less concerned with the WBB's absolute precision as a CoP measurement device. Furthermore, assuming there is no drift in the WBB's (horizontal) offset error across time (a potential issue which has yet to be explored), it would not influence summary measures like mean sway amplitude, path length, and velocity.

Additional limitations of this study pertain to our experimental setup and procedures. The weight distribution of the inverted pendulum mechanical system does not closely resemble that of a human body, in which two thirds of the body's weight is concentrated at or around the height of the body's CoM [112]. Most of the mechanical system's weight was concentrated at the base with only 28% of the weight loaded at the approximate height of a human body's CoM. So although we acquired promising results, we cannot make confident inferences regarding the WBB's competency in practice until we test a load with a weight distribution more representative of a human body. Furthermore, our simulated postural sway signals (with respect to both sway amplitude and frequency) differ from human sway. As previously discussed, we systematically tested multiple displacement angles and load heights to induce a variety of sway amplitudes and frequencies. Although the load heights were selected according to the approximate height of a human body's CoM [108,109], the selected displacement angles induced higher sway amplitudes than typically seen human postural sway. We were restricted to a relatively large range of displacement angles (θ_i = 2°, 4° and 6°) due to the limited precision of the device used to measure the displacement angles. If we were able to reduce and restrict our range (*e.g.*, to θ_i = 0.5°, 1.0° and 1.5°), we would have induced sway amplitudes that were more similar to human postural sway. We expect a lower CoP measurement error when using the WBB to measure human postural sway since human sway tends to be lower in amplitude relative to our simulated postural sway amplitudes and since we determined error to be a function of sway amplitude in this study. Lastly, we only assessed one-dimensional sway and a limited range of sway frequencies (ω = 0.4, 0.5 and 0.6 Hz induced by h = 1100, 1000 and 900 mm, respectively). The range of frequencies tested is comparable to the mean frequencies found in both healthy young and old adults during quiet stance with both eyes opened and eyes closed [35], however a higher frequency range (1–10 Hz) [113] should be tested in order to translate our findings to more challenging sway conditions that elicit an increase in postural sway (*e.g.*, Romberg, standing on foam, or tandem stance) and/or to human populations with known postural instabilities and abnormal postural sway.

So although we have identified the WBB's CoP measurement error under controlled dynamic conditions, future work is needed before the WBB can be used as the sole postural

sway measurement device in the clinical research and rehabilitation research domains. In agreement with Pagnacco *et al.* [105], we do not recommend the use of the WBB as a clinical diagnostic tool. The WBB was designed and manufactured for entertainment purposes and lacks the accuracy, precision, and reliability required of medical devices. In future work, human postural sway must be measured under a variety of sway conditions and in many human populations (differentiated by both age and health status) simultaneously with both the WBB and force plate in order to characterize CoP measurement error under uncontrolled dynamic conditions. Once the WBB's CoP measurement error is fully characterized and accounted for, the WBB could substitute for a laboratory-grade force plate in situations where lower accuracy and precision is acceptable, such as for frequent, longitudinal monitoring of postural sway for older adults in a small clinic or home environment.

2.1.5. Contributions

Contributor	Affiliation(s)	Support Provided
Tamara Hayes (*late PhD advisor*)	ORCATECH, BME Department	-contributed to study design -provided some materials for data acquisition
Robert Peterka (*DAC member*)	BME Department	-contributed time and materials to build the mechanical system -guided CoP derivations -assisted with CoP signal processing -served as a co-author: reviewed and enhanced the manuscript in preparation for publication in the *Sensors* journal
Heather Schlueter	BD Laboratory	-assisted with data acquisition
Martina Mancini	BD Laboratory	-assisted with CoP signal processing and analysis -contributed to interpretation of results -served as a co-author: reviewed and enhanced the manuscript in preparation for publication in the *Sensors* journal
Fay Horak (*PhD advisor*) (*DAC member*)	BD Laboratory, BME & Neurology Departments	-provided laboratory space and equipment for data acquisition -contributed to interpretation of results -served as a co-author: reviewed and enhanced the manuscript in preparation for publication in the *Sensors* journal

CHAPTER 2, Part 2: *Validation Study for the Postural Sway Measurement Device**:** Validating and Calibrating the Nintendo WBB to Derive Reliable Measures of Postural Sway Based on Real Two-Dimensional Postural Sway Signals Acquired from Healthy, Young Adults*

Summary

Objective: To further characterize the Nintendo Wii balance board's (WBB) CoP measurement error, using the "gold standard" laboratory-grade force plate as ground truth, in preparation to use the WBB as the sole CoP measurement device in our in-home study (*Chapter 4*).

Methods: The WBB and a laboratory-grade AMTI force plate (AFP) were used to simultaneously measure the CoP displacement of an uncontrolled dynamic load: human postural sway. Seven healthy young adults (three females, mean age of 32.9 ± 9.7 years) participated in a series of 30-second quiet stance trials while standing in place with a fixed foot position. The subjects performed 3 trials each for 4 different quiet stance conditions: 1.eyes open (EO); 2. eyes closed (EC); 3. standing on foam with eyes open (FEO); and, 4. standing on foam with eyes closed (FEC). The WBB CoP signals were calibrated via two different methods: 1. the pendulum-based calibration method detailed above in *Chapter 2, Part 1*; and 2. a human-based calibration method derived from the human-based postural sway. The CoP measurement error was determined and calibration methods were compared.

Results: The CoP measurement error for the calibrated WBB CoP signals (both pendulum- and human-based) was significantly greater than that for the uncalibrated WBB CoP signals, with the pendulum-based calibrated signal error significantly greater than the human-based calibrated signal error which were significantly greater than the uncalibrated signal error.

Conclusions: There was not a significant difference between the AFP- and WBB-based CoP measures before linear calibration of the WBB CoP signals. Neither calibration method reduced the WBB's CoP measurement error. Despite the significant effort dedicated to calibrating the WBB CoP signals to reduce the WBB's CoP measurement error, it appears as though the uncalibrated WBB CoP signals most accurately quantify CoP in human postural sway. Because of this, neither pendulum- nor human-based calibration will be implemented in *Chapters 4* of this dissertation. The uncalibrated WBB CoP signals will be used to provide CoP estimates during our longitudinal study of postural sway in older adults with MCI.

2.2.1. Introduction

Chapter 2, Part 2 extends beyond *Chapter 2, Part 1* by using real, two-dimensional postural sway signals to characterize the WBB's CoP measurement error. Before implementing the WBB as the sole measurement device, its measurement error must be quantified using uncontrolled, two-dimensional biomedical signals such as in human postural sway. In this study we quantified the WBB's measurement error during quiet stance in seven healthy, young adults. As discussed in *Chapter 1,* quiet stance with no cognitive loading is an easy postural task for a healthy, young adult. In order to elicit more postural sway and in an effort to emulate the mild postural instabilities evidenced in older adults, the difficulty level of the quiet stance condition was modulated. As detailed by Horak *et al.*, spatial orientation in postural control is based on the interpretation of convergent sensory information from the somatosensory, vestibular and visual systems [2]. When you manipulate or remove input from one or multiple systems, a subject's ability to orient one's self in space and maintain postural stability is compromised. We modulated the quiet stance condition by removing visual input (*i.e.*, instructing the subject to close his/her eyes) and by dampening the biomechanical feedback of the support surface (*i.e.*, having the subject stand on foam as opposed to a hard surface, such as the relatively rigid usable surface of the WBB). This study's aim was to extend beyond our first WBB validation study (detailed in *Chapter 2, Part* 1) by quantifying the WBB's CoP measurement error under uncontrolled dynamic conditions, as in human postural sway. Before using the WBB as the sole postural sway measurement device in the clinical research and rehabilitation research domains, it first must be validated against the AFP using real, two-dimensional biomedical signals.

2.2.2. Experimental Methods

The Institutional Review Board at OHSU approved this study's experimental methods and all subjects gave informed written consent prior to participation.

2.2.2.1. Procedures

Seven healthy young adults (three females, mean age of 32.9 ± 9.7 years) participated in a series of 30-second quiet stance trials while standing in place with a fixed foot position. Each subject mounted the WBB (WBB_12 from *Chapter 2, Part 1*), which was mounted and positioned centrally on the force plate, and assumed a fixed foot position. A foam pad was mounted and positioned centrally on the WBB for the two foam conditions. Testing order remained constant across all seven subjects, with four quiet stance conditions (eyes-open (EO), eyes-closed (EC), foam-eyes-open (FEO), and foam-eyes-closed (FEC)) and three consecutive trials per condition for a total of 12 30-second trials per subject. Both measurement devices (the WBB and AFP) acquired two-dimensional CoP displacement data simultaneously.

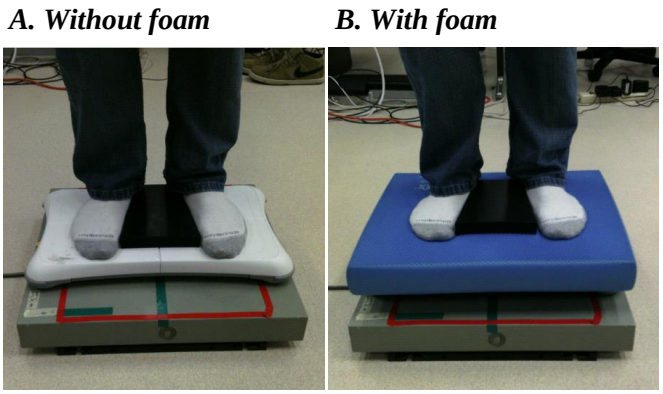

Figure 2.2.1: Experimental setup to measure real, two-dimensional postural sway in healthy young adults across four quiet stance conditions. The subject stood atop the WBB, which was mounted atop the AFP. (**A**) Setup for EO and EC conditions; (**B**) Setup for FEO and FEC conditions. The black reference block was used to ensure a fixed foot position and was removed before data acquisition.

2.2.2.2. Data Acquisition

Prior to data acquisition, pilot data was collected to assess the spectral characteristics of postural sway in healthy young adults. Two healthy young adults (one female, mean age of 28.5 ± 6.4 years) underwent the testing protocol. The majority of the power spectrum was contained below 2.0 Hz, across all four conditions (EO, EC, FEO and FEC) and in both directions (AP and ML). The only condition that contained frequencies higher than 2.0 Hz (up to 4.0 Hz) was FEC. Our findings are consistent with previous findings

regarding the spectral characteristics of postural sway in healthy, young adults [35]. But to be overly cautious and avoid violating the Nyquist-Shannon sampling theorem [114], we modified our custom-written software to store all WBB samples during data acquisition with the intent to create a time series with equally distributed samples during post-processing. This method is different from our first WBB validation study where we employed our data averaging method during data acquisition, setting the WBB to sample at a rate of ~10.7 Hz (detailed in *Chapter 2, Part 1*). In this study, our second WBB validation study, the WBB sampled at its inconsistent rate with a mean frequency of 50.22 Hz. The time between samples (Δt) varied by a factor of 15.5 ms:

$$\Delta t = n * 15.5,\ n = 0,\ 1,\ 2 \text{ or } 3 \tag{2.2.1}$$

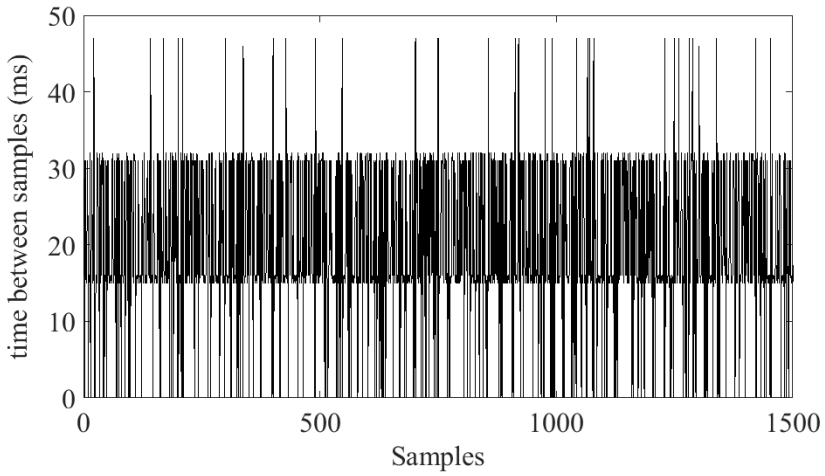

Figure 2.2.2: The WBB's inconsistent sampling rate. The time between samples (Δt) varied by a factor of 15.5 ms. The mean Δt was 19.9 ms, resulting in a mean sampling frequency of 50.22 ± Hz.

Our data averaging method was employed during post-processing to account for the board's sampling restrictions (discussed in *Chapter 2, Part 1*). We averaged across all samples every 50 ms (f_{DA} = 20 Hz). This rate was the fastest usable sampling rate, meaning the specified sampling interval could not be any shorter without producing a data set with missing data points. A sampling rate of 20 Hz is low compared to recommendations in the literature [98] but high enough to capture the spectral characteristics of the postural sway in our seven healthy, young adults under relatively stable postural stance conditions.

The AFP sampled at 100 Hz, and a 10.5 Hz low-pass filter was applied during data acquisition.

2.2.2.3. Data Analysis

All data were analyzed in Matlab R2014a (The MathWorks, Natick, MA, USA).

2.2.2.3.i. CoP Signals

CoP Signal Derivation

Both the WBB- and AFP-based CoP signals were derived based on the methods detailed in *Chapter 2, Part 1* with small adjustments made to the calculations during the FEO and FEC conditions to account for both the height (h_f) and mass (m_f) of the foam pad, which was positioned centrally atop the WBB, which was positioned centrally atop the AFP. The AFP's predicted CoP at the foam surface (CoP_{AFP}'') was calculated by making the following adjustments to Equations 2.1.2-3:

- To calculate *T*, the summed moments about the point of rotation, *R*, Equation 2.1.2 was modified by
    - adding h_f to (h_R + h_{WBB}) to represent the increased length of the lever arm

$$T = CoP_{AFP_x}F_{AFP_z} + (h_R + h_f + h_{WBB})F_{AFP_x} \quad (2.2.2)$$

- To calculate CoP_{AFP}'', Equation 2.1.3 was modified by
    - subtracting the force applied by the foam pad, F_f, from $F_{AFPz'}$ to represent the vertical forces applied to the foam surface, $F_{AFPz''}$

$$CoP_{AFP_x}'' = [T - h_R F_{AFP_x}'']/F_{AFP_z}'' \quad (2.2.3)$$

where, $F_{AFP_x}'' = F_{AFP_x}$, $F_{AFP_z}'' = F_{AFP_z} - F_{WBB} - F_f$, $F_{WBB} = m_{WBB}g$, $F_f = m_f g$, m_{WBB} = the mass of the WBB, m_f = the mass of the foam pad, and g = acceleration due to gravity.

The WBB's predicted CoP at the foam surface (CoP_{WBB}') can be calculated as well using known *T*:

$$CoP_{WBB_x}' = [T - h_R F_{WBB_x}']/F_{WBB_z}' \quad (2.2.4)$$

where, $F_{WBB_x}' = F_{WBB_x} = 0$ since the WBB is unable to measure horizontal forces, and $F_{WBB_z}' = F_{WBB_z} - F_f$. Because $F_{WBB_x}' = F_{WBB_x} = 0$, h_f does not influence CoP_{WBB}'. Equation 2.2.4 relies on information from the AFP, and because the purpose of this work is to be able to

use the WBB as the sole measurement device to estimate CoP, Equation 2.1.1 was used instead to calculate CoP_{WBB}'. Equation 2.1.1 was modified to account for F_f by subtracting F_f from F_{WBBz} across the WBB's four force transducers (TR, BR, TL, and BL). A 30-second bias trial was conducted to determine the four vertical forces applied to the WBB by the foam pad (F_{TRf}, $F_{BRf,}$ $F_{TLf,}$ and F_{BLf}). The four vertical forces attributed by the foam were then subtracted from the vertical forces measured by each of the four force transducers (F_{TR}, $F_{BR,}$ $F_{TL,}$ and F_{BL}) in Equation 2.1.1 to calculate CoP_{WBB}'.

For ease of discussion, from here forward the CoP_{WBB}' and CoP_{AFP}'' signals derived during the FEO and FEC conditions will be referred to as CoP_{WBB} and CoP_{AFP}', respectively.

CoP Signal Processing

The CoP_{WBB} and CoP_{AFP}' signals were processed and time-aligned according to the methods detailed in *Chapter 2, Part 1*.

2.2.2.3.ii. CoP measures

All four time-domain CoP measures detailed in *Chapter 2, Part 1* were derived in this study as well. Two frequency-domain CoP measures replaced the one frequency-domain CoP measure detailed in *Chapter 2, Part 1* (*PFREQ*) to better represent the frequency content of human sway since, in comparison to the pendulum sway, human sway has a broader frequency spectrum (*i.e.*, more than just one (pendulum oscillation) frequency) and contains higher frequencies. The 95% power frequency, *f95*, and the centroidal frequency, *fC*, were included in this analysis for a total of four time-domain measures (*MD, RMS*, *RANGE*, and *MV*) and two frequency-domain measures (*f95*, and *fC*). The *f95* marks the frequency at which 95% of the total power is contained and the *fC* marks the frequency at which the spectral mass is concentrated. Derivations for these two additional frequency-domain measures are detailed elsewhere in Prieto *et al.* [35]. Both the AP and ML CoP signals were used to derive the six CoP measures in this study since human sway is two-dimensional (as opposed to the one-dimensional measures used to quantify the one-dimensional pendulum sway in our first WBB validation study).

2.2.2.3.iii. Quantifying the WBB's Performance by Determining CoP Measurement Error

As in *Chapter 2, Part 1*, the CoP measurement error was differentiated into two parts: CoP signal error and CoP measure error (derivations detailed in *Chapter 2, Part 1*). At first glance, it was clear that the CoP signal error was less in human sway compared to that in pendulum sway (**Figure 2.2.3**). Because of this, a second set of linear regression coefficients were proposed to represent the WBB's CoP signal error in human sway.

2.2.2.3.iv. Linear Calibration of CoP_{WBB} Signals Based on Human Sway

The human-based linear regression coefficients were determined following the methods detailed in *Chapter 2, Part 1*. The human-based *m* coefficients (m_{AP} = 0.981, m_{ML} = 0.987) are significantly less than the pendulum-based *m* coefficients (m_{AP} = 1.099, m_{ML} = 1.097 from **Table 2.1.2**) ($p < 0.001$), suggesting there may be a significant difference in calibration methods. In this study, the CoP_{WBB} signals were linearly calibrated twice, once using the pendulum-based linear regression coefficients, $CoP_{WBBcalib\_pendulum}$, and once using the human-based linear regression coefficients, $CoP_{WBBcalib\_human}$. The pendulum- *vs.* human-based calibration methods were then compared.

2.2.2.3.v. Statistical Analysis

As in *Chapter 2, Part 1*, Pearson's linear correlation coefficients and RMSEs were used to quantify the WBB's CoP signal agreement and error, respectively. A t-test was first performed to confirm that the RMSEs were significantly different from zero before calibration. Then, a 3-way, fixed effects (sway direction, quiet stance condition, calibration method) ANOVA was performed on the RMSEs to assess the main and interaction effects of sway direction (AP, ML), sway condition (EO, EC, FEO, FEC), and calibration method (none, pendulum-based, human-based). A Bonferroni correction was applied to account for multiple comparisons (2 sway directions × 4 quiet stance conditions × 3 calibration methods = 24 comparisons).

As in *Chapter 2, Part 1*, the percent errors in the CoP measures were used to quantify the WBB's CoP measure error. First, one-way, fixed effect (device) ANOVAs were performed on each CoP measure to assess the difference between the AFP- and WBB-based CoP measures during each of the four quiet stance conditions. Then, one-way, fixed

effect (quiet stance condition) ANOVAs were performed on the CoP measure errors to assess the difference in measure error between quiet stance conditions. This analysis was performed both before and after linear calibration of the CoP_{WBB} signals. Lastly, one-way, fixed effect (calibration method) ANOVAs were performed on the CoP measure errors to assess the effect of (both human- and pendulum-based) calibration on CoP measure error.

2.2.3. Results & Discussion

2.2.3.1. CoP Signal Error

The CoP_{WBB} were significantly correlated with the CoP_{AFP}*'* signals during all four sway conditions and in both sway directions ($r > 0.99$) (**Figure 2.2.3**).

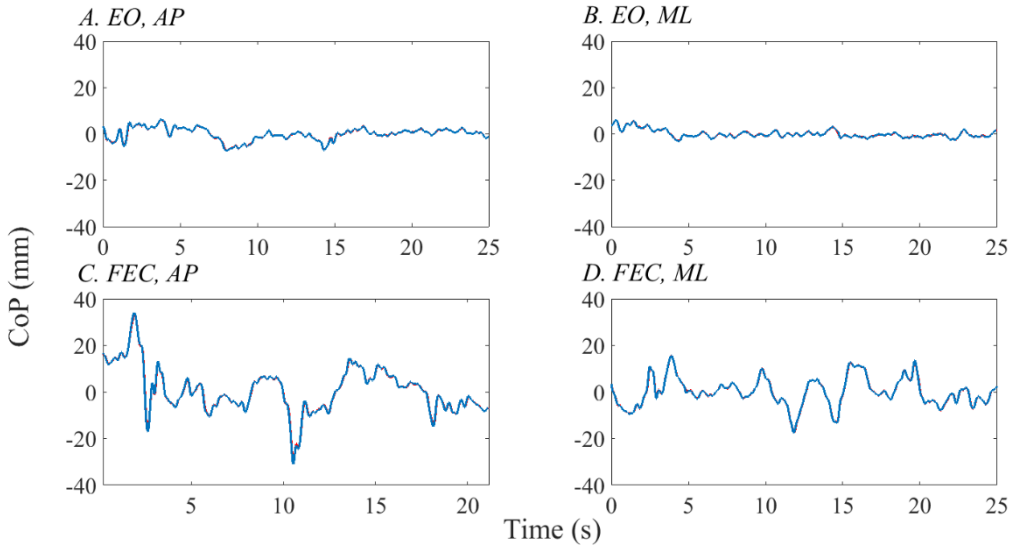

Figure 2.2.3: CoP_{WBB} and CoP_{AFP}*'* signals for a healthy, young adult during the EO and FEC conditions. Postural sway increased as the difficult level of the quiet stance condition increased (from EO (**A** and **B**) to FEC (**C** and **D**)) in both the AP (**A** and **C**) and ML (**B** and **D**) directions. The CoP_{WBB} signals (blue) lay on top of the CoP_{AFP}*'* signals (red). See **Figure 2.2.5** for zoomed-in templates showing the slight difference between the CoP_{WBB} and CoP_{AFP}*'* signals.

The WBBs CoP signal error increased as the amount of postural sway increased, which was induced by increasing the difficulty level of the quiet stance condition (from EO to EC to FEO to FEC) (**Figure 2.2.4,** plots **A** and **B**). The linear trends in CoP signal error were not nearly as strong in human sway as in pendulum sway (compare **Figure 2.2.4,** plots **C** and **D**, to **Figure 2.1.6**). The β coefficients for human sway ($\beta_{AP} = 0.019$, $\beta_{ML} = 0.013$ from

Figure 2.2.4, plots **C** and **D**) are significantly less than that for pendulum sway (β_{AP} = 0.090, β_{ML} = 0.103 from **Figure 2.1.6** and **Table 2.1.3**) ($p < 0.001$). Note the difference in sway range: sway range is less in the human sway compared to the pendulum sway (approximately 120 mm and 100 mm in AP and ML human sway, respectively; approximately 160 mm in both AP and ML pendulum sway).

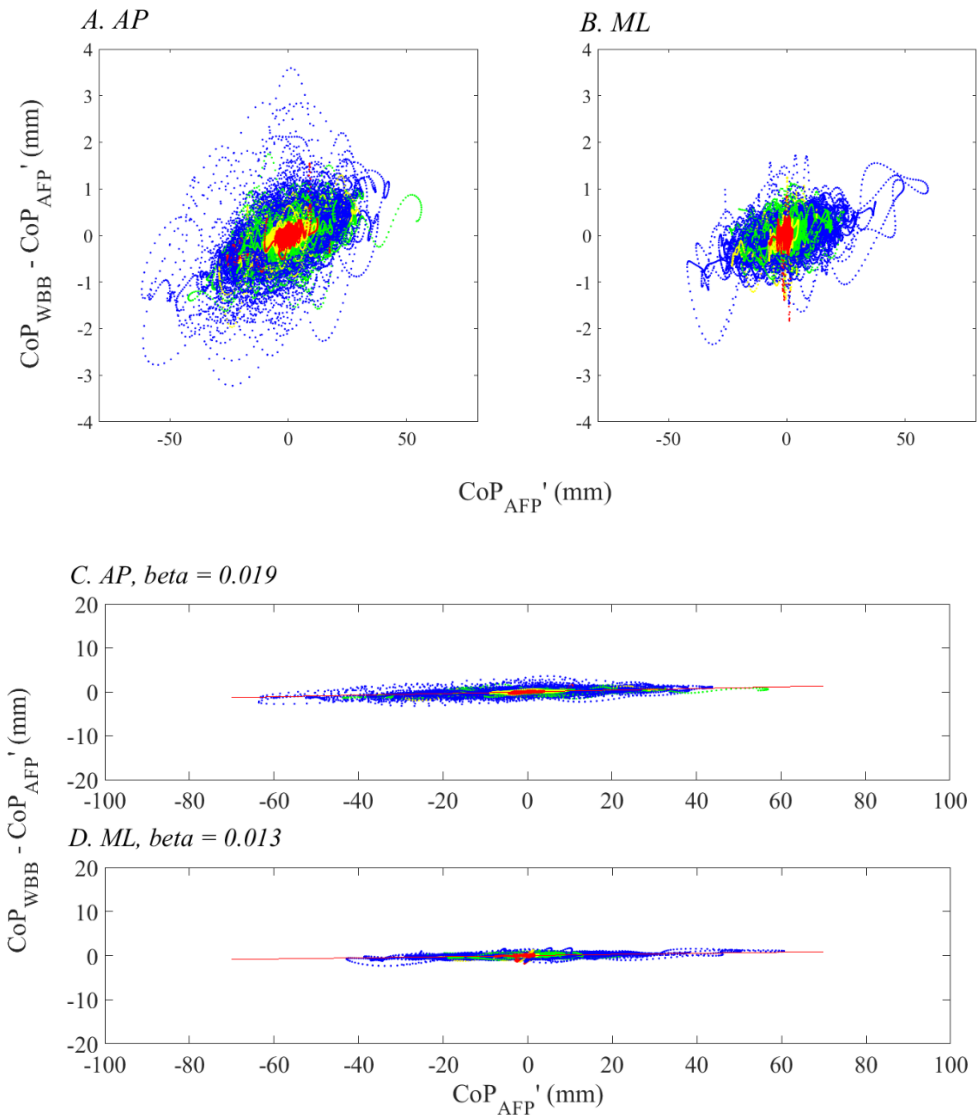

Figure 2.2.4: The WBB's CoP signal error in human sway is less than in pendulum sway: red = EO, yellow = EC, green = FEO, and blue = FEC. Plots (**A**) and (**B**) show the difference in signal error between conditions on unscaled axes to better show the differences in WBB's CoP signal error between quiet stance conditions: signal error increased (marked by larger deviations from zero along the y-axis) as the difficulty level of the quiet stance condition increased (from EO to EC to FEO to FEC). Plots (**C**) and (**D**) show the same data set plotted on scaled axes in order to illustrate the difference in linearity between human and pendulum sway (compare to **Figure 2.1.6**). Note: two different WBB's produced the data in these two figures: WBB_4 in **Figure 2.1.6** and WBB_12 in this figure. The β coefficients associated with WBB_12 for the pendulum sway are β_{AP} = 0.109, β_{ML} = 0.107 from **Table 2.1.3**.

The difference in calibration methods was then compared. The human-based calibration method appeared to adjust the CoP_{WBB} signals better than the pendulum-based calibration method (**Figure 2.2.5**), although the uncalibrated CoP_{WBB} signals appear to agree most with the CoP_{AFP}' signals.

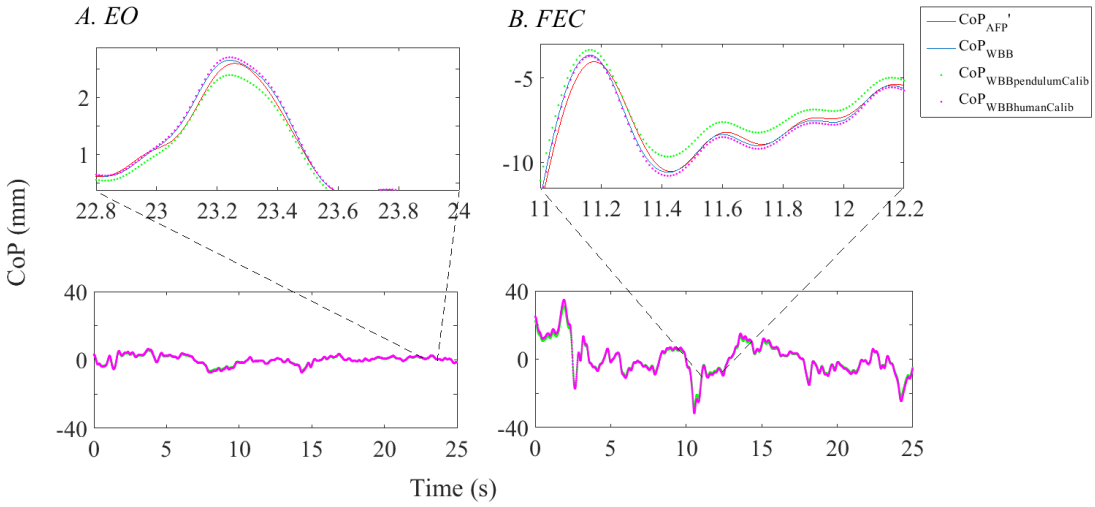

Figure 2.2.5: Comparison of pendulum- *vs.* human-based calibration methods for the CoP_{WBB} signals: red = CoP_{AFP}' signals, blue = CoP_{WBB} signals, green = $CoP_{WBBcalib\_pendulum}$ signals, and magenta = $CoP_{WBBcalib\_human}$ signals. The human-based calibration method appeared to better adjust the CoP_{WBB} signals. Both signals (EO (**A**) and FEC (**B**)) are the AP signals from **Figure 2.2.3**.

The effect of calibration method, as well as sway direction and quiet stance condition, was then quantified using RMSEs (**Figure 2.2.6**). The RMSEs were significantly different from zero before calibration ($p < 0.001$ in both sway directions). There was a statistically significant effect of sway direction, quiet stance condition, and calibration method on the RMSEs. The RMSEs in the AP direction were significantly greater than that in the ML direction ($F_{1,2,3} = 109.07$, $p < 0.001$). The RMSEs in the FEO and FEC conditions were significantly greater than that in the EO and EC conditions, with the FEC RMSEs significantly greater than the FEO RMSEs which were significantly greater than both the EO and EC RMSEs ($F_{3,1,2} = 193.44$, $p < 0.001$). The RMSEs for the calibrated CoP_{WBB} signals (both $CoP_{WBBcalib\_pendulum}$ and $CoP_{WBBcalib\_human}$) were significantly greater than that for the uncalibrated CoP_{WBB} signals, with the pendulum-based RMSEs significantly greater than the human-based RMSDs which were significantly greater than the uncalibrated

RMSDs ($F_{2,3,1}$ = 217.30, p < 0.001). All interaction effects were significant (p < 0.001), meaning the significance of each main effect depends on another main effect.

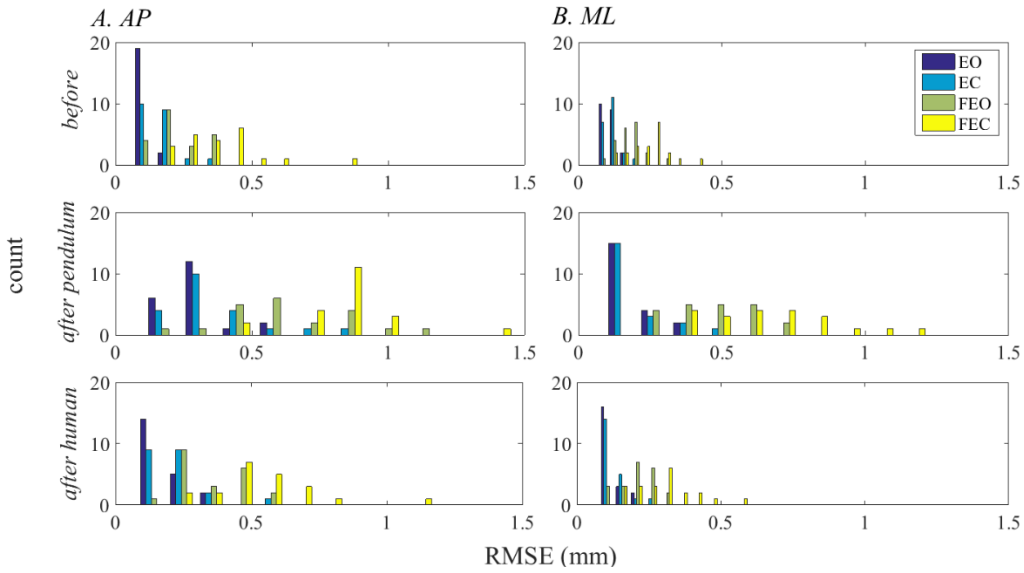

Figure 2.2.6: Effect of both pendulum- and human-based calibration on CoP_{WBB} signal error quantified by RMSEs. This figure shows the distribution of the RMSEs across all four quiet stance conditions (purple = EO, blue = EC, green = FEO, and yellow = FEC) in both the AP (**A**) and ML (**B**) directions, both before and after linear calibration of the CoP_{WBB} signals: "*after pendulum*" refers to the $CoP_{WBBcalib\_pendulum}$ signals, and "*after human*" refers to the $CoP_{WBBcalib\_human}$ signals. Both calibration methods increased the CoP signal error (the pendulum-based calibration more than the human-based calibration).

2.2.3.2. CoP Measure Error

There was not a significant difference between the AFP- and WBB-based CoP measures before linear calibration of the CoP_{WBB} signals (note the low F statistics and high p-values in **Table 2.2.1**).

Table 2.2.1: Means and standard deviations of both AFP- and WBB-based CoP measures during the four quiet stance condition (EO, EC, FEO, and FEC). The *F* statistics and *p*-values are the results from the one-way, fixed effect (device) ANOVAs. The low *F* statistics and high *p*-values show that there is not a significant difference between AFP- and WBB-based CoP measures before linear calibration of the CoP_{WBB} signals.

WITHOUT FOAM								
Measure	***EO condition***				***EC condition***			
	AFP: mean ± std	**WBB: mean ± std**	$F_{1,40}$	***p*-value**	**AFP: mean ± std**	**WBB: mean ± std**	$F_{1,40}$	***p*-value**
MD	3.77 ± 1.78	3.84 ± 1.81	0.01	0.906	4.67 ± 2.27	4.75 ± 2.31	0.01	0.906
RMS	4.40 ± 2.02	4.48 ± 2.06	0.02	0.901	5.47 ± 2.56	5.56 ± 2.61	0.02	0.895
RANGE	22.19 ± 10.14	22.70 ± 10.31	0.03	0.873	28.13 ± 12.49	28.85 ± 12.81	0.03	0.855
MV	7.79 ± 1.92	8.22 ± 1.97	0.53	0.471	10.60 ± 3.12	11.13 ± 3.22	0.29	0.593
f95	1.49 ± 0.41	1.53 ± 0.42	0.06	0.801	1.65 ± 0.41	1.67 ± 0.42	0.01	0.906
fC	0.65 ± 0.18	0.67 ± 0.18	0.07	0.795	0.72 ± 0.18	0.73 ± 0.18	0.04	0.838
WITH FOAM								
Measure	***FEO condition***				***FEC condition***			
	AFP: mean ± std	**WBB: mean ± std**	$F_{1,40}$	***p*-value**	**AFP: mean ± std**	**WBB: mean ± std**	$F_{1,40}$	***p*-value**
MD	8.44 ± 2.73	8.55 ± 2.77	0.02	0.898	11.84 ± 3.37	12:02 ± 3.49	0.03	0.859
RMS	9.61 ± 3.09	9.75 ± 3.14	0.02	0.890	13.65 ± 3.88	13.88 ± 4.00	0.04	0.852
RANGE	50.28 ± 16.90	51.17 ± 17.18	0.03	0.866	72.90 ± 22.19	74.41 ± 22.77	0.05	0.829
MV	20.27 ± 6.85	20.96 ± 7.03	0.10	0.752	36.85 ± 17.31	38.13 ± 18.07	0.06	0.815
f95	1.52 ± 0.30	1.55 ± 0.31	0.08	0.780	1.90 ± 0.44	1.95 ± 0.45	0.09	0.762
fC	0.68 ± 0.13	0.69 ± 0.13	0.12	0.733	0.83 ± 0.17	0.84 ± 0.17	0.08	0.782

There was a significant effect of quiet stance condition on CoP measure error before linear calibration of the CoP_{WBB} signals (note the high *F* statistics and low *p*-values in **Table 2.2.2. A**). The magnitude of percent error in *MD* and *RMS* was significantly less in the FEO condition compared to both the EO and EC conditions. The magnitude of percent error in *RANGE* were significantly less in the FEO condition compared to the EC condition. The magnitude of percent error in *MV* was significantly less in both the FEO and FEC conditions compared to both the EO and EC conditions. (The statistics for the time-domain CoP measure errors are contained in **Table 2.2.2. A.**) The percent errors for *f95* and *fC* are -1.77 ± 2.36 and -1.91 ± 1.02, respectively. There was no significant difference in the

magnitude of percent error between quiet stance conditions for both frequency-domain measures (*f95*: $F_{3,80}$ = 1.24, p = 0.301; *fC*: $F_{3,80}$ = 1.11, p = 0.352).

Table 2.2.2: Time-domain CoP measure (%) errors both before (A) and after (B and C) linear calibration of CoP_{WBB} signals. The *F* statistics and *p*-values are the results from the one-way, fixed effect (quiet stance condition) ANOVAs The high *F* statistics and low *p*-values show that there is a significant difference in CoP measure error between quiet stance conditions. The CoP measure errors are smallest before calibration (**A**). The two frequency-domain CoP measures are not included in this table because the frequency-domain CoP measure errors are not influenced by the linear calibrations.

Measure	EO mean ± std	EC mean ± std	FEO mean ± std	FEC mean ± std	$F_{3,80}$	*p*-value
A. Percent error of CoP_{WBB} signals (*"before"*)						
MD	-1.88 ± 0.36	-1.81 ± 0.36	-1.27 ± 0.49	-1.51 ± 0.64	6.23	0.001
RMS	-1.84 ± 0.36	-1.93 ± 0.34	-1.38 ± 0.51	-1.58 ± 0.65	5.61	0.002
RANGE	-2.41 ± 0.81	-2.55 ± 0.70	-1.82 ± 0.78	-2.01 ± 0.78	4.14	0.009
MV	-5.80 ± 1.91	-5.11 ± 1.09	-3.44 ± 0.66	-3.38 ± 0.45	22.76	<0.001
B. Percent error of $CoP_{WBBcalib\_pendulum}$ signals (*"after pendulum"*)						
MD	7.33 ± 0.33	7.32 ± 0.32	7.79 ± 0.44	7.57 ± 0.58	5.79	0.001
RMS	7.30 ± 0.33	7.22 ± 0.30	7.70 ± 0.46	7.51 ± 0.59	5.14	0.003
RANGE	6.77 ± 0.75	6.65 ± 0.63	7.29 ± 0.71	7.12 ± 0.70	3.89	0.012
MV	3.67 ± 1.72	4.31 ± 0.99	5.81 ± 0.60	5.88 ± 0.41	23.02	<0.001
C. Percent error of $CoP_{WBBcalib\_human}$ signals (*"after human"*)						
MD	-3.62 ± 0.37	-3.62 ± 0.39	-3.00 ± 0.51	-3.22 ± 0.69	7.69	<0.001
RMS	-3.67 ± 0.35	-3.77 ± 0.39	-3.13 ± 0.54	-3.32 ± 0.71	7.12	<0.001
RANGE	-4.21 ± 0.79	-4.39 ± 0.73	-3.57 ± 0.78	-3.77 ± 0.83	4.95	0.003
MV	-7.62 ± 1.99	-6.95 ± 1.13	-5.20 ± 0.70	-5.18 ± 0.47	21.84	<0.001

As shown in **Table 2.2.2**, CoP measure error for the time-domain measures mainly increased with both the pendulum- and human-based calibration (difference between **Table 2.2.2 A, B,** and **C**). Because the magnitude of percent error in the two frequency-domain measure errors does not change with linear calibration of the CoP_{WBB} signals, *f95* and *fC* are not reported in **Table 2.2.2**.

2.2.3.3. Differences between Human- & Pendulum-Based CoP Signals

There was much more CoP measurement error when the WBB quantified pendulum-based signals compared to human-produced signals. This is likely due to the many

differences between the controlled, simulated sway signals (produced by the inverted pendulum model) and the uncontrolled, real human sway signals (produced by healthy, young adults) (discussed in detail in Section 2.1.4). Because the inverted pendulum's CoM shifted much faster (higher sway velocity) and further (larger sway range) than that during human postural sway, there were significantly more shear and horizontal force components contained within the pendulum-produced CoP signals. The WBB is composed of just vertical force sensors and therefore cannot measure the shear and horizontal components of the CoP trajectory. This technological limitation of the WBB likely explains why there was significantly more CoP measurement error for the pendulum-based CoP signals compared to the human-based CoP signals.

The distributions of the human- and pendulum-based CoP data sets are shown in **Figure 2.2.7**. Upon visual inspection, it appears as though the human- based CoP signals (both AP and ML) follow exponential distributions with strong peaks at zero, rapid decay, and heavy tails (**Figure 2.2.7, A & B**). This distribution pattern may help explain why the human-based calibration method did not reduce the WBB's CoP signal error (quantified by RMSEs in **Figure 2.2.6**). Unlike the pendulum-based CoP data set, most of the human-based CoP data is concentrated around a CoP displacement value of zero (as shown in **Figure 2.2.4**). By visually comparing the human- to the pendulum-based distributions (**Figure 2.2.7 A & B** *vs.* **Figure 2.2.7 C & D**), we can deduce that the 95% confidence interval for the human-based CoP data is much smaller compared to that for the pendulum-based CoP data (range of approximately 20mm and 120mm for the human- and pendulum-based CoP data, respectively). This may help explain why a linear correction significantly reduced the WBB's CoP signal error for the pendulum-based CoP data set but had a limited (negative) effect on the WBB's CoP signal error for the human-based CoP data set (shown in **Figure 2.2.6**). We conclude that a linear correction was not an appropriate calibration procedure for the human data set: it had no-to-little effect on the majority of the data (since the majority of the human CoP values were very small) and it appeared to induce a small amount of error for the few larger CoP values (values shown by the tails of the histograms in **Figure 2.2.7 A & B** and errors quantified by the RMSEs in **Figure 2.2.6**).

Despite significant effort, we still cannot explain why the human-based calibration had a (slight) negative effect on the CoP measurements: the human-based linear calibration coefficients were derived from the human CoP data set and a slight linear trend does exist in the WBB's CoP signal error when measuring human CoP (Figure 2.2.4). For reference, the CoP signal errors for the human-based calibrated and uncalibrated CoP_{WBB} signals are strongly correlated (Pearson's correlation coefficient equal 1.0 for both CoP directions).

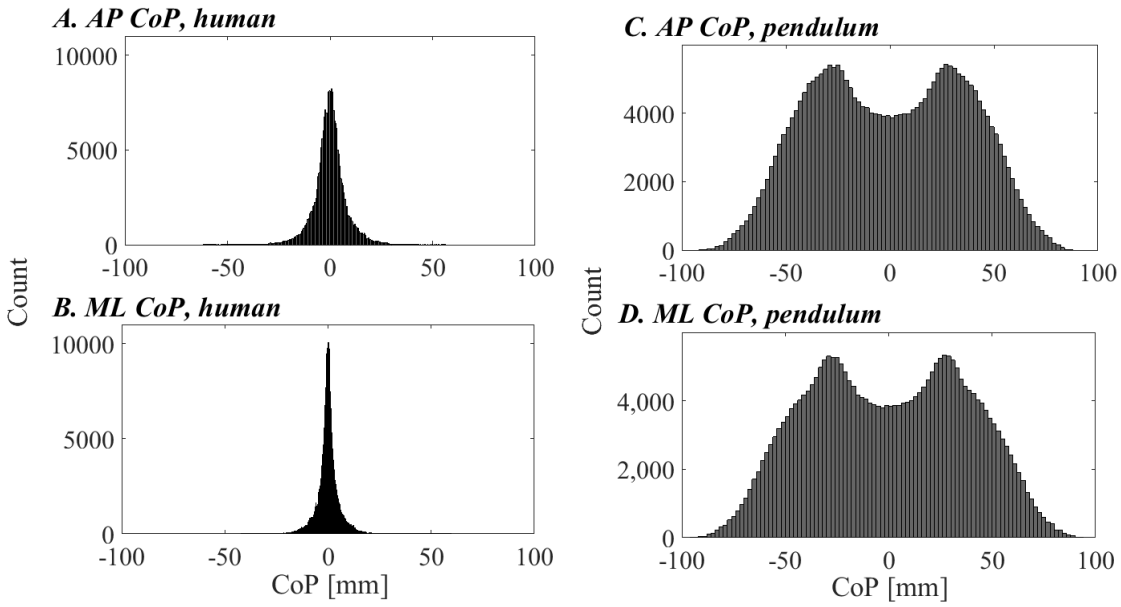

Figure 2.2.7: Histograms to show the distributions of the human- *vs*. pendulum-based CoP data. Plots **A & B** show the exponential distributions of the human-based data in both the AP and ML directions, respectively. [The human data set consists of 210000 total data points: 2500 data points per trial (sampling frequency of 100 samples/second x 25-second worth of data per trial), 12 trials per subject (4 conditions x 3 trials per condition), and 7 subjects = 2500 x 12 x 7 = 210000 total.] Plots **C & D** show the distribution of the pendulum-based data in both the AP and ML directions, respectively. [The pendulum data set consists of 270000 total data points: 2500 data points per trial (sampling frequency of 100 samples/second x 25-second worth of data per trial), 9 trials per WBB (3 displacement heights x 3 displacement angles), and 12 WBBs = 2500 x 9 x 12 = 270000 total.] Our experimental setup in *Chapter 2, Part 1* induced the non-normal distributions in **C & D.** [The combination of the three different displacement heights (h = 900, 1000, and 1100mm) and three different displacement angles (θ = 2, 4, and 6º) produced non-normally distributed CoP displacements when collapsing all 9 CoP displacement conditions together.] For each plot, the x-axis represents CoP displacement (in mm) and the y-axis represents the count (*i.e.*, the number of data points in the data set corresponding to the specific CoP displacement value on the x-axis). This figure shows the ground truth data (CoP quantified by the "gold standard" force plate).

2.2.4. Conclusions

In *Chapter 2, Part 1* we discuss WBB's limited accuracy and precision due to several mechanical and electronic limitations innate to the measurement device. The WBB's has substantially low resolution (0.5 mm), low and inconsistent sample rate (time jitter), low signal to noise ratio, and tends to produce missing data due to occasional electronic glitches

during data acquisition [104]. Because the WBB has low resolution, and because human-based CoP tends to be limited in range (**Figure 2.2.7**) with the majority of CoP displacements falling below ± 10 mm, there appears to be no advantage to calibrating our human-based CoP data set. Here in *Chapter 2, Part 2* we show that there was not a significant difference between the AFP- and WBB-based CoP measures before linear calibration of the CoP_{WBB} signals (**Table 2.2.1**). We then show that neither calibration method reduces the WBB's CoP measure error (**Figure 2.2.6** and **Table 2.2.2**). Although we do not fully understand why the human-based calibration method does not reduce error, we attempt to explain this as best we can. Despite the significant effort dedicated to calibrating the CoP_{WBB} signals to reduce the WBB's CoP measurement error, it appears as though the uncalibrated CoP_{WBB} signals most accurately quantify CoP in human postural sway. Because of this, neither pendulum- nor human-based calibration were implemented in *Chapters 4* of this dissertation. The uncalibrated CoP_{WBB} signals were used to provide CoP estimates during our longitudinal assessment of postural sway in older adults with MCI.

2.2.5. Contributions

Contributor	Affiliation(s)	Support Provided
Heather Schlueter	BD Laboratory	-assisted with data acquisition
Martina Mancini	BD Laboratory	-assisted with CoP signal processing and analysis -provided guidance in statistical analysis -contributed to interpretation of results -provided feedback during manuscript preparation
Robert Peterka (*DAC member*)	BME Department	-provided feedback during manuscript preparation -provided some assistance during data analysis and interpretation
Jeffrey Kaye (*DAC member*)	ORCATECH, LAADC, BME & Neurology Departments	-provided feedback during manuscript preparation
Peter Jacobs (*DAC chair*)	BME Department	-provided feedback during manuscript preparation
Fay Horak (*PhD advisor*) (*DAC member*)	BD Laboratory, BME & Neurology Departments	-provided laboratory space and equipment for data acquisition -contributed to interpretation of results -provided feedback during manuscript preparation

***CHAPTER 3**: Cross-Sectional Study of Postural Sway in MCI: Using an Accelerometer to Quantify Postural Sway during Quiet Stance with Cognitive Loading in Older Adults with MCI*

Summary

Objective: Our study objective was to characterize the associations between cognitive status and postural control in older adults during quiet stance both with (dual-task) and without (single-task) domain-specific cognitive loading.

Hypotheses: Our hypotheses were: 1. Older adults with MCI will have more postural sway and higher postural dual-task costs compared to cognitively intact older adults since reduced postural control and dual-tasking ability has been observed in older adults with cognitive impairment; and, 2. Attention- and executive function-based cognitive loads will elicit higher postural dual-task costs compared to memory-based cognitive loads since attentional and executive control influences posture.

Methods: Twenty-nine older adults (10 intact, 19 MCI) Twenty-nine subjects enrolled in ORCATECH studies were recruited for this pilot study. Three different domain-specific cognitive loads were presented to each subject during quiet stance, each designed to tax a specific cognitive domain (*e.g.*, attention, memory, and executive function). Postural sway was quantified using an accelerometer mounted to the subject's posterior trunk and objective postural sway measures were derived from the accelerometry data.

Results: Higher sway jerk and frequency differentiated the MCI group from the intact group during the single-task condition. Lower postural dual-task costs in sway path length, jerk, and frequency differentiated the MCI group from the intact group during the dual-task conditions. The executive function-based load elicited significantly lower postural- dual-task costs compared to the other two domain-specific cognitive loads. Although there was no interaction effect between cognitive status and cognitive load, the separation between cognitive status groups appeared to be most pronounced during the attention-based dual-task condition.

Conclusions: Our findings suggest that mild postural instabilities do occur during early cognitive decline (as in MCI) and quantifying postural sway under the dual-task condition could help to further differentiate postural sway in older adults with MCI from cognitively intact older adults. This is the first study to quantify both postural sway jerk and frequency during cognitive dual-tasking in older adults with and without MCI. Both postural sway measures expressed sensitivity to MCI status under both single- and dual-task conditions. If our findings hold with a larger, more diverse sample population, lower than normal postural dual-task costs may suggest mild cognitive decline. Future studies of postural sway and dual-task cost in MCI might provide more insight as to why older adults with MCI are at a higher risk of falls. Such knowledge would yield opportunity for the development and implementation of therapeutic interventions and aid in fall prevention.

3.1. Introduction

In *Chapter 1* we explained the use of cognitive-postural dual-tasking to study the relationship between cognition and postural control. Here in *Chapter 3* we use the dual-task paradigm to examine postural sway in older adults with and without MCI under dual-task conditions and assess the effect different cognitive task types have on postural sway.

3.1.1. Background

Attentional and/or executive capacity consistently emerge as strong predictors of postural control and decline; cognitive deficits relating to attentional and/or executive control have been associated with poor performance on complex mobility tasks, other postural instabilities, and frequent falls [41,65,115-118]. Attention is the anatomical network responsible for processing incoming or attended-to excitation to influence the operation of other brain networks and is often considered a specific executive function [116]. Executive functions are defined as higher cognitive processes necessary for planning, monitoring, and executing complex sequences of goal-driven actions [119]. When attentional and/or executive functioning is compromised, problems with information processing, resource allocation and flexible set shifting (all essential functions for dual-tasking) arise. This chapter explores whether cognitive tasks designed to specifically tax attention and/or executive function interfere more with postural control, quantified by a higher postural dual-task cost, compared to other domain-specific cognitive tasks (*e.g.*, memory-based tasks).

3.1.2. Objectives & Hypotheses

This study quantified postural sway during quiet stance in both cognitively intact and mildly cognitively impaired older adults under both single- and dual-task conditions. Our main objective was to characterize the associations between cognitive status (intact *vs.* MCI) and postural control both with (dual-task) and without (single-task) domain-specific cognitive loading.

Our main objective yields two hypotheses:

Hypothesis I: We hypothesize that older adults with MCI will have more postural sway and higher postural dual-task costs compared to cognitively intact older adults since

reduced postural control and dual-tasking ability has been observed in older adults with cognitive impairment.

Hypothesis II: We hypothesize that attention- and executive function-based cognitive loads will elicit higher postural dual-task costs compared to memory-based cognitive loads since attentional and executive control influences posture.

If both the postural and cognitive task compete for the same collection of neural resources during the dual-task condition the older adult's dual-tasking ability will likely be impaired, which may be evidenced by a higher postural dual-task cost.

3.2. Experimental Methods

The Institutional Review Board at OHSU approved this study's experimental methods and all subjects gave informed written consent prior to participation.

3.2.1. Subjects

Twenty-nine older adults enrolled in Oregon's Center for Aging & Technology (ORCATECH) studies were recruited for this pilot study. Twenty-one subjects (10 intact, 11 MCI) were recruited from either ORCATECH's Living Laboratory (OLL) study or from the Intelligent Systems for Assessing Age Change (ISAAC) study, detailed elsewhere in [86]. Both the OLL and ISAAC studies are a part of the Oregon Alzheimer's Disease Center (OADC), the core program at OHSU's Layton Aging & Alzheimer's Disease Center, meaning the 21 subjects from OLL/ISAAC undergo comprehensive neuropsychological testing on an annual basis. The remaining eight subjects (8 MCI) were recruited from ORCATECH's Conversational Engagement Study (CES), a study that is not a part of the OADC, meaning these eight subjects have not undergone comprehensive neuropsychological testing. Subject characteristics by cognitive status group (intact *vs.* MCI) are contained in **Table 3.1**. All 29 subjects were ambulatory, community-dwelling older adults that met the following inclusion criteria: free of physical impairment that significantly inhibits stability; no walking aid (*i.e.*, walker or cane); no known visual, vestibular, or somatosensory impairment greater than what is normal for one's age; and, either classified as "cognitively intact" or "mildly cognitively impaired" (*i.e.*, MCI). All

subjects provided written informed consent, approved by the institutional review board at OHSU.

Table 3.1: Subject characteristics, by cognitive status group

	Intact	***MCI***	**Group differences** $F_{1,27}$, p
# of subjects	10	19	----------
Sex (% female) (#)	80 (8)	74 (14)	----------
Race (% non-white) (#)	10 (1)	32 (6)	----------
Age (yrs) (mean ± std)	88.2 ± 4.9	82.4 ± 7.2	**5.10, 0.032***
Education (yrs) (mean ± std)	15.0 ± 1.6	16.1 ± 2.6	1.39, 0.249
MMSE Score	28.8 ± 1.2	28.1 ± 1.6	1.69, 0.205
Tinetti Balance Score**	1.9 ± 3.1	2.6 ± 3.3	0.21, 0.651
**8 subjects (all MCI) did not have Tinetti Balance Scores			

There was a significant difference in age between cognitive status groups, with the intact group significantly older than the MCI group ($F_{1,27}$ = 5.10, p = 0.032 from **Table 3.1**). There was not a significant difference in years of education, MMSE Scores, and Tinetti Balance Scores between the two cognitive status groups.

3.2.2. Clinical Diagnostic MCI Criteria

Cognitive status for the 21 OLL/ISAAC subjects was determined based on OADC's annual clinical and neuropsychological testing, detailed elsewhere in [1,86]. The conventional Petersen/Winblad criteria as operationalized by the Alzheimer's Disease Neuroimaging Initiative (ADNI) was used to diagnose MCI, detailed elsewhere in [24,25]. Impaired cognitive function was operationalized using the domain-specific neuropsychological tests detailed elsewhere in Kaye *et al.* [86] and was defined as a score of 1.5 SDs or more below the model-derived predicted mean value, adjusted for age, education and sex. In this study, all 11 OLL/ISAAC subjects classified as "MCI" or "intact" were diagnosed based on their most recent annual neuropsychological evaluation. Because all eight CES subjects did not undergo comprehensive neuropsychological testing, their cognitive status was operationalized by the global clinical dementia rating (CDR): all eight CES subjects were classified as "MCI" based on a CDR score of 0.5.

3.2.3. Procedures

The subject performed a series of four 60-second trials during quiet stance both with (three trials) and without (one trial) cognitive loading. Each of the three cognitive dual-task conditions consisted of a cognitive load designed to tax specific cognitive domains (**Table 3.2**). Before each dual-task, the subject was given clear instructions and an opportunity to train to ensure that the subject conceptually understood the specific cognitive task (described in **Table 3.3**). The subject was free to rest between tasks to minimize the effect of physical and mental fatigue on postural performance. Task sequence (**Table 3.2**) was consistent across all 29 subjects.

Table 3.2: The three cognitive loads used for dual-tasking during quiet stance

Trial *(in sequence)*	**Cognitive domain(s)**	**Cognitive test**	**Abbr.**
1	Attention	Alpha-Numeric Sequencing Task	ANST
2	----------	----------	single
3	Memory	Hopkins Verbal Learning Task, delayed recall	HVLT
4	Executive function	Altered Simon Task, incongruent condition	AST

Table 3.3: Administration of the three cognitive dual-tasks

Dual-task *(in sequence)*	**Description of and instructions for each cognitive dual-task**
ANST	ANST is a simple, easy-to-administer, cognitive task used (in both the clinic and laboratory) to tax attentional set shifting, information processing, and working memory [120]. The subject was instructed to stand quietly while counting and reciting the alphabet, alternating between number and letter. *E.g.*, "1-A-2-B-3-C-4-D, *etc.*" The subject was instructed to pick up where he/she left off if he/she made a mistake and/or forgot his/her place in the alpha-numeric sequence. Performance on ANST was used to quantify attention in this study.
HVLT	HVLT is a clinical neuropsychological test designed to test both short- and long-term memory function. Instructions were administered according to the HVLT instruction manual [121] with one exception – subject sat during encoding and stood during recall. The subject had three practice trials to learn a list of 12 words (3 categories, 4 words/category) (encoding). To test short-term memory, the subject was then instructed to stand quietly while recalling the list of 12 words he/she just learned (immediate recall). To test long-term memory function, the subject was instructed to stand quietly while recalling the list of 12 words he/she learned 20-25 minutes prior (delayed recall). Performance during delayed recall was used to quantify memory function in this study.
AST	AST is an altered version of the Simon Task, a neuropsychological test designed to test executive function [122-125]. The subject wore headphones and heard the word "LEFT" or "RIGHT" in either the *left* or *right* ear. The subject was instructed to stand quietly while saying what ear he/she heard the word in and *not* the word itself. For the congruent condition (mild difficulty level), the word "LEFT" was transmitted via the *left* earphone and the word "RIGHT" was transmitted via the *right* earphone. For the incongruent condition (moderate difficulty level), the word "LEFT" was transmitted via the *right* earphone and the word "RIGHT" was transmitted via the *left* earphone. Performance during the more difficult (incongruent) condition was used to quantify executive function in this study.

Performance on the three cognitive dual-tasks was used to quantify cognition during quiet stance. [A significant limitation of this study was our inability to reliably measure cognitive performance during all three cognitive dual-tasks. A wireless microphone was used to record our subjects' verbal responses during the cognitive dual-task conditions. The audio recordings were to be transcribed and used to measure cognitive performance. Unfortunately, the wireless microphone frequently malfunctioned resulting in a significant amount of missing data. Fortunately though, the subjects' verbal responses were also manually recorded as well during two out of the three cognitive dual-tasks, so cognitive performance data was missing for only one cognitive dual-task (ANST).]

Posturography was used to quantify postural sway during quiet stance. An inertial sensor (Opal monitor, APDM, Inc.), composed of a tri-axial accelerometer and gyroscope, was mounted to the subject's posterior trunk (L5 lumbar vertebrae level) near the approximate location of the body's CoM (**Figure 1.2** from *Chapter 1*). Tri-axial acceleration signals were acquired from the inertial sensor, processed, and used to derive the objective postural sway measures.

3.2.4. Acc Signal Processing

All Acc signals were processed using Matlab R2015a (The MathWorks, Natick, MA, USA). Tri-axial acceleration signals were collected with a 108-Hz sampling frequency and transformed to a horizontal-vertical coordinate system to account for the inherent (slight) tilt of the inertial sensor when mounted to the posterior trunk [58]. The two-dimensional (AP and ML), horizontal acceleration signals were then zero-meaned and filtered with a 3.5 Hz cut-off, zero-phase, low-pass Butterworth filter [37].

3.2.5. Outcome Measures

3.2.5.i. Cognitive Performance Measures

Cognitive performance for the attention-based cognitive dual-task (ANST) was not quantified due to technical errors (detailed above in *Section 3.2.3*). In the memory-based cognitive dual-task (HVLT), cognitive performance was quantified by the number of words recalled (in percent, out of 12). In the executive function-based cognitive dual-task (AST), cognitive performance was quantified by the number of cues accurately identified (in percent, out of 16).

3.2.5.ii. Postural Performance Measures

Measures of postural sway and postural dual-task cost were used to quantify postural performance. All measures of postural sway and dual-task cost were derived using Matlab R2015a. Four objective postural sway measures were carefully selected to represent different and independent features of the postural sway signal: total sway path length (*TPATH*) [35], mean sway velocity (*MV*) [35,126,127], normalized mean sway jerk (*NJERK*) [37], and centroidal sway frequency (*fC*) [35,126,127] (**Table 3.4**). All four postural sway measures were derived from the resultant planar (two-dimensional,

horizontal) acceleration (Acc) signals. Measure derivations are detailed elsewhere in Mancini *et al.* [63].

Table 3.4: Acc-based postural sway measures

Measure	Description / Computation	Units
TPATH	Total sway path length: the total length of the Acc trajectory	mm/s^2
MV	Mean sway velocity: the mean of the time integral of the Acc trajectory	mm/s
NJERK	Normalized mean sway jerk: the mean of the time derivative of the Acc trajectory, normalized by sway range (squared) and the time duration of the trial	---------
fC	Centroidal sway frequency: the frequency at which the spectral mass is concentrated	*Hz*

Postural dual-task costs were used to quantify the effect of a specific cognitive load (**Table 3.2**) on postural performance during quiet stance. The postural dual-task cost [100*(dual-task condition – single-task condition)/single-task condition] was calculated for each postural sway measure (**Table 3.4**) during each dual-task condition (Trials 1, 3 and 4 in **Table 3.2**) using Trial 2 in **Table 3.2** as the single-task measurement. Higher costs are positive in value and represent a larger increase in sway from the single- to dual-task condition.

3.2.6. Statistical Analysis

All statistical analyses were performed using Matlab R2015a. Data from 26 subjects (9 intact, 17 MCI) were included in the statistical analysis. Equipment malfunctioned for 2 MCI subjects. One intact subject was an outlier (postural sway, quantified by all four postural sway measures, was greater than 2.5 standard deviations from the group means under the single-task condition). Non-normally distributed data were log-transformed to achieve normal distributions prior to the statistical analyses detailed below.

3.2.6.i. Cognitive Performance

To investigate the effect of cognitive status (intact, MCI) on cognitive performance during the dual-task conditions, one-way, fixed effect (cognitive status) ANOVAs were performed on the cognitive performance measures.

3.2.6.ii. Postural Performance

First, postural sway during the single-task condition was analyzed. Each subject's 60-second single-task condition was used to represent the subject's postural sway during quiet stance. To investigate the effect of cognitive status (intact, MCI) on postural sway without cognitive loading, one-way, fixed effect (cognitive status) ANOVAs were performed on the four postural sway measures (**Table 3.4**). Statistical significance was determined at the 5% level.

Second, postural sway during the dual-task conditions was analyzed. To investigate the effect of both cognitive status (intact, MCI) and cognitive load (attention-based, memory-based, executive function-based) on postural sway during the three 60-second dual-task conditions, two-way, fixed effect (cognitive status, cognitive load) ANOVAs were performed on the four postural sway measures. Then, to investigate the effect of both cognitive status and cognitive load on postural dual-task cost, two-way, fixed effect (cognitive status, cognitive load) ANOVAs were performed on the four measure-specific dual-task costs. Statistical significance was determined at the 5% level. A Bonferroni correction was applied to account for multiple comparisons (3 different cognitive loads), adjusting the significant p-value from 0.050 to 0.017 ($\alpha = 0.050$, $m = 3$ dual-task conditions, critical value = $\alpha/m = 0.050/3 = 0.017$). Because all four postural sway measures have been determined to be independent of one another [126,127], each quantifying a distinct and separate feature of postural sway, the critical value was not adjusted for repeated measures.

3.3. Results

3.3.1. Cognitive Performance

There was no statistically significant difference in cognitive performance between the two cognitive status groups during the dual-task conditions. Cognitive performance for the attention-based cognitive dual-task (ANST) was not quantified due to technical errors. In the executive function-based cognitive dual-task (AST), all but two subjects (1 intact, 1 MCI) earned a perfect score, meaning there was no difference in executive function-based cognitive performance between groups. Additionally, there was no group difference in

cognitive performance on the memory-based cognitive dual-task (HVLT) ($F_{1,24}$ = 0.49 p = 0.490).

3.3.2. Postural Performance

3.3.2.i. Postural Sway during the Single-Task Condition

Postural sway jerk (*NJERK*) and frequency (*fC*) were significantly higher in the MCI group compared to the intact group during quiet stance with no cognitive loading (the single-task condition) (**Table 3.5, Figures 3.1-2**).

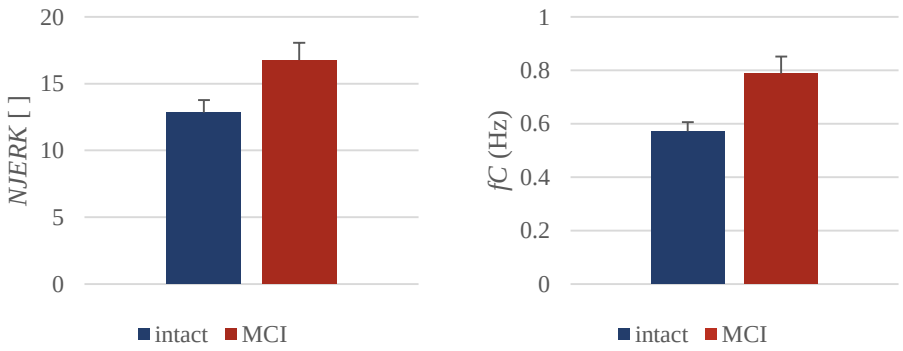

Figure 3.1: Higher postural sway jerk (*NJERK*) and frequency (*fC*) during the single-task condition (quiet stance with no cognitive loading) was associated with MCI. Histograms show the group means and SEs. *NJERK* and *fC* were significantly higher in the MCI group (see statistical results in **Table 3.5**).

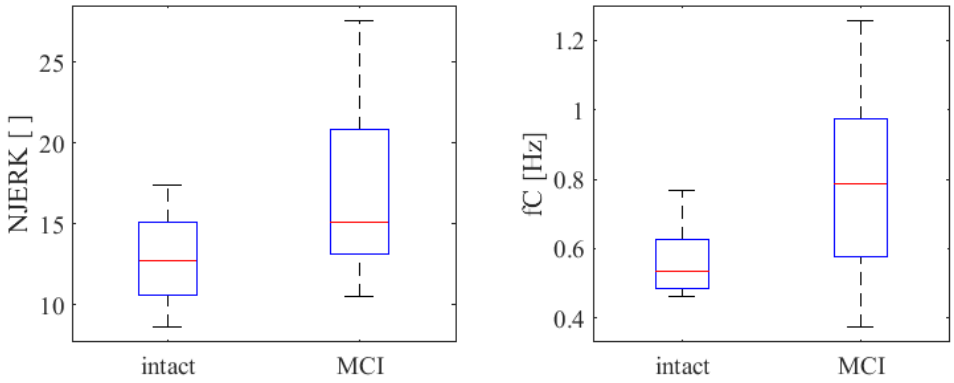

Figure 3.2: Box plots of *NJERK* and *fC* during the single-task condition to show the (group- and measure-specific) non-normal distributions of and outliers in the data in **Figure 3.1**. The horizontal red lines represent the group medians, the edges of the boxes mark the 25th and 75th percentiles, the whiskers extend to the most extreme data points that are not outliers (quantified as > Q_3 + 1.5*(Q_3-Q_1) or < Q_1 – 1.5*(Q_3-Q_1), where Q_1 and Q_3 represent the 25th and 75th percentile, respectively).

There was no significant difference in postural sway path length (*TPATH*) and velocity (*MV*) between the two cognitive status groups during the single-task condition. The group means and standard errors (SE) for the four postural sway measures during the single-task condition are reported in **Table 3.5**.

Table 3.5: Effect of cognitive status on postural sway measures under the single-task condition

Measure	***Intact*** Group mean ± SE	***MCI*** Group mean ± SE	**Effect of cognitive status**	
			$F_{1,24}$	p
TPATH	89.22 ± 10.92	124.69 ± 14.67	2.93	0.100
MV	11.44 ± 2.10	8.63 ± 1.69	1.91	0.180
NJERK	12.85 ± 0.91	16.77 ± 1.28	**4.77**	**0.039***
fC	0.57 ± 0.03	0.79 ± 0.06	**4.88**	**0.037***

*all non-normally distributed data (all data for a given single-task measure, collapsed across both cognitive status groups) were log-transformed to achieve normal distributions prior to the one-way, fixed effect ANOVAs
*reached statistical significance, *critical value = α < 0.05*

3.3.2.ii. Postural Sway & Dual-Task Costs during the Dual-Task Conditions

Main Fixed Effect of Cognitive Status

There was no significant difference in dual-task postural sway between the two cognitive status groups when collapsing across the three dual-task conditions. The group-

specific postural sway measures during the three dual-task conditions are contained in **Table 3.6** and the statistical results are contained in **Table 3.8.**

Table 3.6: The dual-task postural sway measures during the three dual-task conditions, by cognitive status group

Measure	Dual-task conditions		
	Attention Group mean ± SE	**Memory** Group mean ± SE	**Executive function** Group mean ± SE
A. Intact			
TPATH	206.63 ± 33.74	154.30 ± 22.91	101.75 ± 8.90
MV	8.84 ± 1.55	16.32 ± 4.18	8.86 ± 1.30
NJERK	21.97 ± 1.98	16.50 ±1.34	16.07 ± 1.68
fC	0.94 ± 0.09	0.69 ± 0.07	0.75 ± 0.07
B. MCI			
TPATH	175.67 ± 23.42	171.01 ± 19.31	146.26 ± 19.12
MV	9.37 ± 1.56	7.51 ± 1.13	8.43 ± 1.16
NJERK	18.68 ± 1.29	17.62 ± 1.53	17.75 ± 0.83
fC	0.85 ± 0.04	0.78 ± 0.06	0.87 ± 0.05

There was, however, a significant difference in postural dual-task costs between groups (**Table 3.8, A**). The costs in *TPATH*, *NJERK*, and *fC* were significantly lower in the MCI group compared to the intact group when collapsing across all three dual-task conditions. There was not a statistically significant effect of cognitive status on the *MV* cost. The difference in postural dual-task costs are shown in **Figures 3.3-4**.

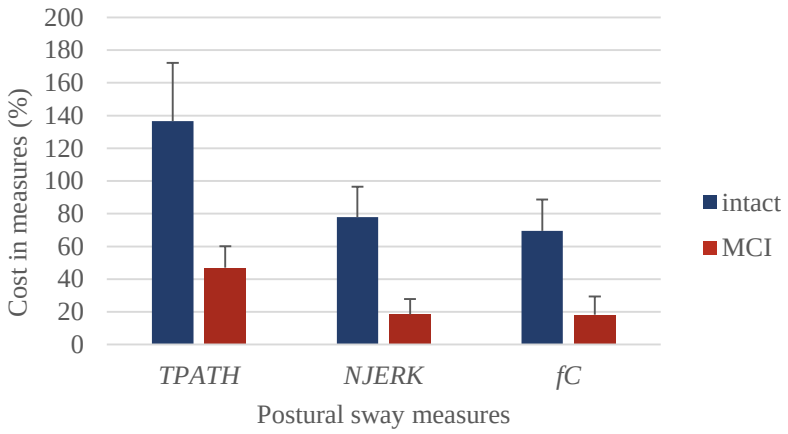

Figure 3.3: Lower postural dual-task sway costs were associated with MCI. Histograms show the group means and SEs. The costs in *TPATH*, *NJERK*, and *fC* were significantly lower in the MCI compared to the intact group. This figure shows the significant difference in postural dual-task cost between groups for the three sensitive measures. This histogram shows the group means and SEs for *TPATH*, *NJERK* and *fC* costs during the attention-based dual-task condition.

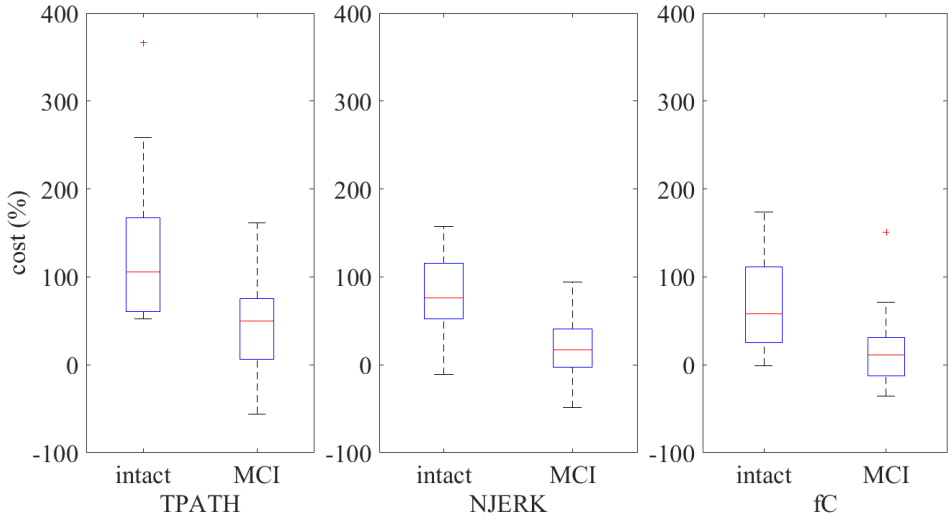

Figure 3.4: Box plots of the group-specific postural dual-task costs for the three sensitive measures during the attention-based dual-task condition to show the (group- and measure-specific) non-normal distributions of and outliers in the data in **Figure 3.1.3**. The horizontal red lines represent the group medians, the edges of the boxes mark the 25th and 75th percentiles, the whiskers extend to the most extreme data points that are not outliers, and the red crosses represent the outliers (quantified as > Q_3 + 1.5*(Q_3-Q_1) or < Q_1 – 1.5*(Q_3-Q_1), where Q_1 and Q_3 represent the 25th and 75th percentile, respectively).

The postural dual-task costs (in percent) in the four postural sway measures (*TPATH*, *MV*, *NJERK*, and *fC*) for the two cognitive status groups (intact and MCI) during the three dual-task conditions (attention-, memory-, and executive function based) are reported in **Table 3.7**.

Table 3.7: The measure-specific postural dual-task costs (in %) during the three dual-task conditions, by cognitive status group

Measure	Dual-task conditions		
	Attention	**Memory**	**Executive function**
	Group mean ± SE	Group mean ± SE	Group mean ± SE
A. Intact			
TPATH	136.49 ± 35.63	85.18 ± 35.20	19.00 ± 6.62
MV	3.72 ± 29.27	60.07 ± 31.20	16.87 ± 36.71
NJERK	77.86 ± 18.66	33.12 ± 12.27	26.79 ± 11.62
fC	69.43 ± 19.16	22.29 ± 12.15	33.87 ± 14.18
B. MCI			
TPATH	47.08 ± 13.14	49.38 ± 15.42	19.34 ± 9.31
MV	74.40 ± 44.26	55.01 ± 37.65	62.09 ± 32.76
NJERK	18.50 ± 9.33	10.94 ± 11.34	13.82 ± 8.67
fC	18.28 ± 11.19	1.89 ± 7.18	7.82 ± 6.88

Main Fixed Effect of Cognitive Load

There was no significant difference in dual-task postural sway between the three different dual-task conditions for both cognitive status groups. There was, however, a significant difference in postural dual-task cost between the three different dual-task conditions. There was a significant effect of cognitive load on the dual-task cost in *TPATH* when analyzing across both cognitive status groups. The executive function-based cognitive load elicited a significantly lower cost in *TPATH* compared to both the attention- and memory-based cognitive loads (**Figures 3.5-6**). There was no effect of cognitive load on the other three postural dual-task costs (*MV, NJERK,* and *fC* costs) (**Table 3.8, B**).

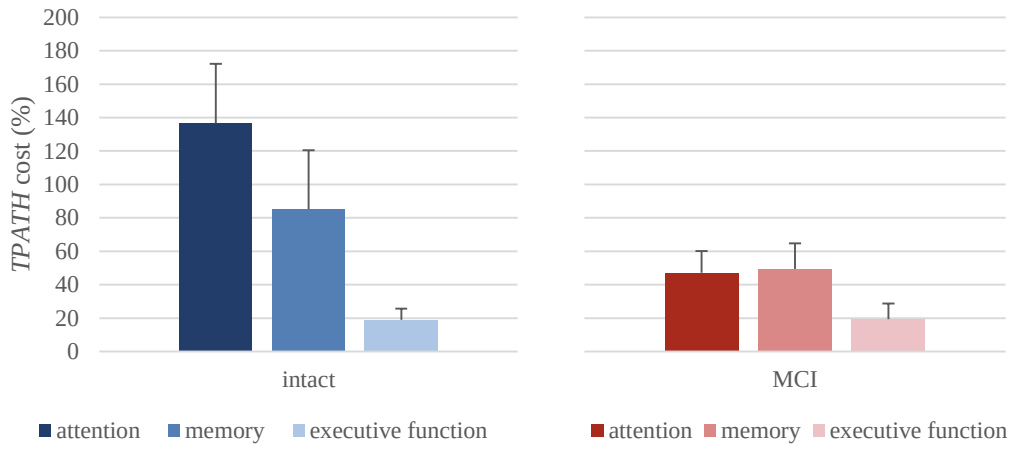

Figure 3.5: The executive function-based cognitive load elicited a significantly lower postural dual-task cost (in *TPATH*). For each cognitive status group (intact = blue; MCI = red), the cost in *TPATH* is plotted during each of the three dual-task conditions (attention-based condition = dark shade; memory-based condition = medium shade; executive function-based condition = light shade). This histogram shows the group means and SEs for *TPATH* cost during the three different dual-task conditions.

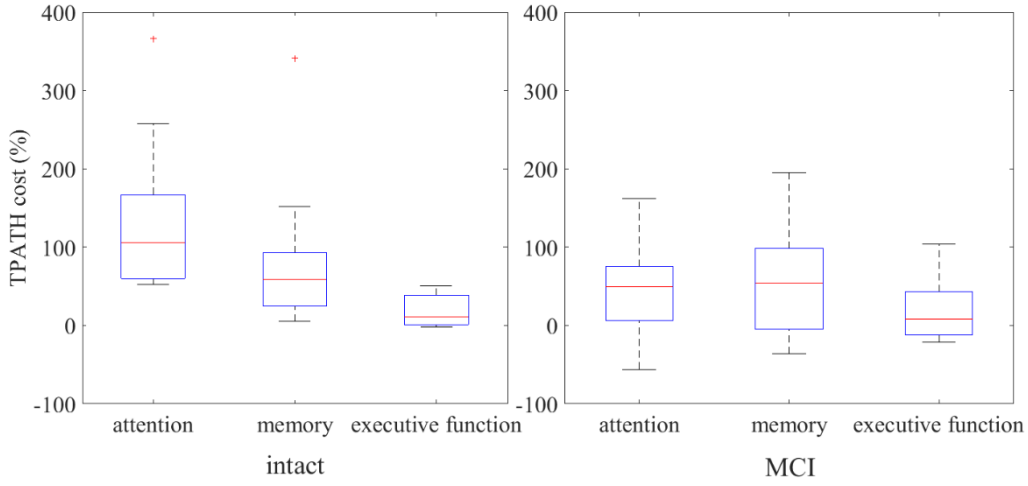

Figure 3.6: Box plots of the group-specific postural dual-task costs in *TPATH* during all three dual-task conditions to show the (group- and condition-specific) non-normal distributions of and outliers in the data in **Figure 3.5**. The horizontal red lines represent the group medians, the edges of the boxes mark the 25th and 75th percentiles, the whiskers extend to the most extreme data points that are not outliers, and the red crosses represent the outliers (quantified as $> Q_3 + 1.5*(Q_3-Q_1)$ or $< Q_1 - 1.5*(Q_3-Q_1)$, where Q_1 and Q_3 represent the 25th and 75th percentile, respectively).

Interaction between the Two Main Fixed Effects: Cognitive Status & Cognitive Load

There was no interaction between the two main fixed effects (cognitive status and cognitive load) when analyzing both postural sway and postural dual-task costs, showing no evidence that the significant effects of cognitive status depends on the specific cognitive load and vice versa (**Table 3.8, C**).

Table 3.8: Main and interaction effects for the two-way, fixed effects ANOVAs on postural sway and postural dual-task costs during the dual-task conditions

Measure	Dual-task		Dual-task costs	
	$F_{1,2,2}$	*p*	$F_{1,2,2}$	*p*
A. Main effect of cognitive status				
TPATH	0.31	0.579	**6.75**	**0.011***
MV	3.05	0.085	0.79	0.378
NJERK	0.02	0.900	**9.33**	**0.003***
fC	0.16	0.687	**12.30**	**0.001***
B. Main effect of cognitive load				
TPATH	4.33	0.017	**6.85**	**0.002***
MV	0.53	0.589	0.26	0.773
NJERK	2.81	0.067	2.14	0.125
fC	3.71	0.029	3.23	0.046
C. Interaction effect of cognitive status & cognitive load				
TPATH	1.32	0.274	2.09	0.131
MV	2.36	0.102	1.14	0.324
NJERK	1.42	0.247	1.09	0.343
fC	0.81	0.450	0.70	0.499

**all non-normally distributed data (all data for a given dual-task measure or cost collapsed across both cognitive status groups and all three dual-task conditions) were log-transformed to achieve normal distributions prior to the two-way, fixed effect ANOVAs
*reached statistical significance after correcting for multiple comparisons (Bonferroni)
α = 0.05,
m = 3 dual-task conditions,
critical value = α/m < 0.05/3 < 0.017

3.4. Discussion

3.4.1. Main Findings

3.4.1.i. Postural Sway and Postural Dual-Task Costs

Postural sway jerk and frequency differentiated between the intact and MCI groups under the single-task condition (*i.e.*, quiet stance with no cognitive loading) with higher sway jerk and frequency associated with MCI. Our first hypothesis is partially supported by this finding: more postural sway, which is often interpreted as less postural control, was observed in the MCI group. Higher jerk is thought to be attributed to frequent corrections of postural sway direction and has been evidenced in Parkinson's disease (PD), an older adult population known for postural instability and increased fall risk. Higher jerk may reflect attempts to compensate for poor proprioceptive control of posture with longer-loop, visual postural feedback; it may also reflect increases in axial rigidity at the trunk (the location of the inertial sensor during this study) [37,63]. Sway frequency has been found to increase with age and is thought to represent postural instability and age-related deficits in the postural control system [35]. Lower sway frequencies (compared to age-matched controls), however, have been evidenced in PD [37,63]. Although both PD and MCI are independent risk factors for falls [128], and both PD and postural instability predict cognitive decline [20], our findings on postural sway frequency in MCI are not consistent with that in PD because we observed higher frequencies in the MCI group.

There was no difference in postural sway path length and mean velocity (two out of our three time-domain distance measures) between the intact and MCI groups at baseline, a finding that does not support the literature since distance measures were found to be sensitive to MCI status in the five previous studies that objectively quantified postural sway in MCI [27,46-48,73]. Although not significantly different, path length was higher and mean velocity was lower in the MCI group. Our velocity finding is not consistent with other studies because Mignardot *et al.* [48] and Deschamps *et al.* [46] found sway velocity measures to be higher in MCI. To reiterate, there was no effect of cognitive status on mean sway velocity in our small pilot study of 10 intact and 19 MCI subjects. There are several differences between our study and the Mignardot and Deschamps studies that could attribute to our inconsistent results: 1. Our study was much smaller than the other two

studies (611 and 175 subjects in the Mignardot and Deschamps studies, respectively), so we may simply not have a large enough sample size to observe postural sway velocity-based differences between groups; 2. Although we used the same MCI criteria (Petersen/Winblad as operationalized by ADNI [24,25]), our neuropsychological assessment battery used for the criteria is much more extensive than that used in the other two studies. As detailed elsewhere in Kaye *et al.* [86], we use 2-4 classic neuropsychological tests per cognitive domain to quantify cognitive domain-specific functioning. Because Mignardot and Deschamps' neuropsychological testing is much less extensive than ours, it is likely that our MCI status definitions (which are, in significant part, derived from the testing battery) are quite different. A subject classified as "MCI" according to Mignardot and Deschamps could possibly be classified as "intact" according to our methods since our testing battery is much more thorough and, in turn, likely more sensitive and less likely to produce false positives; and, 3. Our postural sway velocity-based measures quantify different aspects of CoP velocity dynamics and may be the reason why we did not observe a cognitive status effect on our velocity measure. The most sensitive velocity-based measure in the Mignardot and Deschamps studies is the average absolute maximal velocity (AAMV), which quantifies the bounding limits of CoP velocity dynamics and is detailed elsewhere in [129]. We used a more widely-accepted velocity-based measure, mean sway velocity (*MV*) (our feature selection is justified and defined above in Section 3.2.5.ii). In sum, there are several fundamental differences in our experimental methods that account for our differing results.

When domain-specific cognitive loads were applied to the postural task (*i.e.*, quiet stance) in an effort to increase the difficulty level of the overall testing condition, the separation between cognitive status groups became more pronounced. The postural dual-task costs however were lower in the MCI group compared to the intact group, a finding that does not support our first hypothesis. We predicted postural dual-task costs to be higher in the MCI group since reduced postural control and dual-tasking ability has been observed in older adults with cognitive impairment. This finding opposes the underlying theory of the cognitive-postural dual-task paradigm [74,76,130,131]: if the individual's cognitive and/or postural control is impaired, he/she most likely has limited neural attentional

resources and will be less likely to adequately regulate both tasks during dual-task conditions, resulting in higher dual-tasks costs compared to the intact control. We observed the opposite in our sample population: our MCI group had lower postural dual-task costs (quantified by sway path length, jerk, and frequency) compared to the intact group.

Both groups had positive dual-task costs, meaning the cognitive tasks interfered with the postural task represented by an increase in postural sway from the single- to dual-task condition. This finding is consistent with the literature: an added cognitive task yields a decrease in postural control in older adults tending to both a cognitive and postural task [74,84,132-134]. The MCI group had significantly more postural sway (quantified by sway jerk and frequency) than the intact group at baseline, but there was no difference in postural sway between cognitive status groups during the dual-task conditions. The significantly lower postural dual-task costs (in sway path length, jerk, and frequency) in the MCI group (although still positive in value) might in part be attributed by the already significant amount of postural sway (relative to the intact group) at baseline. It is possible that the MCI group was already approaching their limits of stability during quiet stance so an added cognitive load may not have had as much of an effect on their postural response (in comparison to the intact group who had significantly much less sway at baseline and may have, in turn, had more room to increase in sway before pushing the limits of stability).

If mild postural instability is in fact a hallmark feature of MCI [48], it is possible that older adults with MCI are aware of the subtle changes in their postural control system and, in turn, may pay more close attention to their sway when instructed to stand quietly. According to the "constrained action hypothesis" [135,136], consciously controlling one's movement interferes with the coordination of automatic processes responsible for regulating the movement. Conversely, diverting attention away from the movement (and towards a secondary task) enables the automatic processes to operate unconstrained, in turn generating movement more efficiently [137]. This hypothesis could help explain our findings of more single-task sway and less dual-task cost in the MCI group: under the single-task condition, the mildly posturally impaired MCI subject may over-control his/her sway resulting in significantly more postural sway compared to the intact subject; but when the MCI subject's attention is directed towards something else, such as the cognitive tasks

in our dual-task condition, the MCI subject's automatic control of posture may take over resulting in more similar sway to the intact subject with no postural instabilities.

The "posture first hypothesis" [78] could offer another possible explanation as to why we observed lower postural dual-task costs in the MCI group. Assuming mild postural instability is a hallmark feature of MCI, older adults with MCI would chose the "posture first" strategy when a cognitive task was added to the postural task since they would already be experiencing mild postural instability before the additional load. In contrast, cognitively intact older adults could afford to reallocate more attention away from the postural task and to the cognitive task due to their intact postural control (relative to age) and limited amount of postural sway at baseline. If the older adult has insufficient neural attentional resources to adequately regulate both the cognitive and postural task, she will likely choose the "posture first" strategy, abandoning the less critical (cognitive dual-) task in effort to maintain postural stability and prevent a fall [74,131]. Our older adults with MCI may have had lower postural dual-task costs compared to cognitively intact older adults if the added cognitive load had overtaxed the cognitive and/or postural control systems. But because we did not repeat the protocol while our subjects were sitting and because our cognitive performance data set lacks significance, we are unable to quantify the cognitive dual-task cost and, in turn, make strong inferences regarding the amount of cognitive effort exerted on the added cognitive task and the trade-off between cognitive and postural control.

3.4.1.ii. Domain-Specific Cognitive Loads

Although executive function has been identified as a significant contributor to postural control, our chosen executive function-based task elicited significantly lower postural dual-task costs in both cognitive status groups. We suspect this may be due to the ease of our chosen executive function-based task (AST). All but two subjects (1 intact,1 MCI) earned a perfect score on the AST task. The AST task did not appear to be challenging enough to elicit cognitive performance-based differences between cognitive status groups. This observed ceiling effect was confirmed by the subjects' feedback: when prompted, all subjects reported on the ease of the task – "No, it did not seem challenging". Perhaps a more taxing executive function-based task (*e.g.,* AST with mixed (congruent and incongruent) cues) would compete more for the collection of neural resources required for

the postural task, increasing the difficulty level of the dual-task condition and likely eliciting a higher dual-task cost.

Trends in our data suggest that the attention-based load may elicit the highest postural dual-task costs in a larger sample population. Also, the separation between cognitive status groups appeared to be most pronounced during the attention-based dual-task condition. This finding supports our second hypothesis: although our executive function-based load elicited the lowest postural dual-task costs (likely due to the task's ceiling effect), our attention-based load appeared to elicit relatively high postural dual-task costs and seemed to best differentiate between groups.

Since no interaction effect (between cognitive status and cognitive load) reached statistical significance, the effect of MCI status on postural cost likely does not depend on the specific type of cognitive loading. Nonetheless, using an attention-based cognitive load may best serve as a sensitive cognitive dual-task for identifying older adults with (mildly) limited cognitive reserve (*e.g.*, MCI) since it appeared to be the task that induced the most amount of postural sway and the highest postural dual-task cost. Tending to two tasks at once requires a certain amount of attentional set shifting, information processing, and working memory (a completely different entity than short- or long-term memory), and as previously stated, the amount of cognitive processing required for a given dual-task condition depends on both the complexity of the two tasks as well as the capacity of the individual's cognitive reserve. Our chosen attention-based task (ANST) was designed to tax these specific cognitive functions, which may be why this cognitive load appeared to compete for the most amount of shared resources. As previously stated, memory (specifically long-term, which was the type of memory taxed in our chosen memory-based task (HVLT)) has not been postulated as a cognitive function necessary for postural control, so it is likely HVLT did not compete for the same neural resources required for postural stability during quiet stance. Nonetheless HVLT elicited statistically similar postural dual-task costs to that elicited by ANST in this study, suggesting the two tasks were of similar difficulty levels and required similar amounts of attentional resources.

3.4.2. Study Limitations

The main limitation of this study was our inability to quantify the cognitive dual-task costs, inhibiting us from fully interpreting our unpredicted results. An important note: this protocol was performed as an exploratory pilot study to investigate the older adult's ability to perform a variety of cognitive tasks during quiet stance. We were mainly interested to know whether or not older adults (both cognitively intact and mildly cognitively impaired) could safely perform certain tasks without significantly compromising postural control. This pilot was performed in preparation for our in-home study of postural sway during cognitive dual-tasking (*Chapter 4* of this dissertation) and was not designed for the purpose of a thorough investigation. Although our study design is lacking an important feature (measurement of cognitive dual-task costs), we still report interesting results. We used objective postural sway measures to differentiate MCI from cognitively intact controls under both postural single-task and cognitive-postural dual-task conditions.

The age gap between cognitive status groups (intact *vs.* MCI) is another major concern associated with this pilot study. We did not adjust for age in our statistical analyses because we did not have enough statistical power given our small sample population. Although we drew from age-matched pools during subject recruitment, we ended up with a six year difference between the intact group and MCI groups once all subjects were recruited and tested. During recruitment we found older adults with MCI less likely to participate in our study compared to the cognitively intact older adults. Because this study served as preliminary work for a more extensive study of postural sway and cognitive dual-tasking in MCI, we were primarily driven by a time constraint and less concerned about our subjects' specific age. Since this pilot study we have been more stringent during subject recruitment since a six year age gap (*e.g.*, early eighties *vs.* mid-late eighties) may differentiate the groups based on underlying age-related pathologies and/or may dilute any important findings pertaining to disease-related pathologies. For future studies (and specifically, for our longitudinal study of postural sway in MCI, *Chapter 4*) we have/will recruit our MCI group first and age-match the cognitively intact group accordingly.

Although our sample population was small (10 intact, 19 MCI), our findings are promising given the statistically significant *p*-values even after conservatively accounting

for our multiple comparisons via a Bonferroni correction (three different cognitive loads). Similar investigations should be conducted on larger, more diverse samples to assess the significance of our findings. If lower postural dual-task costs differentiate MCI subjects from intact subjects in a larger, more diverse population, objective postural sway measures and dual-task costs may be implemented as early markers of MCI.

3.5. Conclusions

Our findings suggest that mild postural instabilities do occur during early cognitive decline (as in MCI) and quantifying postural sway under the dual-task condition could help to further differentiate postural sway in older adults with MCI from cognitively intact older adults. This is the first study to quantify both postural sway jerk and frequency during cognitive dual-tasking in older adults with and without MCI. Both postural sway measures expressed sensitivity to MCI status under both single- and dual-task conditions. If our findings hold with a larger, more diverse sample population, lower than normal postural dual-task costs may suggest mild cognitive decline. Future studies of postural sway and dual-task cost in MCI might provide more insight as to why older adults with MCI are at a higher risk of falls. Such knowledge would yield opportunity for the development and implementation of therapeutic interventions and aid in fall prevention.

3.6. Contributions

Contributor	Affiliation(s)	Support Provided
Tamara Hayes (*late PhD advisor*)	ORCATECH, BME Department	-contributed to study design -provided materials for data acquisition -assisted with Acc signal processing and preliminary analysis -contributed to preliminary interpretation of results
Diane Howieson	LAADC	-provided guidance for selection of cognitive tasks
Colette Duncan	LAADC	-assisted with subject selection during recruitment
Sylvia Salazar	LAADC	-assisted with subject selection during recruitment
Nora Mattek	ORCATECH, LAADC	-assisted with subject selection during recruitment -provided clinical and neuropsychological data -provided guidance in statistical analysis
Rajal Cohen	BD Laboratory	-inspired executive function domain cognitive task
Ed King	BD Laboratory	-built auditory device necessary to implement executive function domain task
Ryan Meyer	BD Laboratory	-assisted with data acquisition
Martina Mancini	BD Laboratory	-assisted with Acc signal processing and analysis -provided guidance in statistical analysis -contributed to interpretation of results -provided feedback during manuscript preparation
Nicole Sharma	ORCATECH	-reviewed manuscript before submission
Robert Peterka (*DAC member*)	BME Department	-provided feedback during manuscript preparation
John Nutt (*DAC member*)	Neurology Department	-provided feedback during manuscript preparation
Jeffrey Kaye (*DAC member*)	ORCATECH, LAADC, BME & Neurology Departments	-provided feedback during manuscript preparation
Peter Jacobs (*DAC chair*)	BME Department	-provided guidance in statistical analysis -provided feedback during manuscript preparation

Fay Horak (*PhD advisor*) (*DAC member*)	BD Laboratory, BME & Neurology Departments	-provided materials for data acquisition -provided guidance in statistical analysis -contributed to interpretation of results -provided feedback during manuscript preparation

CHAPTER 4: *Longitudinal Study of Postural Sway in MCI: Using the Nintendo WBB to Quantify Postural Sway during Quiet Stance both with and without Cognitive Loading in Older Adults with MCI in the Home for 30 Days*

Summary

Objectives: Our study objectives were to: 1. Determine the feasibility of daily, in-home monitoring of postural sway and cognitive dual-tasking in an older adult population with and without mild cognitive impairment; 2. Assess the reliability of objective postural sway measures across time; 3. Characterize the associations between cognitive status and postural sway both with (dual-task) and without (single-task) cognitive loading longitudinally; and, 4. Characterize the day-to-day variability in postural sway in an older adult population with and without mild cognitive impairment.

Hypotheses: Our study hypotheses were: 1. Our in-home study of postural sway and cognitive dual-tasking will be feasible in our older adult population with and without mild cognitive impairments; 2. Objective postural sway measures will exhibit good test-retest reliability; 3. Older adults with lower cognitive functioning will have more postural sway; and, 4. Older adults with lower cognitive functioning will have higher day-to-day variability in postural sway.

Methods: Twenty subjects (10 intact, 10 MCI) enrolled in ORCATECH's OLL and ISAAC studies were recruited. A Nook tablet and Nintendo Wii balance board (WBB) were integrated into ORCATECH's current in-home technological platform to quantify postural sway (both with and without cognitive loading) daily for 30 days. Five objective postural sway measures were derived from the two-dimensional postural sway (CoP) signals and were used to quantify daily postural sway (during both the single- and dual-task condition) and dual-task cost measures. The feasibility of the in-home study and potential group differences in subject adherence were assessed. The test-retest reliability of objective postural sway measures was assessed. The means and variability in postural sway and postural dual-task cost across the 30-day monitoring period were analyzed both between and across cognitive status groups.

Results: Monitoring of postural sway during dual-task conditions was determined to be feasible within the in-home monitoring environment. All five objective postural sway measures exhibited good test-retest reliability across the 30-day monitoring period. When analyzing between cognitive status groups, there was significantly higher day-to-day variability in the dual-task cost in sway frequency in the MCI group compared to the intact group. When analyzing across cognitive status groups, there were linear relationships observed between postural sway variability and cognitive functioning (indexed by cognitive global z-scores): more variability in time-domain postural sway (indexed by sway distance and area) and less variability in frequency-domain postural sway (indexed by centroidal sway frequency) was associated with lower cognitive functioning.

Conclusions: In-home monitoring of daily postural sway proved to be feasible. Objective postural sway measures were reliable when acquired daily for 30 days. Variability measures of postural sway were found to be related to cognitive functioning, with more variability in time-domain

postural sway and less variability in frequency-domain postural sway associated with lower cognitive functioning. Analyzing postural sway across cognitive status groups proved to be of significance, suggesting that more descriptive measures of cognitive status (spectrum instead of binary data) are necessary to observe the relationship between postural instability and mild cognitive dysfunction. Our small pilot study conducted on a small time scale motivate the large-scale implementation of this research over a more extended period of time (*e.g.*, months, years, and even decades). Tracking longitudinal changes in postural sway may further our understanding of early-stage motor decline and its association with cognitive decline and may aid in the early detection of dementia during the preclinical stages.

4.1. Introduction

4.1.1. Longitudinal Study Design

Chapter 4 extends beyond *Chapter 3* by assessing postural sway on a frequent, "longitudinal" basis. Due to the time constraints inherent to PhD research, we monitored postural sway and postural dual-task cost daily for only 30 days. Within this chapter, our use of the term "longitudinal" simply refers to daily measures acquired over a relatively short time course (*e.g.*, weeks or months).

4.1.2. Background Summary

In *Chapter 1, Section 1.8* we detailed the fundamental insufficiencies in the current paradigm of infrequent measures (of both cognitive and physical performance). Infrequent measures reflect one instance of performance, do not measure changes in performance variability over time, and in turn may mask true status and decline in cognition and/or postural control [86]. In *Chapter 1, Section 1.9* we detailed the pathophysiological association between cognitive and motor control. A marked increase in functional variability (either cognitive or motor) often occurs before the clinical manifestations of functional decline [89,90]. And because changes in sensorimotor control have been shown to far precede changes in cognition [91,92], longitudinally monitoring a motor function (*e.g.*, postural sway) may yield early detection of progressive motor decline and has potential to predict cognitive decline [49].

4.1.3. Study Foci

Our first focus for this longitudinal study was to determine the feasibility of daily, in-home monitoring of postural sway in both cognitively intact and mildly cognitively impaired older adults. If proven feasible, this study will lay the foundation to extract frequent, longitudinal measures of postural sway from the natural home environment to track changes in the neural control of posture across time.

Our second focus was to characterize the dynamic time-course of postural sway in both cognitively intact and mildly cognitively impaired older adults. Only one study to date has monitored postural sway daily in the home in older adults: McGrath *et al.* [138] determined the stability of daily, in-home postural sway measures in cognitively intact older adults

over the course of 8 weeks. Although daily postural sway expressed good statistical reliability (ICC > 0.7) across the 8-week monitoring period, the researchers observed a significant amount of variability in day-to-day postural sway both between (37-107%, depending on the postural sway measure) and within (17-56%, depending on the postural sway measure) subjects. McGrath *et al.* concluded that "the idea of applying a group-focused approach at an individual level may result in misclassifying important changes for a particular individual. Early detection of deterioration can only be achieved through the creation of individual trajectories for each person, that are inherently self-referential" [138]. To the best of our knowledge, a longitudinal, in-home study of postural sway in mildly cognitively impaired older adults (*i.e.*, MCI) has not yet been done. As expressed by McGrath *et al.*, "establishing natural patterns of variation in the day-to-day signal, occurring in the relative absence of functional decline or disease, would enable us to determine thresholds for changes in postural control from baseline" [138]. Thus in principle, establishing the variability patterns present during the initial stages of functional decline and/or disease state (*e.g.*, MCI) would enhance our ability to develop biomarkers for early decline. The research conducted within the framework of this study holds great clinical weight since the characterization of both natural aging and disease-related patterns could enable early detection and prevention of bio-psycho-social decline that threatens the independence and quality of life within our aging population [138].

4.1.4. Quantifying Cognitive Functioning Beyond MCI Status

Chapter 4 extends beyond *Chapter 3* by using cognitive global z-scores to quantify cognitive functioning within both the intact and MCI groups. So, in addition to analyzing postural sway between cognitive status groups (intact *vs.* MCI), we used global z-scores to analyze postural sway across groups for a more in-depth analysis of postural sway and cognitive status.

4.1.5. Objectives & Hypotheses

This study quantified postural sway during quiet stance in both cognitively intact and mildly cognitively impaired older adults under both single- and dual-task conditions daily for 30 days. Our four main objectives were: 1. To determine the feasibility of daily, in-

home monitoring of postural sway and cognitive dual-tasking in an older adult population with mild cognitive impairment; 2. To assess the reliability of objective postural sway measures across time; 3. To characterize the associations between cognitive status and postural sway both with (dual-task) and without (single-task) cognitive loading longitudinally; and, 4. To characterize the day-to-day variability in postural sway in both cognitively intact and mildly cognitively impaired older adults.

Our four objectives yield four hypotheses:

Hypothesis I: We hypothesize that our in-home study of postural sway and cognitive dual-tasking will be feasible in our older adult population with mild cognitive impairments. We are optimistic about feasibility because: 1. The successful implementation of our cross-sectional study (detailed in *Chapter 3*); and, 2. The overall impressive adherence-to-protocol history within our ORCATECH cohort.

Hypothesis II: We hypothesize that objective postural sway measures will exhibit good test-retest reliability. Our prediction is based on previous findings from a similar study design [138].

Hypothesis III: We hypothesize that older adults with lower cognitive functioning will have more postural sway since previous studies have shown cognitive decline to degrade postural control. We expect the differences in postural sway between cognitive status groups to be more pronounced under the dual-task condition due to the added cognitive load.

Hypothesis IV: We hypothesize that older adults with lower cognitive functioning will have higher day-to-day variability in postural sway since previous studies have shown increased variability in a (motor or cognitive) function during the initial stages of functional decline.

4.2. Experimental Methods

The Institutional Review Board at OHSU approved this study's experimental methods and all subjects gave informed written consent prior to participation.

4.2.1. Subjects

Twenty subjects (10 intact, 10 MCI) enrolled in ORCATECH's OLL and ISAAC studies were recruited for this study (**Table 4.1**). All subjects were ambulatory,

community-dwelling older adults that met the following inclusion criteria: free of physical impairment that significantly inhibits stability; no walking aid (*i.e.*, walker or cane); no known visual, vestibular, or somatosensory impairment greater than what is normal for one's age; and, either classified as "cognitively intact" or "mildly cognitively impaired" (*i.e.*, MCI). All subjects provided written informed consent, approved by the institutional review board at OHSU.

Table 4.1: Subject characteristics, by cognitive status group

	Intact	***MCI***	**Group differences**	
			$F_{1,18}$	***p***
# of subjects	10	10	-----	-------
Sex (% female) (#)	70 (7)	60 (6)	-----	-------
Race (% non-white) (#)	0 (0)	10 (1)	-----	-------
Age (yrs) (mean ± std)	88.0 ± 7.6	86.1 ± 6.0	0.38	0.547
Education (yrs) (mean ± std)	14.9 ± 2.1	14.6 ± 2.7	0.08	0.785
MMSE Score [29]	29.2 ± 1.3	27.7 ± 2.4	3.07	0.098
Cumulative Illness Rating Scale [139]	20.5 ± 2.3	19.5 ± 2.5	0.87	0.362
Geriatric Depression Scale [140]	0.6 ± 0.7	0.6 ± 0.7	0.00	1.000
Tinetti Balance Score [32]	2.7 ± 4.1	2.3 ± 2.5	0.07	0.793

There was no difference in age, years of education, MMSE Scores, Cumulative Illness Rating Scale, Geriatric Depression Scale, and Tinetti Balance Scores between the two cognitive status groups. [Note: there have been many different scoring systems reported for the Tinetti Balance Score [141]. At OHSU's LAADC, balance is measured on a scale of 0-26 with lower scores indicating better performance [86].]

4.2.1.i. New Clinical Diagnostic MCI Criteria

Cognitive status for all 20 subjects was determined based on OADC's annual clinical and neuropsychological testing, detailed elsewhere in [1,86]. Diagnosis of MCI was consistent with the new comprehensive neuropsychological Jak/Bondi criteria detailed in [31], which depends on: (a) domain-specific cognitive impairment operationalized using the domain-specific neuropsychological tests detailed elsewhere in Kaye *et al.* [86] and defined as a score of at least 1 SDs or more below the age-stratified normative data on at least two tests within one or more of the six cognitive domains (1. memory; 2. language;

3. executive function; 4. processing speed; 5. working memory; and, 6. visual perception/construction); (b) nonfulfillment of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) criteria for dementia; (c) preserved general cognitive functions as confirmed by a score of 24 or above on the MMSE; and, (d) absence of severe depression as confirmed by a score of less than 5 on the Geriatric Depression Scale. This actuarial neuropsychological method put forward by Jak and Bondi was designed to balance test sensitivity and reliability and is thought to be more refined than the MCI diagnostic criteria used in *Chapter 3* (the conventional Petersen/Winblad ADNI criteria). In a comparison between these two diagnostic methods, the Jak/Bondi criteria appears to remove the 'false positive' diagnoses produced by the Petersen/Winblad ADNI criteria [142]. MCI status was defined to include subjects who have had at least one MCI classification (according to the Jak/Bondi criteria) in the past, whether or not they were classified as "MCI" at their most recent evaluation.

4.2.1.ii. Cognitive Functioning Defined

Cognitive functioning was defined by cognitive global z-scores. Access to global z-scores enhanced our assessment of postural sway/dual-task cost and cognitive status by enabling an analysis of cognitive functioning across cognitive status groups (as opposed to simply between cognitive status groups, as in *Chapter 3*). Z-scores are more descriptive than MCI status (spectrum *vs.* binary data) and represent the subject's level of cognitive functioning (and severity of cognitive impairment) relative to the group mean. The normative data used to derive the z-scores were drawn from the first (baseline) evaluation of all (>3000) cognitively intact subjects from OHSU's LAADC.

Global and domain-specific z-scores were derived from the subjects' most recent domain-specific neuropsychological test scores and were used to classify the subjects as "intact" or "MCI" according to the Jak/Bondi criteria. Note that six out of our ten MCI subjects were classified as "intact" according to the Jak/Bondi criteria at their most recent evaluation. Nonetheless, there was a significant difference in the z-scores between our two cognitive status groups (**Table 4.2**). The group means and SEs for the z-scores, as well as the effect of cognitive status on the z-scores (quantified by one-way, fixed effect (cognitive status) ANOVAs), are reported in **Table 4.2**. Despite the "intact" classification for six out

of our ten MCI subjects, all z-scores (one global measure and six domain-specific measures) were significantly lower in the MCI group.

Table 4.2: Global and domain-specific z-scores for the two cognitive status groups

Cognitive domains	*Intact* mean ± SE	*MCI* mean ± SE	Group differences	
			$F_{1,18}$	*p*
Global	0.61 ± 0.20	-0.41 ± 0.14	**17.37**	**0.001***
Memory	0.72 ± 0.29	-0.52 ± 0.34	**7.57**	**0.013***
Language	1.11 ± 0.44	-0.29 ± 0.27	**7.26**	**0.015***
Executive function	0.88 ± 0.27	-0.10 ± 0.21	**8.42**	**0.010***
Processing speed	0.39 ± 0.13	-0.17 ± 0.21	**5.11**	**0.038***
Working memory	0.13 ± 0.20	-0.75 ± 0.27	**6.95**	**0.017***
Visual perception/construction	0.45 ± 0.24	-0.67 ± 0.16	**14.44**	**0.001***

*reached statistical significance, $p < 0.05$

**NOTE: the degrees of freedom associated with the F statistic for the processing speed domain are 1,16 ($F_{1,16}$) and for the visual perception/construction domain are 1,17($F_{1,17}$) due to 2 subjects- and 1 subject-worth of missing data, respectively*

Two out of the 20 subjects (both MCI) were unable to complete the full test battery during their most recent neuropsychological evaluation due to progressive macular degeneration. One of these MCI subjects was unable to complete all tests required to derive the processing speed z-score; and the other MCI subject was unable to complete all tests required to derive both the processing speed and visual perception/construction z-scores. For these two subjects, the global z-score was derived from only 4 or 5 cognitive domains-worth of data (as opposed to all 6 cognitive domains specified above in **Table 4.2**).

4.2.3. Procedures

4.2.3.i. Experimental Setup & Daily Testing Protocol

A Nook tablet and Nintendo Wii balance board (WBB) were integrated into ORCATECH's current in-home technological platform to quantify postural sway (both with and without cognitive loading) daily for 30 days. The WBB was positioned on an uncarpeted floor forearm's distance away from a wall and was used to quantify postural sway via the displacement of the subject's center of pressure (CoP) projected on the WBB's usable surface. The subject's feet were traced with tape on the WBB's usable surface to ensure a fixed foot position over the course of the 30-day monitoring period. The WBB

transmitted CoP data to the tablet via a Bluetooth connection. The tablet was mounted on a wall at eye-height and served as the user-interface, running a custom-designed/built application that walked the subject through his/her three-minute daily routine. The tablet was used to acquire CoP data from the WBB and cognitive performance data input by the subject. Upon completion of the daily routine, the tablet automatically transmitted both the postural (CoP) and cognitive performance data to ORCATECH's data repository via a wireless internet connection. The in-home setup is shown in **Figure 4.1**.

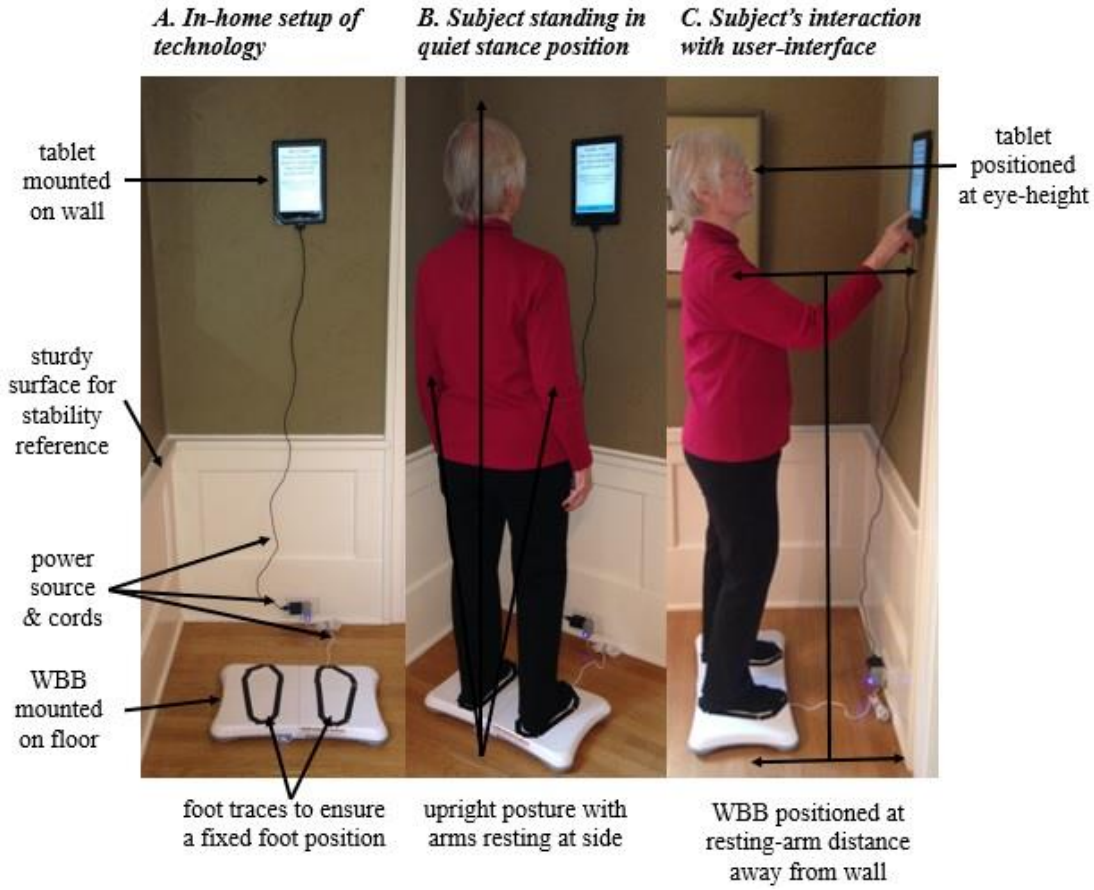

Figure 4.1: The in-home setup of the Nook tablet and the Nintendo WBB to acquire daily CoP-based postural sway measures. (**A**) Shows the in-home setup of our technological platform: The WBB was mounted on the uncarpeted floor parallel to the wall and the tablet was mounted and levelled the wall. The subject's feet were traced with tape on the WBB's usable surface to ensure a fixed foot position. Both devices were plugged into a power source to run continuously throughout the 30-day monitoring period. The system was positioned near a sturdy surface so the subject could grab hold and regain postural stability if need be. (**B**) Shows the subject during quiet stance: Standing without shoes in a comfortable, natural upright posture with a fixed foot position, arms resting at side, looking straight ahead. (**C**) Shows the position of the WBB and tablet relative to the wall and subject. The WBB was positioned at the subject's resting-arm's distance away from the wall to ensure a comfortable reach when interacting with the tablet. The tablet was centered relative to the WBB and positioned on the wall at the subject's eye-height.

The custom-written application ran continuously over the course of the 30-day monitoring period on the tablet and responded each day when the subject stepped on the WBB. The application provided the subject with detailed instructions and administered two

quiet stance trials: one 30-second trial without cognitive loading followed by one 60-second trial with cognitive loading (a daily word search task). At the end of the 60-second trial the subject was asked to report the solution to the word search by answering a multiple choice question via touching the tablet fixed to the wall. The subject was instructed to simply guess if he/she was unable to solve the word search within the 60 allotted seconds or if he/she forgot the answer. A mock-up of the application's detailed instructions, daily word search task, and multiple choice question are shown in **Figure 4.2**.

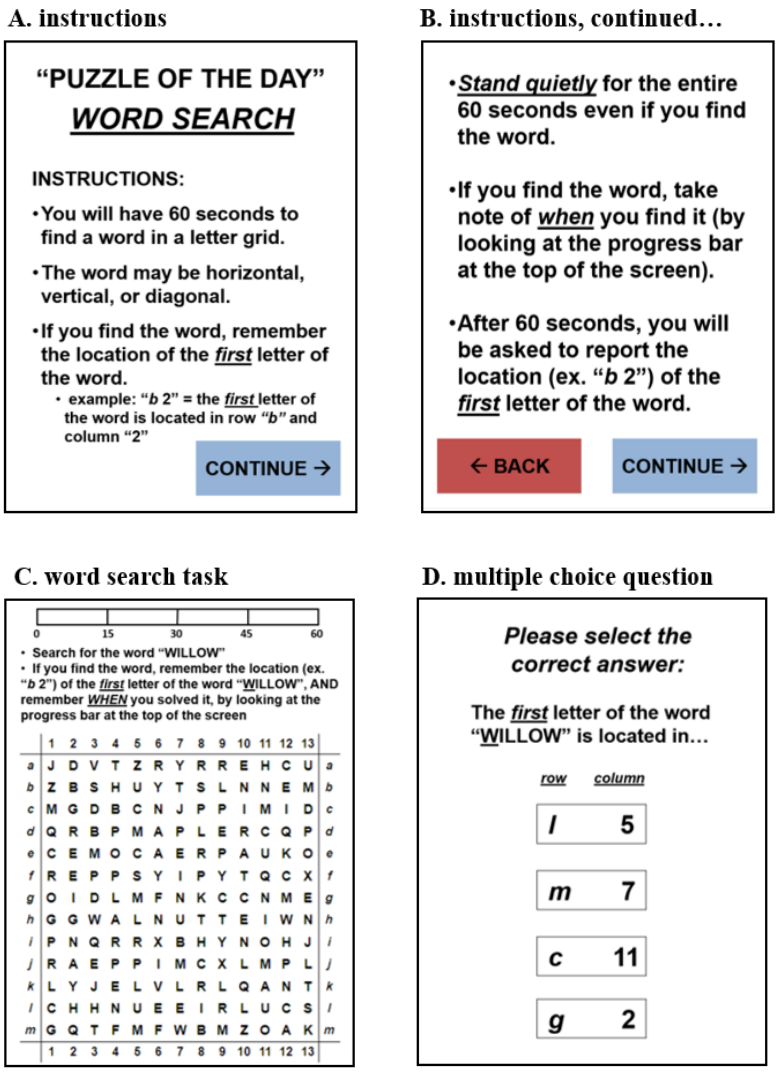

Figure 4.2: The user-interface for the daily postural dual-task condition: a mock-up of the application's detailed instructions (**A-B**), the daily word search task (**C**), and the multiple choice question (**D**). **A-B**: the subject was able to toggle back and forth to ensure he/she was clear on the instructions: the subject had to press "CONTINUE" to begin his/her daily word search task, ensuring he/she was ready for the 60-second dual-task trial to begin. **C**: the word search task served as the cognitive load during 60 seconds of quiet stance: the progress bar at the top of the screen tracked the subject's time. **D**: after 60 seconds passed, the multiple choice question automatically appeared; the subject was instructed to simply guess if he/she was unable to solve the word search within the 60 allotted seconds or if he/she forgot the answer.

4.2.3.ii. Cognitive Task Selection Process

Selection of the cognitive task type was mainly driven by this study's main purpose – to quantify postural sway daily across time. Because we sought to quantify postural sway during quiet stance, we were unable to administer a task that required either a verbal or physical response during the 60-second trial because articulation and/or physical movement would disrupt the postural sway signal. Cognitive task selection was also driven by restrictions inherent to an in-home study design. Because the daily cognitive task was "self"-administered via the tablet, we were limited in our ability to quantify effort exerted on the cognitive task. And because our primary drive was to preserve the integrity of the postural sway signal, we were limited in our ability to quantify actual cognitive performance (*i.e.,* if we would have allowed our subjects to respond as soon as they found the word in the letter grid we would have been able to measure response time, a more descriptive outcome measure than simply "correct" or "incorrect"; but because we placed greater value on 60 seconds of uninterrupted quiet stance, we compromised the value of our cognitive performance measure). To reiterate, the purpose of the cognitive load was to draw neural attentional resources away from the postural task and to the cognitive task in effort to increase the difficulty level of the quiet stance condition.

4.2.3.iii. Subject Training & Support

A substantial amount of time was dedicated to train each subject (1-2 hours per subject) to ensure full comprehension of the daily in-home testing protocol. Great emphasis was placed on "standing quietly" during the training process: subjects were informed of the study's main aim – "to measure one's ability to stand quietly daily for 30 days." Each subject had ample opportunity to practice quiet stance before testing. The 30-day in-home monitoring period did not begin until the subject felt capable, comfortable, and confident in his/her ability to adhere to the procedures detailed during the training process. Each subject was provided with a cell phone number to call if he/she had any questions or concerns and was encouraged to call at any time/day.

4.2.4. CoP Signal Processing

All CoP signals were processed using Matlab R2015a (The MathWorks, Natick, MA, USA). The WBB's CoP signals were derived via the methods detailed in *Chapter 2, Part 2*. As discussed in *Chapter 2, Part 1*, the WBB's mean sampling rate depends on both the device and the operating system of the device used to connect to the WBB. The WBB sampled at a mean rate of ~30 Hz when connected to the Nook tablet (as opposed to mean sampling rate of ~50 Hz when connected to the Microsoft laptop computer used in *Chapter 2*). Because of this, we had reduce the rate of our data averaging method, $f_{DA,}$ from 20 Hz to 10 Hz. Although a sampling rate of 10 Hz is quite low for postural sway compared to recommendations for laboratories in the literature [98], it is high enough to capture the spectral characteristics of the postural sway in our older adult population [114].

All CoP signals (both the 30-second single-task and 60-second dual-task signals) were trimmed to a length of 25-seconds ($3.5*f_{DA}$: $28.5*f_{DA} - 1$) so both the single- and dual-task CoP time series were of the same length and so the first few seconds worth of data were eliminated from the time series. [Note: trimming the end of the trial was not necessary, however a logical trial length was desired (*i.e.*, 25 *vs.* 26.5 seconds), so the end of the trial was trimmed to achieve this.] The first half of the dual-task CoP time-series was used (as opposed to the second half) to increase the probability of quantifying postural sway under the dual-task condition. If the subject solved the word search before the 60-second allotment was over, his/her postural sway during the end of the dual-task trial would likely be more like a single-task condition since he/she would no longer be working to solve the puzzle.

4.2.5. Outcome Measures

4.2.5.i. Cognitive Performance Measure

Cognitive performance was quantified by the subject's performance on the daily word search task. Daily performance was reported as "correct" (1) or "incorrect" (0) and overall cognitive performance was quantified as the percentage of days across the 30-day monitoring period that the subject reported the correct answer to the daily word search task. Limited value was placed on this cognitive performance measure since the way in which

the subject reported his/her answer was through multiple choice, resulting in a 25% chance of getting the correct answer simply by guessing.

4.2.5.ii. Postural Performance Measures

Measures of postural sway and postural dual-task cost were used to quantify postural performance. All CoP-based postural sway measures were derived from the 25-second CoP time series using Matlab R2015a. Four of the five objective postural sway measures were carefully selected to represent distinct and independent features of the postural sway signal [126,127]: mean sway distance (*MD*), mean sway velocity (*MV*), centroidal sway frequency (*fC*), and frequency dispersion (*FD*) (**Table 4.3**). Sway area (*AREA*) was included to model the stabilogram and can be conceptualized as the product of *MD* and *MV* [35]. All five postural sway measures were derived from the resultant planar (two-dimensional, horizontal) CoP signals. Measure derivations are detailed elsewhere in Prieto *et al.* [35].

Table 4.3: CoP-based postural sway measures

Measure	Description / Computation	Units
MD	Mean sway distance: the average distance of the CoP trajectory from the mean CoP	mm
MV	Mean sway velocity: the average velocity of the CoP trajectory	mm/s
AREA	Sway area: estimates the area enclosed by the CoP trajectory per unit time	mm^2/s
fC	Centroidal sway frequency: the frequency at which the spectral mass is concentrated	*Hz*
FD	Frequency dispersion: a unitless measures of the variability in the frequency content of the power spectral density	--------

Postural dual-task costs were used to quantify the effect of the cognitive load on postural performance during quiet stance. The postural dual-task cost calculations were detailed earlier in *Chapter 3*.

4.2.6. Statistical Analysis

Statistical analyses were performed using both Matlab R2015a and IBM SPSS Statistics 22 (IBM Corp., Armonk, NY, USA). Non-normally distributed data were log-

transformed to achieve normal distributions prior to the statistical analyses detailed below. *P*-values were not adjusted due to the limited size of our sample population.

4.2.6.i. Feasibility of In-Home Postural Sway Assessments in Older Adults

To assess the feasibility of an in-home study of daily postural sway and postural dual-task cost in older adults who are either cognitively intact or mildly cognitively impaired, subject adherence was assessed. A t-test was used to assess whether or not there was a difference in subject adherence (quantified by the number of missing days-worth of data due to subject error) between cognitive status groups.

4.2.6.ii. Cognitive Performance & Cognitive Status

To investigate the effect of cognitive status (intact, MCI) on cognitive performance, a one-way, fixed effect ANOVA was performed on the cognitive performance measure.

4.2.6.iii. Reliability of Daily Postural Sway Measures across Time

The stability of postural sway across time was examined using the statistical procedures put forth by McGrath *et al.* [138] to quantify the reliability of our quantitative postural sway measures (**Table 4.3**) acquired daily for 30 days in our 20 non-demented older adults. Intra-class correlation coefficients (ICC(2,k)) [143,144] were calculated for all five postural sway measures extracted from the single-task condition. Standard error of measurement (SEM) was calculated using the formula: $SEM = SD \times \sqrt{1 - ICC}$, where SD was the standard deviation of the mean values across the 20 subjects and ICC was the reliability statistic. Minimum detectable change (MDC) was calculated using the formula: $MDC = SEM \times 1.96 \times \sqrt{2}$, where 1.96 is the Z which is the score associated with the 95% confidence interval and $\sqrt{2}$ is the multiplier to account for uncertainty when multiple tasks are conducted of a measure [145]. Because a complete data set was necessary to calculate the ICC metric, missing days-worth of data were replaced by the subject's mean measurement over the course of the 30-day monitoring period.

4.2.6.iv. Means of Postural Sway & Dual-Task Cost across Time

Pearson's linear correlation was used to assess the association between our clinical (static) postural control measure (Tinetti Balance Score [32], acquired at the subjects' most

recent annual evaluation (**Table 4.1**)) and the monthly means of postural sway and dual-task cost.

Between Cognitive Status Groups

To investigate the effect of cognitive status (intact, MCI) on postural sway and dual-task cost longitudinally, linear mixed effects models were performed on the weekly means of postural sway (during both the single- and dual-task condition) and dual-task cost acquired over the course of the 30-day in-home monitoring period. Subject-specific weekly means were used instead of daily measures to increase statistical power, since 30 data points per subject for a given measure with only 20 subjects (10 per group) is far too many measurements for the statistical model. The first and last day of the 30-day monitoring period were excluded to reduce our data set to 28 days, or four weeks, worth of data. Each weekly mean measure was derived from 4-7 days-worth of data (see **Table 4.4** and **Figure 4.3** for a description of missing data). Cognitive status and time were defined as the two main (fixed) factors; the model assessed both the main and interaction effects of/between these two factors. Subject was defined as a random effect to account for the correlated residuals within each of the 20 subjects.

Across Cognitive Status Groups

To assess whether or not there was an association between cognitive functioning and mean postural sway and/or dual-task cost, cognitive global z-scores were regressed against the monthly means for each measure of postural sway and dual-task cost averaged across the 30-day monitoring period. Linear regression analyses via the least squares method was used.

4.2.6.v. Day-to-Day Variability in Postural Sway & Dual-Task Cost across Time

Pearson's linear correlation was used to assess the association between our clinical (static) postural control measure (Tinetti Balance Score [32], acquired at the subjects' most recent annual evaluation (**Table 4.1**)) and the day-to-day variability in postural sway and dual-task cost.

Between Cognitive Status Groups

The day-to-day variability in postural sway and dual-task cost across time was quantified by calculating the variance in postural sway and dual-task cost across the 30-day monitoring period. To investigate the effect of cognitive status (intact, MCI) on the day-to-day variability in postural sway and dual-task cost, one-way, fixed effect (cognitive status) ANOVAs were performed on the variance measures.

Across Cognitive Status Groups

To assess whether or not there was an association between cognitive functioning and day-to-day variability in postural sway and/or dual-task cost, global z-scores were analyzed against the variance in each measure of postural sway and dual-task cost across the 30-day monitoring period. Linear regression analyses via the least squares method were used.

4.3. Results

4.3.1. Illustration of Postural Sway Quantified by the WBB

Postural sway under both the single- and dual-task condition for a cognitively intact subject is illustrated by stabilograms (**Figure 4.3**). Upon visual inspection, there appeared to be no significant effect of cognitive load on postural sway (*i.e.*, there is no observable difference in postural sway between the single- and dual-task conditions for this one subject on this one study day).

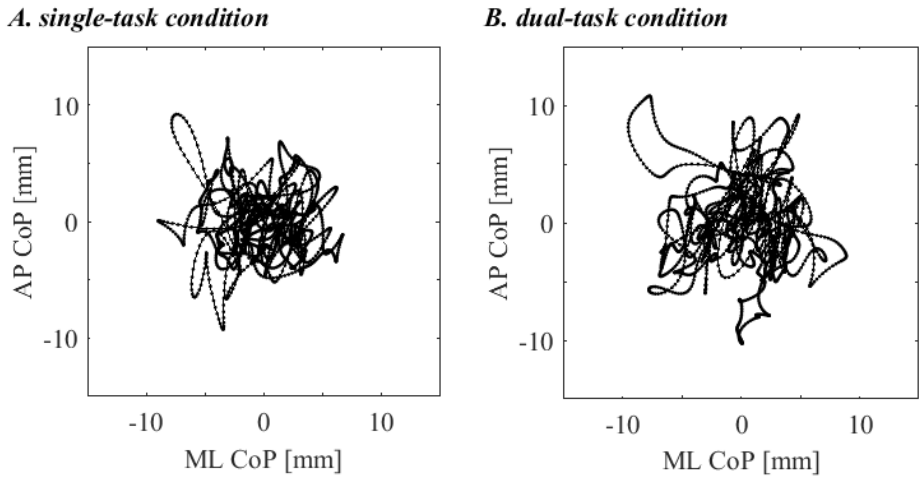

Figure 4.3: Stabilograms illustrating the two-dimensional CoP signals acquired from the WBB under both the single- and dual-task conditions: 25-seconds worth of CoP data for a cognitively intact subject during both the single- and dual-task condition (**A** and **B**, respectively). There is no observable difference between the single- and dual-task stabilograms for this one subject on this one study day. The ML CoP trajectory (x-axis) is plotted against the AP CoP trajectory (y-axis), providing a visual representation/approximation of postural sway area (*AREA*, the one postural sway measure that is conceptualized as the product of two other measures used in this study – *MD* and *MV*).

4.3.2. Feasibility of In-Home Postural Sway Assessments in Older Adults

The total number and percentage of missing days-worth of data are reported in **Table 4.4**. Missing data was often due to technological (*i.e.*, tablet-related) errors: 1. the tablet lost connection to the wireless internet network and did not reconnect automatically; or, 2. the tablet rebooted and did not reinitialize properly. Only two out of the 20 subjects (1 intact, 1 MCI) missed more than one third of the monitoring days. The remaining 18 subjects missed six or fewer out of the 30 days total. On average, there were 2.95 ± 0.72 days, or 9.38 ± 2.39 percent, missing per subject throughout the 30-day monitoring period. The distribution of missing days-worth of data is shown in **Figure 4.4, C**. The distributions of missing days-worth of data due to technological error, subject error, and subject error by group are shown in **Figure 4.4, A, B,** and **D** respectively. There was no difference in subject adherence (quantified by subject error) between cognitive status groups ($p = 0.70$) (**Figure 4.4, D**).

Table 4.4: Feasibility: number of missing days out of 30 days of monitoring. The total number of missing days-worth of data, as well as the number of missing differentiated based on cause: 1. Due to technological error; and, 2. Due to subject error. Feasibility data is separated by cognitive status group (intact (**A**), MCI (**B**)) to assess potential group differences in subject adherence to protocol (quantified by number of missing days due to subject error). There was no difference in subject adherence between cognitive status groups ($p = 0.70$).

SubjID	Number of missing days (#)		Total missing *out of 30*	
	Due to technological error	***Due to subject error***	**(#)**	**(%)**
A. Intact				
2	0	0	0	0.00
3	1	1	2	6.67
4	3	2	5	16.67
5	1	9	10	33.33
10	0	0	0	0.00
12	1	2	3	10.00
14	0	0	0	0.00
15	0	1	1	3.33
18	0	1	1	3.33
19	1	0	1	3.33
Intact group: mean ± SE	**0.70 ± 0.30**	**1.60 ± 0.86**	**2.30 ± 0.99**	**7.67 ± 3.30**
B. MCI				
1	5	6	11	36.67
6	0	0	0	0.00
7	2	2	4	13.33
8	1	4	5	16.67
9	0	0	0	0.00
11	1	0	1	3.33
13	1	5	6	20.00
16	2	0	2	6.67
17	2	2	4	13.33
20	2	1	3	10.00
MCI group: mean ± SE	**1.60 ± 0.45**	**2.00 ± 0.72**	**3.60 ± 1.05**	**12.00 ± 3.49**
Both groups combined: mean ± SE	**1.15 ± 0.28**	**1.80 ± 0.55**	**2.95 ± 0.72**	**9.83 ± 2.39**

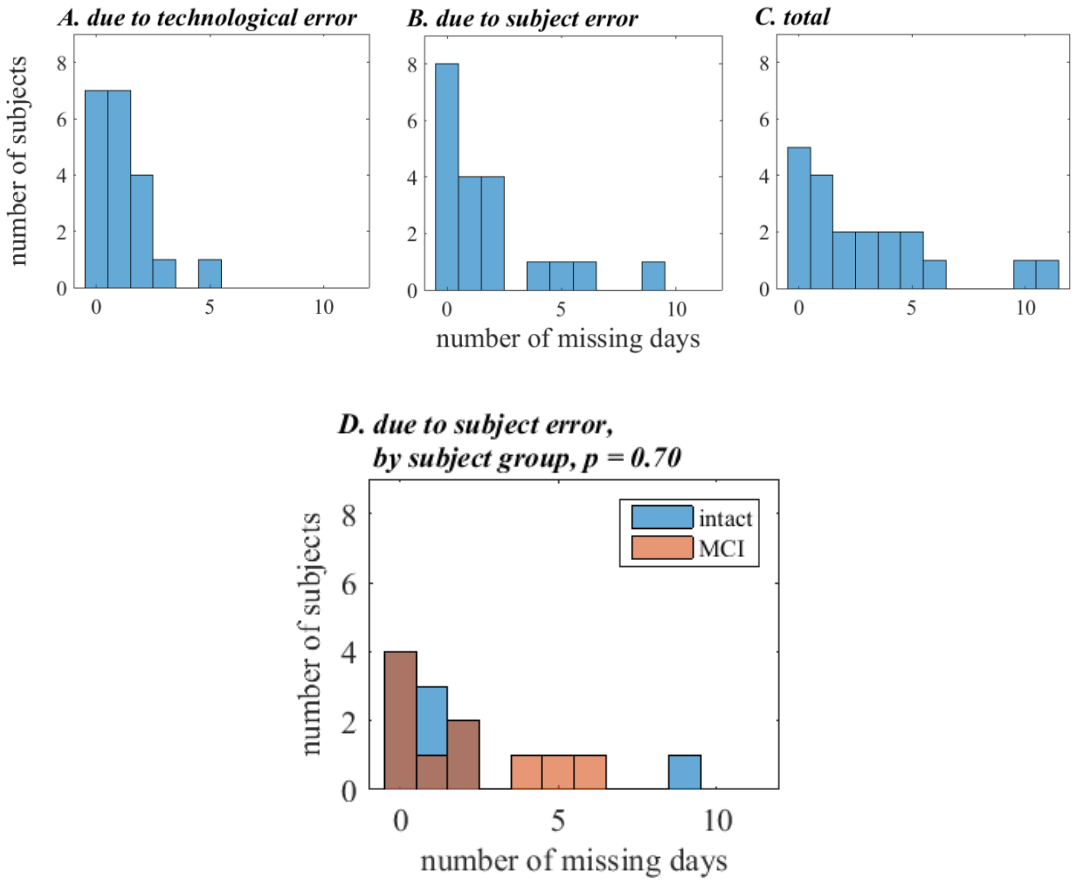

Figure 4.4: Distributions of missing days-worth of data: A. due to technological error; B. due to subject error; C. total; and D. by cognitive status group. Plot D shows the distribution of missing days due to subject error by cognitive status group (intact *vs.* MCI) to assess a potential group-effect on subject adherence to protocol. The maroon/purple color (blend of blue and red) represents group overlaps. There was no difference in subject error between-groups ($p = 0.70$).

4.3.3. Cognitive Performance & Cognitive Status

There was no difference in cognitive performance between the cognitive status groups ($F_{1,18} = 0.97$, $p = 0.338$, **Figure 4.5**).

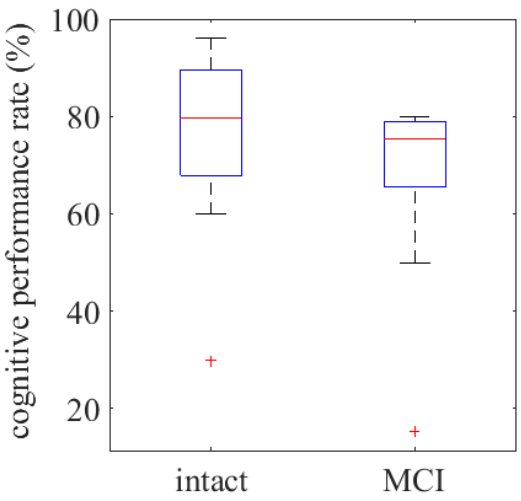

Figure 4.5: Cognitive performance rate (%), by cognitive status group. There was no difference in cognitive performance between the intact and MCI groups. The horizontal red lines represent the group medians, the edges of the boxes mark the 25th and 75th percentiles, the whiskers extend to the most extreme data points that are not outliers (quantified as > Q_3 + 1.5*(Q_3-Q_1) or < Q_1 – 1.5*(Q_3-Q_1), where Q_1 and Q_3 represent the 25th and 75th percentile, respectively).

4.3.4. Reliability of Daily Postural Sway Measures across Time

The test-retest reliability of our five postural sway measures extracted daily during the single-task condition is reported in **Table 4.5**. All five measures exhibited excellent statistical reliability (ICC > 0.90).

Table 4.5: Reliability of the postural sway measures across time. Results from the reliability analysis (put forth by McGrath *et al.* **[138]**) to assess the stability of daily in-home postural sway measures across 30-days of monitoring in 20 non-demented older adults.

Measure	Mean	SD	CoV	ICC	(95% CI)	SEM	MDC
MD	4.22	1.39	32.93	0.987	(0.977 - 0.994)	0.16	0.45
MV	15.29	6.05	39.58	0.994	(0.990 – 0.997)	0.46	1.27
AREA	21.71	14.16	65.20	0.989	(0.980 – 0.995)	1.51	4.18
fC	1.09	0.25	23.10	0.981	(0.966 – 0.991)	0.04	0.10
FD	0.76	0.03	4.05	0.947	(0.908 – 0.976)	0.01	0.02

Means: determined first by calculating the mean across days per subject and then calculating the mean across subjects
Standard deviations (SD): calculated from the SD of the means across subjects
Coefficients of variation (CoV): calculated by taking the ratio of the SD to the mean, expressed as a percentage
Intra-class correlation coefficients (ICC): using Cronbach's alpha.
Standard error of measurement (SEM): $\boldsymbol{SD \times \sqrt{1 - ICC}}$
Minimal detectable change (MDC): $\boldsymbol{SEM \times 1.96 \times \sqrt{2}}$
Note: because a complete data set is necessary to calculate the ICC metric, missing data points (~10% missing per subject, on average) were replaced by the subject's mean measure over the course of the 30-day monitoring period. In doing so, we introduced a certain amount of measurement error to our reliability metric.

The means of and (intra-subject) variability in postural sway across the 30 days, per subject and postural sway measure (extracted daily during the single-task condition) is reported in **Table 4.6**. Subjects are separated by cognitive status group and group statistics are provided. Inter-subject variability by cognitive status group is also reported. Intra- and inter-subject variability ranges from 5-35% and 4-65%, respectively, depending on the postural sway measure. [Intra- and inter-subject variability is quantified by the CoV values contained in **Table 4.6**. The interpretation of CoV values should be approached with caution since CoV is sensitive to small changes in the mean when the mean nears zero (*e.g.*, for the frequency-domain postural sway measures) and may not accurately represent true variation in the measure.]

Table 4.6: Means of and (intra-subject) variability in postural sway across 30 days, per subject and postural sway measure. Subjects are separated by cognitive status group (**A.** intact; **B.** MCI). Group statistics are provided. Inter-subject variability (quantified by CoV) is also reported.

SubjID	*MD*		*MV*		*AREA*		*fC*		*FD*	
	Mean	**Intra-subject CoV**	**Mean**	**Intra-subject CoV**	**Mean**	**Intra-subject CoV**	**Mean**	**Intra-subject CoV**	**Mean**	**Intra-subject CoV**
A. Intact										
2	5.69	16.53	30.11	10.31	52.17	27.97	1.38	13.76	0.71	5.28
3	2.37	26.42	8.26	10.08	6.12	38.90	1.07	20.06	0.77	4.28
4	4.38	23.55	21.64	34.76	26.07	39.82	1.37	28.82	0.77	5.45
5	4.38	16.03	22.71	11.85	27.65	28.58	1.38	11.01	0.72	5.14
10	2.85	24.99	10.32	10.65	9.46	32.97	1.41	23.67	0.76	4.76
12	4.69	17.94	23.83	14.52	35.87	32.59	1.47	17.52	0.75	7.94
14	6.63	19.94	19.93	16.58	41.00	33.90	0.95	17.44	0.76	4.89
15	6.16	20.44	17.32	17.24	35.13	36.85	0.74	16.47	0.75	5.93
18	3.33	22.10	12.53	9.24	13.34	32.96	1.15	19.44	0.78	6.29
19	4.08	18.20	7.49	12.95	9.74	31.31	0.57	16.94	0.80	5.03
means ± SE	4.46 ± 0.44	20.61 ± 1.13	17.41 ± 2.38	14.82 ± 2.38	25.66 ± 4.93	33.59 ± 1.25	1.15 ± 0.10	18.51 ± 1.58	0.76 ± 0.01	5.50 ± 0.33
Inter-subject CoV	31.35		43.27		60.74		27.14		3.53	
B. MCI										
1	2.83	23.55	11.67	3.27	10.88	26.58	1.13	16.32	0.74	8.46
6	3.63	22.88	13.57	13.87	14.70	31.85	1.12	14.82	0.74	5.01
7	4.06	20.23	15.19	11.68	19.35	31.03	0.95	17.42	0.76	6.18
8	4.33	25.60	11.62	12.87	15.42	32.30	0.92	17.67	0.81	4.06

9	2.45	21.65	8.50	9.30	5.69	26.07	1.01	20.47	0.78	4.97
11	3.24	18.24	12.54	10.19	13.11	24.28	1.13	12.43	0.70	5.19
13	3.03	16.45	13.03	14.88	12.29	31.77	1.36	15.00	0.73	6.13
16	4.79	24.02	13.00	18.82	21.05	52.41	0.83	16.60	0.79	4.57
17	4.00	16.32	11.56	12.14	15.29	24.23	0.91	20.84	0.80	4.49
20	7.44	23.36	20.95	15.30	49.87	34.12	0.85	17.05	0.79	5.03
means ± SE	3.98 ± 0.45	21.23 ± 1.04	13.16 ± 1.02	12.23 ± 1.32	17.77 ± 3.82	31.46 ± 2.59	1.02 ± 0.05	16.86 ± 0.80	0.76 ± 0.01	5.41 ± 0.40
Inter-subject CoV	35.53		24.59		67.91		16.06		4.67	
C. Both cognitive status group combined										
means ± SE	**4.22 ± 0.31**	**20.92 ± 0.75**	**15.29 ± 1.35**	**13.53 ± 1.36**	**21.71 ± 3.17**	**32.52 ± 1.42**	**1.09 ± 0.06**	**17.69 ± 0.88**	**0.76 ± 0.01**	**5.45 ± 0.25**
Inter-subject CoV	**32.94**		**39.58**		**65.20**		**23.15**		**4.06**	
Note: See **Table 4.7** for cognitive status group differences (or lack thereof) in postural sway under the single-task condition										

The means of and (intra and inter-subject) variability in postural sway across time is illustrated in **Figure 4.6**. Mean sway distance (*MD*) was selected to visually represent the amount of postural sway in each of the 20 subjects across 30 days of monitoring.

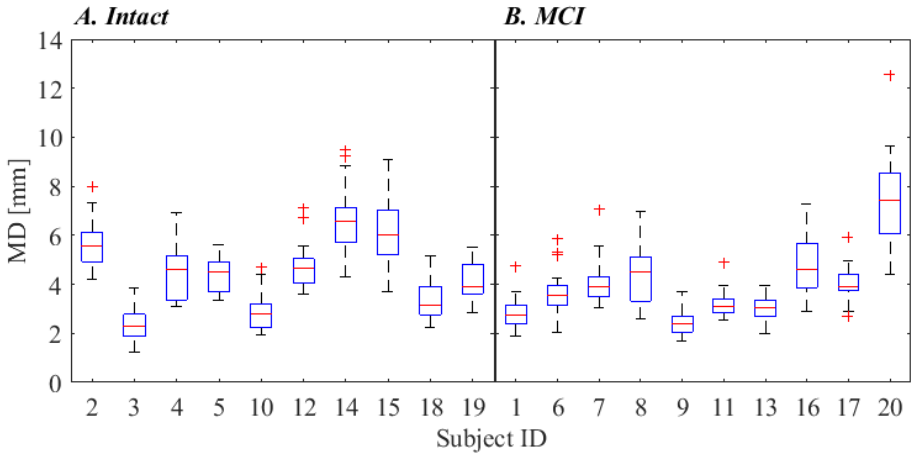

Figure 4.6: Box plots illustrating the subject-specific distribution of postural sway distance (*MD*) across the 30-day monitoring period. The horizontal red lines represent the subject-specific medians, the edges of the boxes mark the 25th and 75th percentiles, the whiskers extend to the most extreme data points that are not outliers, and the red crosses represent the outliers (quantified as > Q_3 + 1.5*(Q_3-Q_1) or < Q_1 – 1.5*(Q_3-Q_1), where Q_1 and Q_3 represent the 25th and 75th percentile, respectively). Each boxplot represents a subject. The first 10 subjects plotted along the x-axis belong to the intact cognitive status group (**A**); the remaining 10 subjects belong to the MCI cognitive status group (**B**).

The autocorrelation put forth by McGrath *et al.* was reproduced in this study. Although not specified, we assume the authors used a biased autocorrelation function to analyze their postural sway time series based on our success in reproducing McGrath's results. The biased autocorrelation for the 30-day *MD* time series at time lags of 1-7 days for all 20 of our subjects is illustrated in **Figure 4.7**. Each subject is represented by a line on the plot, with cognitive status groups separated by color. Maximum lag time was set to 7 days because increased variance is inherent with larger time lags since the estimate of the mean squared value is inherently more variable and less reliable at larger time lags (*i.e.*, fewer data points are used to compute the mean) [111,146].

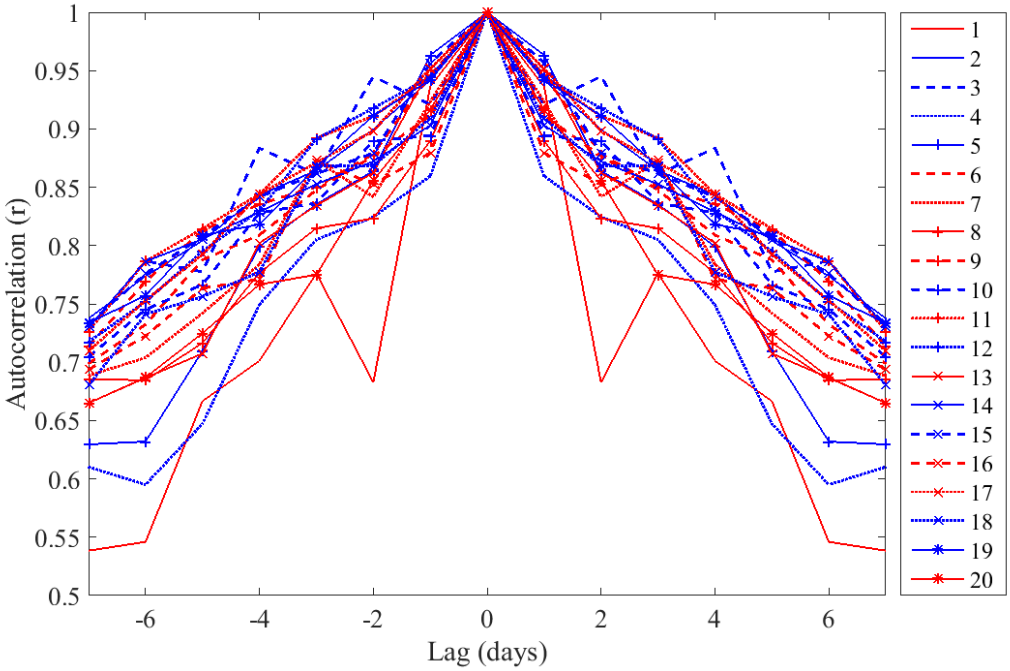

Figure 4.7: Biased autocorrelation function of the 20 subjects' postural sway distance (*MD*) across time (up to 7 days lag). Each line represents a subject (subjID 1-20), with the intact (blue) and MCI (red) subjects separated by color. The x-axis denotes the time lag (in days) and the y-axis denotes the autocorrelation function for a given lag and subject.

This approach is invalid (and likely led to misinterpretation of the data in McGrath's paper) as it does not account for the fact that when shifting one time series relative to the other, fewer data points contribute to the calculation because there is less overlap between the time series. An unbiased autocorrelation function is necessary to account for decreasing data points as time lag increases and is implemented with a scale factor of $1/N - |lag|$, where *N* represents the length of the time series and *lag* represents the time step in days [111,146].

McGrath does not specify how they dealt with missing days-worth of data. If the missing days were simply excluded from the analysis or were replaced with simulated data (*i.e.*, the subject's mean measure over time), a certain amount of error would be introduced to the autocorrelation function: removing a time-step (*i.e.*, a day with missing data) would compromise the information about the specific time-lag linear dependence, and simulating data that is missing (*e.g.*, with the mean measure across time) would produce a potentially inflated autocorrelation value (amount of error will increase as the number of simulated data points increase). To avoid these computational errors, we did not remove the missing

data points from the time series but we did exclude any data couples with missing data points from our autocorrelation calculations. The unbiased autocorrelation function with properly treated missing days-worth of data for the 30-day *MD* time series at time lags of 1-7 days is illustrated in **Figure 4.8**.

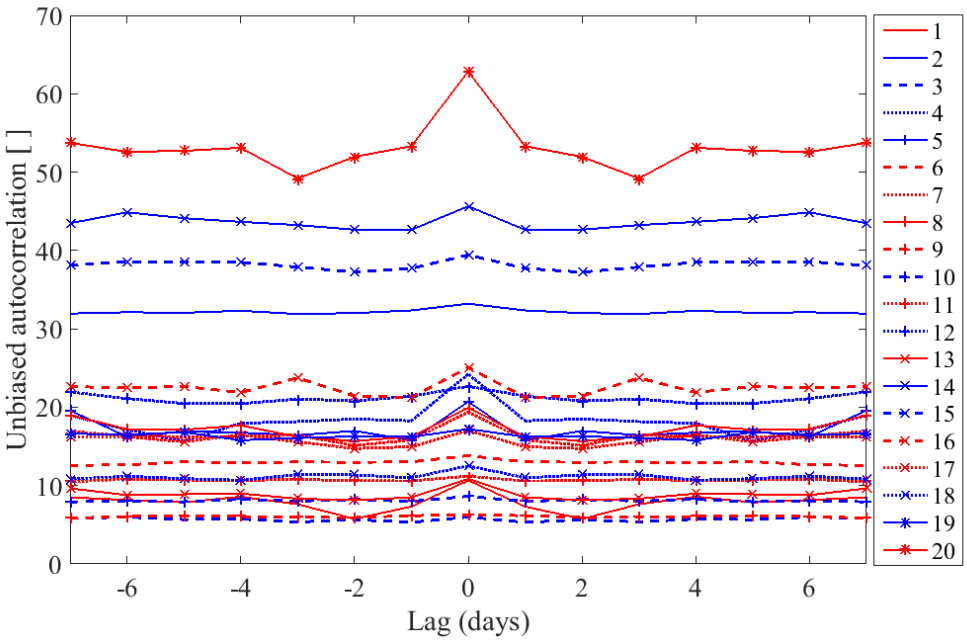

Figure 4.8: Unbiased autocorrelation function illustrating the true autocorrelation of the 20 subjects' postural sway distance (*MD*) across time (up to 7 days lag). Each line represents a subject (subjID 1-20), with the intact (blue) and MCI (red) subjects separated by color. The x-axis denotes the time lag (in days) and the y-axis denotes the autocorrelation function for a given lag and subject.

This analysis was performed on the four other postural sway measures as well. Similar results were produced for all five postural sway measures. The unbiased autocovariance function was then computed to assess whether there were systematic changes in the measures over time. The unbiased autocovariance function for the 30-day *MD* time series at time lags of 1-7 days is illustrated in **Figure 4.9**.

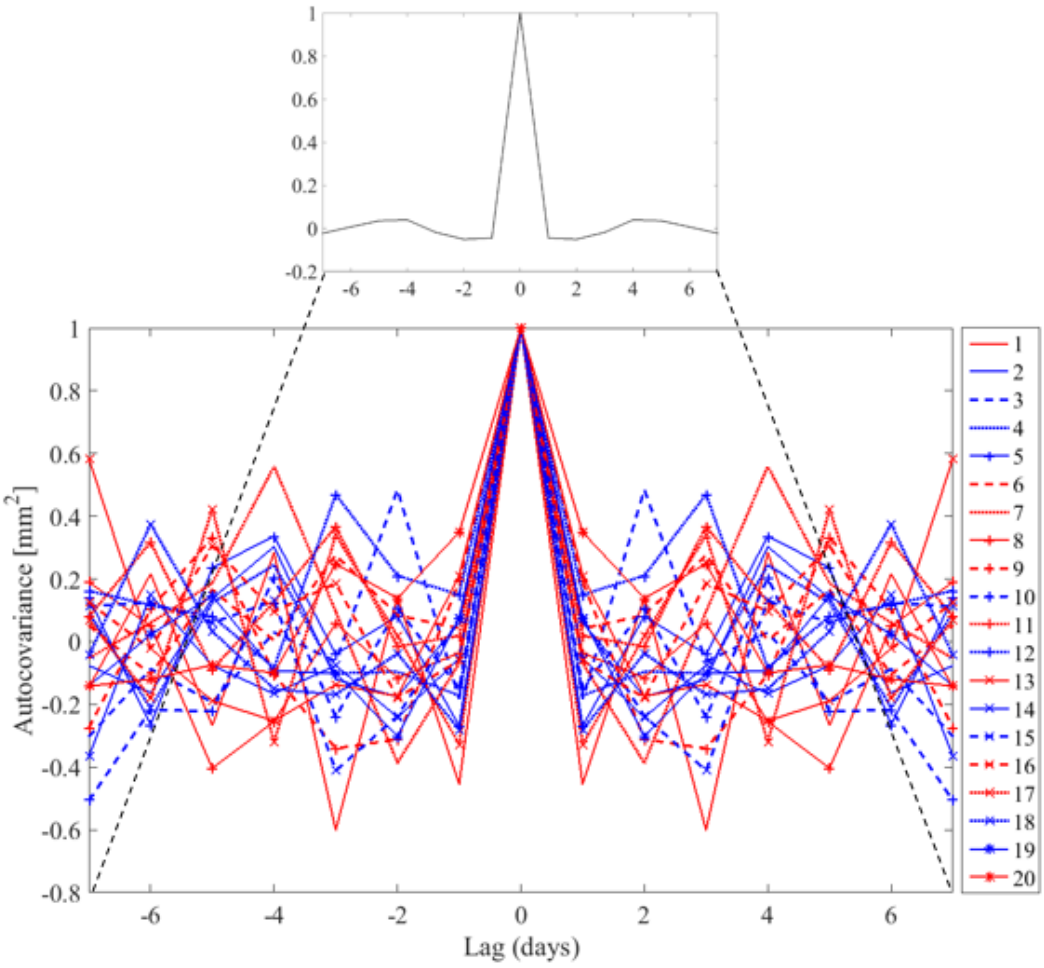

Figure 4.9: Unbiased autocovariance function of the 20 subjects' postural sway distance across time (up to 7 day lag). Each line represents a subject (subjID 1-20), with the intact (blue) and MCI (red) subjects separated by color. The x-axis denotes the time lag (in days) and the y-axis denotes the autocovariance function for a given lag and subject. The small plot projected above the main plot represents the group mean autocovariance averaged across all 20 subjects and shows that there is no systematic change in *MD* over time (for all lags but zero, the autocovariance remains close to zero).

The unbiased autocovariance function (**Figure 4.9**) is quite informative as it can be used to detect time-dependent patterns such as linear trends or periodic variations across days. There are no systematic changes in postural sway *MD* over the course of the 30-day monitoring period (illustrated by the group mean autocovariance value approximately equaling zero for all time lags but zero – up to 7 days lag is shown in **Figure 4.9**). The same time-scale patterns were expressed by postural sway *MV*, *AREA*, *fC*, and *FD*, suggesting that there are no systematic changes in postural sway in our 20 older adults across the 30-day monitoring period. [Note: there is little difference between biased and

unbiased autocovariance functions when there is no systematic change in the measure over time: in autocovariance, the means of the time series are zeroed such that the product of one time series and the shifted time series (at *n lags*) is also close to zero so there is little difference in scaling by $1/N$ or $1/N - |lag|$, where *N* represents the length of the time series and *lag* represents the time step in days.] The unbiased autocorrelation function (**Figure 4.8**) is not very useful since there were no obvious trends in the postural sway time series.

4.3.5. Weekly & Monthly Means of Postural Sway & Dual-Task Cost

The monthly means of (both single- and dual-task) postural sway and dual-task cost were not significantly correlated with The Tinetti Balance Score (Pearson's correlation coefficient, $r < 0.50$).

4.3.5.i. Between Cognitive Status Groups

Lower postural sway measures appeared to be associated with MCI status when measuring postural sway daily for 30 days. Upon visual inspection, the daily group means in *MV, AREA,* and *fC* trended towards separation, with lower mean measures of postural sway in the MCI group. This trend was present under both the single- and dual-task conditions. The daily group means for the five postural sway measures across the 30-day monitoring period are shown in **Figure 4.10**.

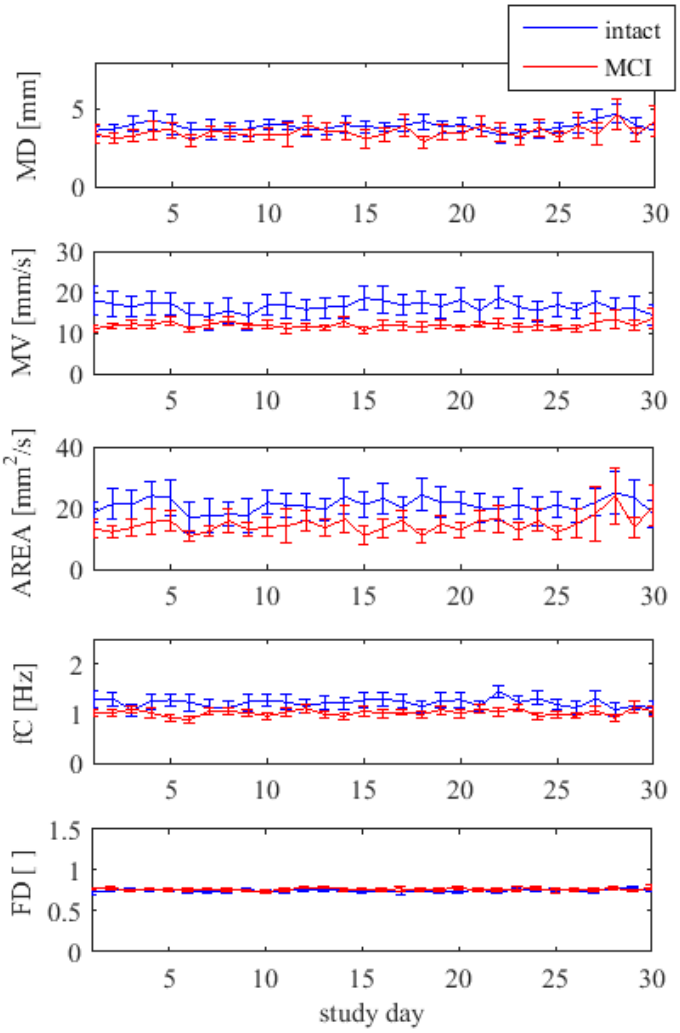

Figure 4.10: The daily group means in three out of the five postural sway measures (*MV*, *AREA*, and *fC*) trended towards separation, with lower mean measures associated with MCI. This figure shows daily group means and distribution (quantified by SE) across the 30-day monitoring period for the five postural sway measures during the dual-task condition.

Despite the group-specific trends in postural sway shown in **Figure 4.10**, there was no difference in weekly mean measures of postural sway between the intact and MCI groups (**Table 4.7**). There was also no difference in weekly mean measures of postural dual-task cost between the intact and MCI groups (**Table 4.7**) and there were no group-specific trends in dual-task cost observed via visual inspection. The statistical results of the linear mixed effects models are reported in **Table 4.7**: there was no effect of cognitive status or time on the weekly group means of postural sway and dual-task cost and there was no interaction between cognitive status and time. Monthly group means (weekly group means

averaged across the four weeks) for postural sway (both single- and dual-task) and dual-task cost are contained in **Table 4.7** for reference.

Table 4.7: Weekly group means of postural sway and dual-task cost across the 4 weeks of in-home monitoring: Results from the linear mixed effects models (fixed effects: cognitive status, time) are reported to show the main and interaction effects on the weekly means of postural sway (single- (**A**) and dual-task (**B**)) and dual-task cost (**C**).

Measure	***Intact*** **Group mean ± SE** *across the 4 weeks*	***MCI*** **Group mean ± SE** *across the 4 weeks*	**Main Effect: *Cognitive Status***		**Main Effect: *Time*** *(by week)*		**Interaction Effect:** *Cognitive Status*Time*		**Information Criteria: Log Likelihood**
			F	**p**	***F***	***p***	***F***	***p***	**-2logΛ**
A. Single-task									
MD	4.44 ± 0.02	3.98 ± 0.08	0.69	0.415	1.19	0.321	0.76	0.522	-230.47
MV	17.34 ± 0.14	13.16 ± 0.17	1.67	0.211	1.62	0.195	0.91	0.441	-264.48
AREA	25.37 ± 0.26	17.75 ± 0.75	1.24	0.279	1.07	0.368	0.91	0.440	-140.14
fC	1.15 ± 0.01	1.02 ± 0.01	1.40	0.250	0.95	0.422	0.29	0.831	-100.90
FD	0.76 ± 0.00	0.76 ± 0.00	0.24	0.628	0.99	0.403	0.65	0.588	-361.75
B. Dual-task									
MD	3.86 ± 0.04	3.50 ± 0.06	0.87	0.362	1.80	0.158	0.13	0.939	-231.61
MV	16.71 ± 0.28	11.87 ± 0.08	1.89	0.185	1.08	0.363	2.36	0.081	-253.63
AREA	21.08 ± 0.41	14.47 ± 0.54	1.40	0.250	0.84	0.476	0.34	0.793	-133.15
fC	1.23 ± 0.01	1.12 ± 0.02	0.73	0.403	2.10	0.110	0.48	0.695	-74.88
FD	0.75 ± 0.00	0.76 ± 0.00	0.46	0.507	0.61	0.609	0.42	0.742	-351.94
C. Dual-task costs (in %)									
MD	-8.72 ± 0.84	-9.01 ± 0.64	0.00	0.988	0.15	0.927	0.14	0.935	634.59
MV	-5.09 ± 0.95	-8.52 ± 1.09	1.18	0.291	0.98	0.407	1.98	0.127	533.61
AREA	-9.16 ± 0.92	-11.54 ± 1.56	0.07	0.795	0.11	0.954	0.53	0.662	694.24
fC	10.51 ± 0.84	12.76 ± 1.04	0.12	0.737	0.39	0.762	0.15	0.932	656.57
FD	-0.57 ± 1.17	0.25 ± 0.37	0.27	0.608	0.21	0.889	0.31	0.820	457.96

Group mean: weekly cognitive status group means of the postural sway measure/cost averaged across the 4 weeks
SE: SEs of weekly cognitive status group means of the postural sway measure/cost across the 4 weeks
*reached statistical significance, $p < 0.05$

4.3.5.ii. Across Cognitive Status Groups

There were no significant linear relationships ($p < 0.05$) between postural sway or dual-task cost and cognitive functioning when analyzing across groups (**Table 4.8**).

Table 4.8: No linear relationships between postural sway or dual-task cost and cognitive functioning. Results from the linear regression analyses are reported to show there were no linear relationships between the monthly means of postural sway (single- (**A**) and dual-task (**B**)) and dual-task cost (**C**) averaged across the 30 days and cognitive global z-scores.

Measure	*A. Single-task*			*B. Dual-task*			*C. Dual-task cost*		
	r	***F***	***p***	***r***	***F***	***p***	***r***	***F***	***p***
MD	-0.34	2.41	0.138	-0.32	2.11	0.163	0.02	0.01	0.931
MV	0.04	0.03	0.870	0.06	0.07	0.799	-0.05	0.05	0.824
AREA	-0.27	0.55	0.468	-0.18	0.57	0.460	-0.06	0.06	0.813
fC	0.43	4.17	0.056	0.29	1.59	0.223	-0.18	0.58	0.457
FD	-0.05	0.05	0.827	-0.12	0.24	0.629	-0.12	0.24	0.631

*reached statistical significance, $p < 0.05$

4.3.6. Day-to-Day Variability in Postural Sway & Dual-Task Cost

The day-to-day variability in (both single- and dual-task) postural sway and dual-task cost were not significantly correlated with The Tinetti Balance Score (Pearson's correlation coefficient, $r < 0.50$), suggesting that the information gleaned from infrequent, clinical measures of (static) postural control does not relate to the information acquired from frequent, in-home postural sway measures since the day-to-day variability in postural sway was found to be associated with both cognitive status (Section 4.3.6.i) and cognitive functioning (Section 4.3.6.ii).

4.3.6.i. Between Cognitive Status Groups

There was significantly higher day-to-day variability in *fC* cost in the MCI group compared to the intact group (**Table 4.9, C, Figure 4.11**). There were no other differences in day-to-day variability between cognitive status groups.

Table 4.9: Variability in postural sway and dual-task cost across the 30 days of in-home monitoring: Results from the one-way, fixed effect (cognitive status) ANOVAs are reported to show the effect of cognitive status on the day-to-day variability (quantified by variance) in postural sway (single- (**A**) and dual-task (**B**)) and dual-task cost (**C**) within the 30-day monitoring period.

Measure	Units	*Intact* Group mean ± SE	*MCI* Group mean ± SE	Effect of *Cognitive Status*	
				$F_{1,18}$	p
A. Single-task					
MD	mm^2	0.85 ± 0.15	0.87 ± 0.27	0.30	0.588
MV	mm^2/s^2	10.94 ± 5.27	3.33 ± 0.94	1.80	0.196
AREA	mm^4/s^2	92.47 ± 25.83	54.38 ± 28.31	1.54	0.231
fC	Hz^2	0.05 ± 0.02	0.03 ± 0.00	1.21	0.286
FD	Hz^2	0.00 ± 0.00	0.00 ± 0.00	0.04	0.845
B. Dual-task					
MD	mm^2	0.68 ± 0.17	0.81 ± 0.28	0.22	0.642
MV	mm^2/s^2	10.45 ± 4.33	2.57 ± 1.32	2.17	0.158
AREA	mm^4/s^2	53.28 ± 14.77	44.05 ± 26.43	1.14	0.300
fC	Hz^2	0.06 ± 0.01	0.05 ± 0.01	0.23	0.641
FD	Hz^2	0.00 ± 0.00	0.00 ± 0.00	0.67	0.424
C. Dual-task costs					
MD	%	721.42 ± 205.69	640.19 ± 165.59	0.07	0.790
MV	%	209.98 ± 49.44	144.09 ± 24.86	1.42	0.249
AREA	%	1593.02 ± 342.03	1245.50 ± 339.89	0.78	0.403
fC	%	551.50 ± 69.09	895.64 ± 133.05	**5.27**	**0.034***
FD	%	59.24 ± 5.05	60.59 ± 6.63	0.03	0.874

Group means: mean day-to-day variability (quantified by variance) averaged across the 10 subjects
SE: SE in day-to-day variability across the 10 subjects
*reached statistical significance, $p < 0.05$

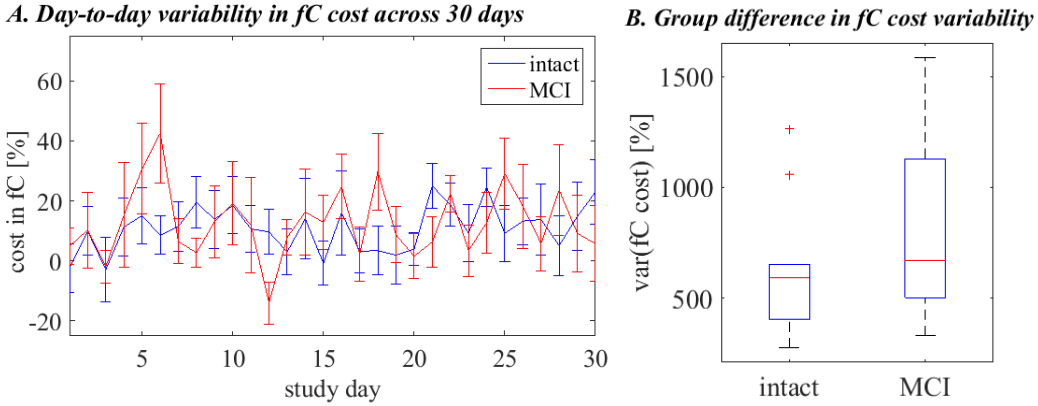

Figure 4.11: The variability in *fC* cost across the 30 days of in-home monitoring was significantly higher in the MCI group. The variability in *fC* cost across the 30-day monitoring period was higher in the MCI group (**A**). This significant group difference is shown by a boxplot (**B**) and is reported above in **Table 4.9, C**. The horizontal red lines in (**B**) represent the group medians, the edges of the boxes mark the 25th and 75th percentiles, the whiskers extend to the most extreme data points that are not outliers, and the red crosses represent the outliers (quantified as > Q_3 + 1.5*(Q_3-Q_1) or < Q_1 – 1.5*(Q_3-Q_1), where Q_1 and Q_3 represent the 25th and 75th percentile, respectively).

4.3.6.ii. Across Cognitive Status Groups

There were significant linear relationships ($p < 0.05$) between postural sway variability and cognitive functioning when analyzing across groups. Under the single-task condition, more variability in *MD* and less variability in *fC* across the 30-day monitoring period was related to lower global z-scores (**Table 4.10, A, Figure 4.12, A & B**). Under the dual-task condition, more variability in both *MD* and *AREA* across the 30-day monitoring period were related to lower global z-scores (**Table 4.10, B, Figure 4.12, C & D and Figure 4.13**). In sum, more day-to-day variability in time-domain postural sway and less day-to-day variability in frequency-domain postural sway was correlated with lower cognitive functioning (quantified by lower global z-scores).

Table 4.10: Linear relationships between the day-to-day variability in postural sway and cognitive functioning. Results from the linear regression analyses are reported to show the significantlinear relationships between the variance in postural sway (both single- (**A**) and dual-task (**B**)) across 30 days and the cognitive global z-scores. There were no significant linear relationships between the variance in postural dual-task cost (**C**) across 30 days and cognitive global z-scores.

Measure	*A. Single-task*			*B. Dual-task*			*C. Dual-task cost*		
	r	***F***	***p***	***r***	***F***	***p***	***r***	***F***	***p***
MD	**-0.48**	**5.51**	**0.031***	**-0.45**	**4.47**	**0.049***	0.08	0.13	0.723
MV	0.18	0.61	0.446	0.16	0.50	0.491	-0.17	0.51	0.485
AREA	-0.25	1.15	0.297	**-0.47**	**5.03**	**0.038***	-0.06	0.06	0.804
fC	**0.46**	**4.91**	**0.040***	0.26	1.33	0.265	-0.27	1.40	0.252
FD	0.21	0.84	0.371	0.05	0.04	0.842	0.00	0.00	0.992

*reached statistical significance, $p < 0.05$

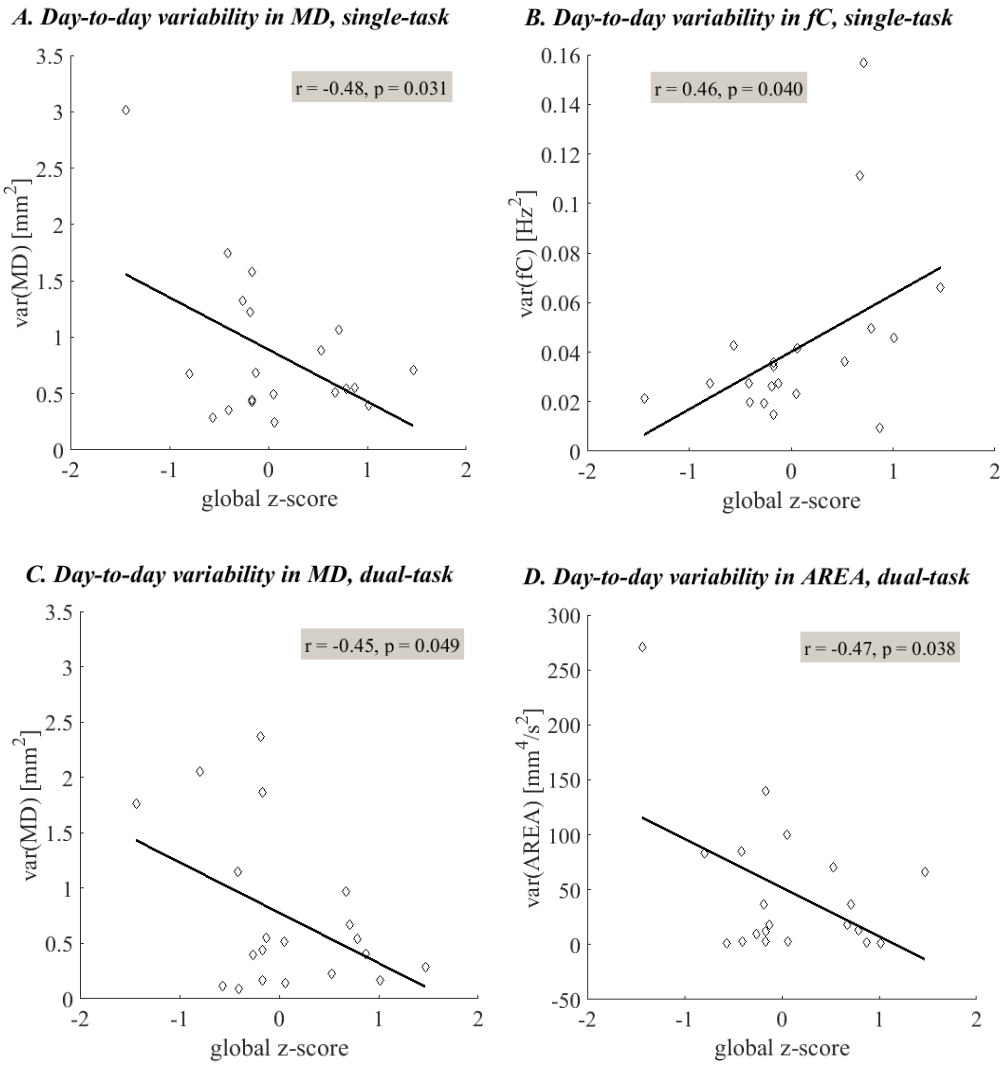

Figure 4.12: Linear relationships between the day-to-day variability in postural sway and cognitive functioning. Linear regression shows significant linear relationships ($p < 0.05$) between the day-to-day variability in postural sway measures and cognitive global z-scores. More variability in time-domain postural sway (quantified by *MD* (**A & C**) and *AREA* (**D**)) and less variability in frequency-domain postural sway (quantified by *fC* (**B**)) is related to lower cognitive functioning (quantified by lower global z-scores). The linear trends observed under the single- and dual-task conditions are shown in plots **A & B** and **C & D**, respectively.

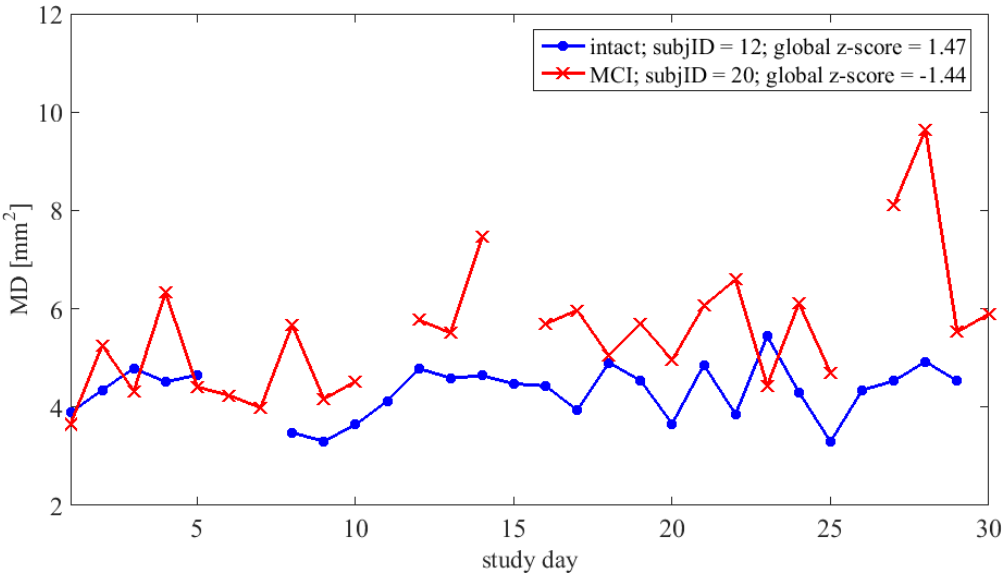

Figure 4.13: *MD* time series illustrating the difference in day-to-day variability between relative high and low cognitive functioning: more variability in *MD* is related to lower cognitive functioning. Daily *MD* measures for two subjects are plotted: the (MCI) subject with the lowest global z-score (in red) and the (intact) subject with the highest global z-score (in blue). The lines are discontinuous due to missing days-worth of data. Both subjects had three days-worth of missing data over the course of the 30-day monitoring period. The intact subject (subjID 12) missed two days due to subject error. The MCI subject (subjID 20) only missed one day due to subject error.

4.4. Discussion

4.4.1. Feasibility

Results from our feasibility analysis support *Hypothesis I*: our in-home study of postural sway and cognitive dual-tasking was feasible in our older adult population – both for cognitively intact and mildly cognitively impaired older adults. Subject adherence to protocol was impressive and there was no difference in adherence between cognitive status groups. This was to be expected within the ORCATECH cohort due to both our subjects' previous experience with longitudinal, in-home studies of aging with technology and the subtlety of impairment within our MCI group. We did not anticipate the MCI group to experience trouble adhering to the testing protocol due to the unobtrusive nature of their mild cognitive impairments (their impairments were classified based on their lack of interference with activities of daily living).

All 20 subjects were recommended for this study based on their reliable, capable and cooperative nature. All have been active participants in ongoing ORCATECH studies for years now, meaning all were comfortable with longitudinal, in-home, technology-driven studies. It is important to note that our cohort may not adequately represent the average older adult within this age group. Similar studies must be conducted with a larger, more diverse sample population before true feasibility can be determined. Nonetheless, this pilot study's feasibility results are promising.

4.4.2. Cognitive Performance

There was no difference in cognitive performance on the daily word search task between the intact and MCI groups. Selection of cognitive task type was both driven and limited by our study's main aim – to acquire sound, meaningful measures of postural sway daily in older adults with and without MCI via in-home monitoring methods. We were driven to select a cognitive task of reasonable difficulty level so it would provide enough cognitive demand and sufficiently draw attention away from the postural and to the cognitive task. We were limited to select a cognitive task without a verbal or physical response (restricting our response type to mental). Both verbal and physical responses would affect CoP: articulation provokes changes in the respiratory pattern, which may in turn be reflected by an increase in postural sway frequency (and hence sway path distance) [75,147]; a physical movement, such as lifting an arm to touch the tablet, would obviously be reflected by an increase in postural sway as well. Maintaining the integrity of the postural sway signal remained our primary focus in this study. In turn, limited effort was placed on acquiring a meaningful cognitive performance measure based on the restrictions associated with our experimental setup and primary outcome measure (*i.e.*, postural sway) as well as those inherent to in-home study designs.

Our daily cognitive task, the word search, is not a classic neuropsychological test and was not designed to tax a specific cognitive function. [We consider our word search puzzle to be more of a global cognitive task: it has visuospatial and working memory components – as the subject searches the letter grid for the word; executive function and supervisory/divided attention components – as the subject performs the puzzle, maintains postural stability, meanwhile tracking this/her progress relative to the time remaining in

the trial; and, a possible short-term memory component – as the subject consciously works to remember the solution to the puzzle, assuming the subject solves the puzzle with time remaining in the 60-second dual-task condition.] Because the word search puzzle is an "off-the-shelf" task and is not classically used to measure cognition, it mainly served as a cognitive distraction in this study and was not expected to differentiate between cognitive status groups. The way in which it taxed cognition (and the sensitivity of the task itself) remains unknown in our older adult populations under our cognitive-postural dual-task conditions.

We acquired clinical feedback from several LAADC/ORCATECH researchers and staff throughout the user-interface design and development phase in an effort to increase the likelihood of successful implementation and meaningful data acquisition within our specific cohort. We also tested our system with two older adults before beginning testing for this study. We were relatively confidant in the clarity of phrasing, instruction, and format for our daily in-home routine. Upon implementation though, we observed consistent and sustained confusion on one element of our daily routine. After inputting their answer to the multiple choice question, the subjects were prompted to tell us whether or not they guessed when responding to the multiple choice question (a simple "yes" or "no" response). For some reason, the phrasing of this question seemed to confuse at least a third of our subjects. After clarifying the meaning of the question, most subjects remained confused and sustained this confusion over the course of the 30-day monitoring period. [I routinely called to check-in with these subjects and asked whether or not they found the word in their daily word search puzzle. I then asked whether or not they guessed when responding to the multiple choice question. The subjects' responses were inconsistent and showed that they remained confused about the question's intent.] Because this confusion often led to incorrect responses, we are unsure how often our subjects actually guessed the answer. In hindsight, we simply should have had an "I don't know" option for the multiple choice question. This would have been clearer, avoided confusion, and would have allowed us to place more weight on our cognitive performance outcome measure. As is, we are unsure of the amount of error within our cognitive performance measure (*i.e.*, how often a successful response was simply due to chance). In sum, because our cognitive performance

measure lacked precision, accuracy and overall significance, we were not surprised to see no effect of cognitive status on cognitive performance in this study.

4.4.3. Reliability of Daily Measures

Our longitudinal findings support the conclusions made by McGrath *et al*. on the stability of daily in-home measures of postural control [138]. All five of our objective postural sway measures exhibited excellent statistical reliability (ICC > 0.90), supporting *Hypothesis II*. It is important to note though that by replacing missing data points with the subject's mean measure, we introduced a certain amount of measurement error to our reliability metric: as the number of missing days-worth of data increases, the accuracy of the ICC metric decreases. Because each subject on average only missed 2.95 ± 0.72 days out of the total 30, we consider there to be a limited amount of error in the ICC metric due to missing data. It is also important to note that the ICC values may have been inflated by the quantity of our repeated measures. On average, each subject was assessed 27 out of the 30 total days; the weight of error variance decreases as the quantity of repeated measures increases, which could in turn inflate the ICC values [148].

The ICCs in this study ranged between r = 0.908 and 0.995 (**Table 4.5**) suggesting that there was considerably greater inter- *vs.* intra-subject variability. This suggests that there is a need for more individual–based healthcare approaches. While group (inter-subject) analyses are important, early detection of functional decline can only be operationalized via the assessment of individual (intra-subject) time-course trajectories, which are inherently self-referential. Individual time-series analyses of postural control would expose the natural dynamic patterns of an individual's postural control system across time and may reveal pattern changes preceding or paralleling functional decline.

We also quantified SEM and MDC metrics for each postural sway measures to assess measure stability across the 30-day monitoring period (**Table 4.5**). The SEM value is beneficial as it provides an absolute index of reliability (as opposed to ICC, a relative reliability measure) and can be used to define the difference needed between a subject's day-to-day postural sway for the difference to be considered real (MDC values) [145]. McGrath and colleagues discuss the value and limitations of these metrics given their current clinical application [138]: currently SEM and MDC values are derived from group

means and are used to identify when an individual has significantly deviated from the group mean. But since we, like McGrath, consider individual-based methods to be the most beneficial type of healthcare approach, more meaningful (SEM and MDC) metrics would be that derived from one subject (as opposed to one group) over time.

Our observed intra- (5-35%) and inter- (4-65%) subject variability in postural sway across time was less than that observed by McGrath (17-56% and 37-107% for intra- and inter-subject variability, respectively) (**Table 4.6**). Because our battery of objective postural sway measures is similar to McGrath's, postural sway feature selection most likely does not account for this difference in results. The time course of our study was half the length of McGrath's study (4 *vs.* 8 weeks) and our subjects were ~15 years older than in McGrath's study (mid-late 80's *vs.* early 70's). A shorter monitoring period and older cohort may have contributed to the lower amount of observed intra- and inter-subject variability. Perhaps the day-to-day (week-to-week, month-to-month, *etc.*) variability in postural sway increases as the time scale increases. And perhaps our older cohort is less stable due to the age-related effects on postural control, which may be expressed by a reduced amount of day-to-day postural sway variability (a concept supported by the literature: too much or too little variability in a given function is an indication of functional decline [149]). Although we did not observe as much intra-subject variability as McGrath, we did observe some variability that characterizes the natural fluctuation in postural sway in older (mid-late 80's) non-demented old adults.

Neither the intra- nor inter-variability in postural sway was correlated with The Tinetti Balance Score (Pearson's correlation coefficient, $r < 0.50$). Our findings support McGrath's conclusion that the observed variation in postural sway (at least for our 10 intact subjects) are not necessarily "aberrant movement patterns, but are seemingly representative of natural movement variability," which in turns motivates the use of postural sway variability as a sensitive biomarker for early motor and/or cognitive decline [138].

The unbiased autocovariance function was used to assess whether there were time-dependent patterns such as linear trends or periodic variations in postural sway across days. There were no systematic changes in all five objective postural sway measures over the course of the 30-day monitoring period (illustrated by the group mean autocovariance value

approximately equaling zero for all time lags but zero – up to 7 days lag is shown in **Figure 4.9**), suggesting that the postural sway in older adults both with and without MCI is a stationary process when bound by a relatively small time scale (*e.g.*, one month).

4.4.4. Postural Sway & Dual-Task Cost

4.4.4.i. Weekly & Monthly Means

The group-specific postural sway trended towards separation with more postural sway associated with the intact group during both the single- and dual-task conditions (there were no group-specific trends observed in postural dual-task cost) when comparing the (daily (**Figure 4.10**) and weekly (**Table 4.7**)) means of postural sway between cognitive status groups. Furthermore, there were no linear relationships between postural sway (under either the single- or dual-task condition) and cognitive functioning (indexed by cognitive global z-scores) when analyzing across cognitive status groups. These findings do not support *Hypothesis III* since we predicted older adults with lower cognitive functioning (as in MCI) to have more postural sway.

4.4.4.ii. Day-to-Day Variability

Only one (dual-task cost) measure differentiated the day-to-day variability in postural sway between cognitive status groups (**Table 4.9**). There was significantly higher day-to-day variability in the dual-task cost in sway frequency (quantified by centroidal frequency, *fC*) in the MCI group compared to the intact group (**Figure 4.11**). This finding supports *Hypothesis IV*: more variability in postural dual-task cost (a specific motor function) was associated with MCI (a population that is in the initial stages of functional decline). Perhaps an older adult with intact cognitive functioning has a more consistent set-switching strategy when dual-tasking [150,151] (quantified by less day-to-day variability in postural dual-task cost) compared to an older adult with mildly impaired cognitive functioning. Studies have shown an age-effect on dual-task ability and set-switching strategy: older adults experience higher (cognitive) dual-task (switch) costs and are less able to switch cognitive strategies compared to younger adults [151]. It is likely that the age-effect on set-switching is exacerbated in the presence of cognitive impairment due to decreased cognitive flexibility,

which may be expressed by less consistent set-switching strategies across time (and quantified by more day-to-day variability in dual-task cost) in older adults with MCI.

The day-to-day variability in the four other dual-task cost measures and all five postural sway measures (from both the single- or dual-task conditions) did not differentiate between cognitive status groups. As mentioned in *Chapter 1*, this is the first study to quantify postural sway frequency in older adults with MCI. Results from this study suggest that postural sway frequency (specifically centroidal frequency) may be an important feature to quantify and track since it was the only measure to differentiate between the intact and MCI groups in this study.

Our findings associated with day-to-day variability were amplified when analyzing across our cognitive status groups, further supporting *Hypothesis IV*. There were linear relationships observed between postural sway variability and cognitive functioning: more variability in time-domain postural sway (indexed by sway distance (*MD*) and area (*AREA*)) and less variability in frequency-domain postural sway (indexed by centroidal sway frequency (*fC*)) was associated with lower cognitive functioning (indexed by lower cognitive global z-scores) (**Figure 4.12**).

Upon visual inspection of **Figure 4.12**, potential outliers are observed in the data. In two out of three of the time-domain plots (*MD* from the single-task condition (**Figure 4.12, A**) and *AREA* from the dual-task condition (**Figure 4.12, D**)), the subject with the lowest cognitive functioning (SubjID = 20, global z-score = -1.44, MCI status) had significantly more variability in time-domain postural sway across the 30-day monitoring period compared to the other 19 subjects. The negative linear relationships observed in **Figure 4.12 A & D** did not hold after removing this subject from the datasets: for *MD* under the single-task condition, $r = -0.17$ and $p = 0.481$; for *AREA* under the dual-task condition, $r = -0.12$ and $p = 0.618$. In sum, the negative linear relationships observed in **Figure 4.12 A & D** were dependent upon the one subject with significantly more postural sway variability in *MD* and *AREA*. We are hesitant to consider this subject as an outlier though since this is the subject with the lowest cognitive functioning (quantified by the lowest cognitive global z-score) and, as discussed in *Chapter 1*, *Section 1.1.8*, increased variability in motor function has been observed during the initial stages of cognitive decline. Because both the

cognitive and postural control systems have been shown to demonstrate an initial period of increased variability during the depreciation of physiologic reserve [90], and because the clinical manifestations of postural decline have been shown to precede that of cognitive decline [91,92] (discussed in greater detail below in *Chapter 5, Section 5.1.3*), the postural profile expressed by this subject may in fact be indicative of his/her true cognitive state. To determine whether or not this subject is actually an outlier, a more extensive study must be conducted with a larger sample population consisting of a more diverse spread of cognitive functioning (*i.e.*, subjects with more severe cognitive impairments must be tested as well to determine whether increased variability in time-domain postural sway is in fact related to lower cognitive functioning).

There were two potential outliers in the one frequency-domain plot in **Figure 4.12** (plot **B**): two cognitively intact subjects (SubjID = 4, global z-score = 0.72; SubjID = 10, global z-score = 0.67) had significantly more variability in frequency-domain postural sway across the 30-day monitoring period compared to the other 18 subjects. The positive linear relationship between cognitive functioning and day-to-day variability in centroidal frequency (*fC*) was still present after removing the potential outliers from the dataset. In fact, the linear trend was stronger after removing these two intact subjects: $r = 0.52$ and $p = 0.026$. These results are promising: the positive linear relationship between cognitive functioning and sway frequency variability remained (and strengthened) after removing two potential outliers, 10% of the complete dataset. If this positive linear relationship holds with a larger, more (cognitively) diverse sample population, the variability in postural sway frequency may prove to be an important feature relating to cognitive functioning and decline in older adults.

4.4.4.iii. Importance of Across-Group Analyses

Our findings would be limited if we were restricted to only between-group analyses. When simply analyzing between the two cognitive status groups, it appeared as though there was no effect of cognitive status on postural sway variability across the 30-day monitoring period. But when utilizing cognitive global z-scores to quantify cognitive functioning as opposed to just MCI status (*i.e.*, spectrum *vs.* binary data), significant linear relationships between postural sway variability and cognitive functioning emerged. Using

a more descriptive measure of cognitive status (cognitive global z-scores *vs.* MCI status/diagnosis) appears to be important when studying the relationship between postural sway, the variability in postural sway across time, and cognition.

4.4.5. Study Limitations

4.4.5.i. MCI Recruitment

The number of OLL/ISAAC subjects classified as "MCI" during their most recent annual neuropsychological evaluation was reduced after implementing the more refined Jak/Bondi MCI diagnostic criteria. With a reduced number of MCI subjects available to us, we had to modify our MCI status definition in order to have enough MCI subjects for this study. Instead of only recruiting subjects classified as "MCI" in their most recent evaluation, we redefined our MCI status definition to include subjects who have had at least one MCI classification in the past, whether or not they were classified as "MCI" at their most recent evaluation. Note that MCI status at a given annual evaluation often transitions into or out of MCI, or even between MCI subtypes (from aMCI to naMCI and vice versa). This variability reflects the challenges associated with accurately classifying cognitive status based on a single evaluation, and in turn motivates the implementation of frequent assessments via longitudinal, in-home monitoring methods. As discussed in *Chapter 1* and again above in this chapter, the variability in a given function (*e.g.*, cognitive performance) increases with age and further during the initial stages of functional decline. Because of this, it is challenging to accurately define cognitive status during the initial stages of cognitive decline (*i.e.*, MCI) via cross-sectional methods.

Our MCI recruitment pool was reduced from our cross-sectional to our longitudinal study due to two main reasons: 1. After implementing the new MCI algorithm, many OLL/ISAAC participants who were originally classified as "MCI" (using the Petersen/Winblad ADNI criteria) were now classified as "intact" (according to the new, more sensitive Jak/Bondi criteria); and, 2. Many of our MCI subjects from the cross-sectional study (classified using the Petersen/Winblad ADNI criteria) were no longer interested in study participation by the time we began recruiting for our longitudinal study. [Studies have shown that as cognitive decline manifests in the older adult, she tends to withdraw from her usual activities of daily living which results in reduced activity levels

and social isolation [152]]. Our limited access to MCI subjects yielded a much smaller sample population than originally planned for, which in turn limited our statistical power. Because of this, we had to restrict the number of statistical analyses performed to preserve what limited statistical power we had. Even though we had domain-specific cognitive z-scores for all 20 subjects, we did not present results from across-group analyses on postural sway and domain-specific cognitive functioning. If we were to report domain-specific functioning (detailed in **Table 4.1**) as possible factors, we would decrease the statistical power of our results six-fold (since there are six different cognitive domains). To assess potential associations between postural sway and domain-specific cognitive functioning, a much larger sample population is needed. [Postural sway and domain-specific cognitive functioning should be a research topic of great interest since domain-specific cognitive functions control posture and domain-specific cognitive dysfunctions have been associated with postural instability (as discussed in *Chapter 3*).]

4.4.5.ii. In-Home Technological Setup

As discussed above in *Section 4.3.2* and reported in **Table 4.4**, a significant amount of missing data was due to technological error (*i.e.*, issues with our in-home technological setup and specifically with the tablet). The Nook tablet played an integral role in our experimental design: it served as the user-interface (running a custom-designed/built application that walked the subjects through the three-minute daily routine); it acquired and stored cognitive performance data input by our subjects; it retrieved CoP-based postural sway data acquired from the Nintendo WBB; and, it automatically transmitted all in-home data to ORCATECH's data repository via a wireless internet connection immediately following data acquisition. Although the Nook tablet possessed all technological specifications required for the uses noted above, it proved to be an unreliable, unsustainable device in the field, becoming increasingly more unreliable/unsustainable as time passed. Detailed below are the main tablet-based issues encountered during the in-home data acquisition period: 1. often, the tablet would spontaneously shut-down and would not reboot properly; 2. occasionally, the tablet would lose connectivity to its wireless internet network and would not reconnect automatically; and, 3. occasionally, the tablet would neither store nor transfer acquired data. These issues appeared to be non-systematic

and therefore could neither be reproduced nor fixed in the laboratory. Given the limited time and resources available to develop and support this in-home technology, we were restricted in our ability to improve the setup. Mainly, we had to focus on maintaining the current system and responding immediately when the tablet malfunctioned in order to preserve/achieve the best dataset possible. [It is important to note that these issues did not occur during the many months of testing prior to data acquisition – these issues occurred after the study began and increased in frequency as time passed.]

In theory, our in-home technological setup was fluid, efficient, and reliable and required a relatively limited amount of effort when integrating it into ORCATECH's current in-home technological platform. In practice, our in-home technological setup proved to be unsustainable, unreliable, and dependent upon full-time monitoring and maintenance. As is, our technology is not suitable for future use. However, if one were to invest a sufficient amount of time and resources into technological development (*i.e.*, more than what was allotted for the purpose of this PhD research) and were willing to dedicate more funds to the purchase of a (higher quality) tablet, we are confident that this in-home technological setup could be successfully developed, implemented and sustained on a large-scale.

4.5. Conclusions

In-home monitoring of daily postural sway proved to be feasible. Objective postural sway measures were reliable when acquired daily for 30 days. Variability measures of postural sway were found to be related to cognitive functioning, with more variability in time-domain postural sway and less variability in frequency-domain postural sway associated with lower cognitive functioning. Analyzing postural sway across cognitive status groups proved to be of significance, suggesting that more descriptive measures of cognitive status (spectrum instead of binary data) are necessary to observe the relationship between postural instability and mild cognitive dysfunction. Our small pilot study conducted on a small time scale motivate the large-scale implementation of this research over a more extended period of time (*e.g.*, months, years, and even decades). Tracking longitudinal changes in postural sway may further our understanding of early-stage motor

decline and its association with cognitive decline and may aid in the early detection of dementia during the preclinical stages.

4.6. Contributions

Contributor	Affiliation(s)	Support Provided
Tamara Hayes (*late PhD advisor*)	ORCATECH, BME Department	-contributed to preliminary study design
Colette Duncan	LAADC	-assisted with subject selection during recruitment
Nora Mattek	ORCATECH, LAADC	-assisted with subject selection during recruitment -provided clinical and neuropsychological data
Jon Yeargers	ORCATECH	-built application for in-home data acquisition -setup in-home data transfer and storage
Nicole Sharma	ORCATECH	-provided technical support during in-home data acquisition -reviewed manuscript before submission
Ben Davis-Bloom	ORCATECH	-provided technical support during in-home data acquisition
Thomas Riley	ORCATECH	-assisted with data-pulls from data repository
Johanna Austin	ORCATECH	-assisted with data-pulls from data repository
Martina Mancini	BD Laboratory	-assisted with data and statistical analyses -contributed to interpretation of results -provided feedback during manuscript preparation
Robert Peterka (*DAC member*)	BME Department	-provided feedback during manuscript preparation -significantly contributed to autocorrelation and autocovariance analysis and interpretation
John Nutt (*DAC member*)	Neurology Department	-provided feedback during manuscript preparation
Jeffrey Kaye (*DAC member*)	ORCATECH, LAADC, BME & Neurology Departments	-contributed to preliminary study design -provided feedback during manuscript preparation
Peter Jacobs (*DAC chair*)	BME Department	-provided guidance in statistical analysis -provided feedback during manuscript preparation
Fay Horak	BD Laboratory,	-contributed to study design

(*PhD advisor*) (*DAC member*)	BME & Neurology Departments	-provided materials for data acquisition -contributed to interpretation of results -provided feedback during manuscript preparation

CHAPTER 5: *Conclusions & Future Direction*

5.1. Conclusions

5.1.1. Summary of PhD Research Findings

In *Chapter 2,* we conducted two validation studies in effort to fully characterize the WBB's CoP measurement error and prepare for the use of the WBB as the sole CoP measurement device in our longitudinal, in-home study (*Chapter 4*). A "gold standard" laboratory-grade force plate was used as our ground truth in both validation studies. In *Chapter 2, Part 1,* we validated the WBB against the force plate using simulated, one-dimensional postural sway signals produced by an inverted pendulum mechanical model. We observed a significant effect of sway amplitude, frequency, and direction on the WBB's measurement error and propose a linear signal adjustment to calibrate the WBB-based CoP (CoP_{WBB}) signals and help reduce CoP measurement error. A version of *Chapter 2, Part 1* was published in the journal *Sensors* on September 29, 2014 (ISSN 1424-8220). In *Chapter 2, Part 2,* we validated the WBB against the force plate using real, two-dimensional postural sway signals produced by healthy young adults. We observed far less CoP measurement error with real, biomedical signals. We proposed an alternative linear signal adjustment based on human postural sway to better fit the CoP_{WBB} signals. We then compared our calibrated CoP_{WBB} signals produced by our two linear calibration procedures to the uncalibrated CoP_{WBB} signals and determined that, despite the effort invested in calibration, the uncalibrated CoP_{WBB} signals contained less measurement error and best represented human postural sway.

In *Chapter 3,* we conducted a cross-sectional study on postural sway, postural dual-task cost, and MCI. We used a body-worn inertial sensor to characterize the associations between cognitive status (intact *vs.* MCI) and postural control in older adults during quiet stance both with (dual-task) and without (single-task) cognitive loading. We found objective Acc-based measures of postural sway to differentiate between cognitive status groups. Both measures of postural sway (extracted from the single-task condition) and postural dual-task costs (extracted from the dual-task conditions) separated the MCI from the intact group. Our cross-sectional findings suggested that quantifying postural sway

under the dual-task condition may help differentiate postural sway in older adults with MCI from cognitively intact older adults.

In *Chapter 4,* we conducted a longitudinal, in-home study of postural sway in MCI within the ORCATECH framework. We integrated a Nintendo WBB and a Nook tablet into ORCATECH's current technological platform to administer cognitive tasks and extract objective measures of postural sway and postural dual-task cost. We monitored both cognitively intact and mildly cognitively impaired older adults daily for 30 days. We used the uncalibrated CoP_{WBB} signals to provide daily estimates of postural control. We determined daily, in-home monitoring of postural sway and cognitive dual-tasking in an older adult population with MCI to be feasible within our cohort. We determined objective postural sway measures to be reliable across 30 days. And, we characterized the association between mean and variability measures of postural sway and cognitive functioning. We found time-domain postural sway variability to be higher and frequency-domain postural sway to be lower in older adults who tested lower in cognitive functioning. Our findings suggested that changes in postural sway variability across time may serve as a sensitive biomarker for early cognitive decline.

5.1.2. Comparison of our Cross-Sectional vs. Longitudinal Studies

5.1.2.i. Different Findings: Postural Sway Dual-Task Costs

Our findings from our cross-sectional study of postural sway, dual-tasking and MCI (*Chapter 3*) were not supported by our longitudinal analysis (in *Chapter 4*). Postural dual-task costs did not consistently separate the MCI group from the intact group longitudinally. Furthermore, postural dual-task costs were positive in value in our cross-sectional study and negative in value in our longitudinal study in both the intact and MCI groups. Cognitive task/response-type and experimental setup may help explain our inconsistent postural dual-task cost results.

Both the cognitive task and task response-type differed between our cross-sectional and longitudinal studies. All three cognitive dual-tasks from our cross-sectional study were designed to tax specific cognitive domains (1. attention; 2. long-term memory; and 3. executive function; **Tables 3.2-3**) and had verbal responses. The cognitive dual-task in our longitudinal study (the word search puzzle) was predominantly a visuospatial and working

memory-based task (as discussed in *Chapter 4*) with a nonverbal response. Because articulation provokes changes in the respiratory pattern and has been shown to increase postural sway (quantified by a positive postural dual-task cost) [75,147], the difference in task response-type alone could help explain the difference between our cross-sectional and longitudinal findings. Studies have shown postural sway to increase with the addition of verbal mental tasks [153,154] and decrease with the addition of nonverbal mental tasks [130,155]. Furthermore, other studies have shown that mental tasks with visuospatial and working memory components (as in the word search puzzle from our longitudinal study) have less of an influence on postural sway compared to other mental tasks (*e.g.*, verbal fluency- and serial subtraction-based tasks, similar to the cognitive dual-tasks from our cross-sectional study) [156]. Therefore, the differences in both cognitive task and task response-type may explain why there were positive postural dual-task costs in our cross-sectional study (quantified by both time- and frequency-domain measures, **Table 3.7**) and negative postural dual-task costs in our longitudinal study (quantified by time-domain frequency measures, **Table 4.7**).

Another contributing factor to our inconsistent results may be the difference in experimental setup between our cross-sectional and longitudinal studies. In our cross-sectional study, our subjects were simply instructed to stand quietly while looking straight ahead during the single-task condition. All objects within our subjects' field of vision were stationary, so the amount of visual fixation/focus was likely less than if there was a moving object within the subjects' field of vision (as in our longitudinal study). During the single-task condition in our longitudinal study, our subjects followed the same procedure – they stood quietly while looking straight ahead. This condition was different though since by looking straight ahead, the subjects were visually fixated on the tablet's screen (since the tablet was mounted on the wall at eye-level height). A progress bar was displayed on the screen to mark time. Because the progress bar tracked real time, and because real time is continuous, there was a constantly-moving object within the subjects' field of vision throughout the entire duration of the single-task condition. Visual tracking is a cognitive task and has been shown to influence postural sway [74], so it is possible that our single-task condition for our longitudinal, in-home study was not in fact a single-task condition.

It is likely that there was less of a change in postural sway between our "single-" and dual-task conditions in our in-home study since our baseline measures were not actually baseline. For future studies, the user-interface must be modified so all objects visible to the subject during the quiet stance condition remain stationary. This flaw in our experimental setup could help explain the differences in our results regarding postural dual-task costs.

In our longitudinal study, the weekly means of postural dual-task cost were negative in value in both the intact and MCI groups (quantified by our time-domain postural sway measures in **Table 4.7, C**), meaning that our time-domain postural sway measures decreased in the presence of the cognitive dual-task. Although we anticipated postural dual-task costs to be positive in our longitudinal study (in line with our cross-sectional results), we were not alarmed by this finding. As detailed in *Chapter 1*, the direction (*i.e.*, positive *vs.* negative) of postural dual-task cost depends on several features, including the cohort characteristics (*i.e.*, healthy young adults *vs.* healthy old adults *vs.* impaired adults (*e.g.*, PD, AD, MCI, cerebellar disorders, *etc.*)), the primary postural task type (*e.g.*, simple quiet stance *vs.* quiet stance with augmented somatosensory, visual, and/or vestibular inputs, as in Jacobi *et al.* [61]), the secondary cognitive task type (*i.e.*, designed to tax global *vs.* domain-specific cognitive functioning), the cognitive task response type (*e.g.*, verbal *vs.* nonverbal), as well as the postural sway outcome measures (*e.g.*, time- *vs.* frequency-domain measures, mean *vs.* variance measures, *etc.*). In sum, because many important factors contribute to the directional effect of a cognitive task on postural sway and because many of these factors differ between our cross-sectional and longitudinal studies, the determination of the exact causes of the inconsistency between our cross-sectional and longitudinal findings on postural dual-task costs would require additional research.

5.1.2.ii. Different Methods: Postural Sway Measurement Device

As discussed in *Chapter 1*, Postural sway was quantified by either the movement of the body's center of pressure (CoP) or the acceleration (Acc) of the body's CoM. Currently, both CoP- and Acc-based measurement devices are used to quantify postural sway. Acc-based measures have been validated against the "gold standard" CoP-based measures (acquired from a laboratory-grade force plate) as accurate and reliable measures of postural sway during quiet stance [58,59]. Because Acc- and CoP-based measures are strongly

correlated, Acc-based measurement devices are often used in place of the force plate because body-worn inertial sensors are practical, inexpensive, unobtrusive and can easily be used in the small clinic and/or home environment [37].

We used a body-worn inertial sensor (an Acc-based measurement device) to quantify postural sway in our cross-sectional study (*Chapter 3*) because we had not yet completed our validation of the Nintendo WBB. After quantifying the WBB's CoP measurement error and determining it an appropriate CoP-based measurement device for the purpose of this PhD research (detailed in our two validation studies, *Chapter 2*), we used the WBB to quantify postural sway in our longitudinal study (*Chapter 4*). Postural sway feature selection for our longitudinal study was driven by our desire to compare our results from *Chapter 4* to results from *Chapter 3*. In *Chapter 3*, we derived total sway path length, mean sway velocity, normalized sway jerk, and centroidal sway frequency from the Acc-based postural sway signals. In *Chapter 4*, we also derived mean sway velocity and centroidal sway frequency from the CoP-based postural sway signals. Total sway path length however was not included in *Chapter 4* because the CoP-based derivation for total sway path length is simply a function of mean sway velocity and the duration of the trial [35]. Mean sway distance was used instead and served as the distance measure in *Chapter 4*. Normalized sway jerk also was not included in *Chapter 4* because jerk (the first derivative of acceleration, the third derivative of position) lacks precision when derived from CoP-based signals. Sway area and sway frequency dispersion were included in *Chapter 4* for reasons detailed in Section 4.2.5.ii.

In summary, three different postural sway measures (sway distance, velocity, and frequency) can be compared between *Chapter 3* and *Chapter 4*. So although our postural sway signal acquisition methods differ between our cross-sectional and longitudinal studies, we can still compare our results and do not attribute our inconsistent findings to the change in postural sway measurement device type (CoP *vs.* Acc).

5.1.2.iii. Significant Postural Sway Measures

In our cross-sectional study (*Chapter 3*), normalized sway jerk and centroidal sway frequency were higher in the MCI group compared to the intact group during the single-task condition. Furthermore, the postural dual-task costs in sway path length, normalized

sway jerk, and centroidal sway frequency were lower in the MCI group compared to the intact group during the dual-task conditions. There was no significant difference in mean sway velocity between the intact and MCI groups during both the single- and dual-task conditions.

In our longitudinal study (*Chapter 4*), the day-to-day variability in centroidal sway frequency cost (*i.e.*, the postural dual-task cost in centroidal sway frequency) was higher in the MCI group compared to the intact group. Furthermore, more day-to-day variability in mean sway distance and sway area and less day-to-day variability in centroidal sway frequency was related to lower cognitive functioning (indexed by cognitive global z-scores). There was no significant difference in monthly mean postural sway measures between the intact and MCI groups and there were no linear relationships between mean postural sway measures and cognitive functioning during both the single- and dual-task conditions. In sum, variability-based postural sway measures appear to be more significant than mean-based postural sway measures when studying the relationship between postural sway and cognitive status/functioning across time within our small sample of 20 older adults.

As discussed above in Section 5.1.2.i, the significance of postural dual-task costs (in both the time- and frequency-domain) and MCI in our cross-sectional study (*Chapter 3*) did not hold longitudinally (*Chapter 4*). Although our results from *Chapter 3* were not confirmed in *Chapter 4*, examining both time- and frequency-domain sway measures proved to be significant in both studies. Specifically, sway distance (either sway path length (*Chapter 3*) or mean sway distance (*Chapter 4*)), sway area (*Chapter 4*), and centroidal sway frequency (both *Chapters 3 & 4*) may be the best metrics to use when studying the potential relationship between postural sway (and postural sway variability) and cognitive status/functioning in the older old (*i.e.*, 80's – 90's) adult population.

It is important to note that our longitudinal study in *Chapter 4* served as an exploratory research pilot study – we had a large number of hypotheses, we ran many statistical models, and we had a small sample population. Because of this, we did not adjust our *p*-values when determining statistical significance for our postural sway measures. In turn, the conclusions drawn from our longitudinal results in *Chapter 4* should be received with

caution. Further research with a larger sample population is necessary before strong conclusions can be drawn.

If we were to account for multiple comparisons with a Bonferroni correction in *Chapter 4*, we would have had to divide our *p*-value of 0.05 by 15 [5 postural sway measures (mean sway distance, mean sway velocity, mean sway area, centroidal sway frequency, and frequency dispersion) × 3 measure types (single-task condition, dual-task condition, and dual-task cost)], resulting in a significant *p*-value of < 0.003. We ran power calculations to determine the sample sizes necessary to achieve statistical significance with adjusted *p*-values: in *Chapter 4*, Section 4.3.6.i (our between-group analysis, **Table 4.9**), a sample population of at least 54 (27 in both the intact and MCI groups) would be necessary to observe the group difference in postural dual-task cost illustrated in **Figure 4.11**; in *Chapter 4*, Section 4.3.6.ii (our across-group analysis, **Table 4.10**), a sample population of at least 56 would be necessary to observe the relationships between postural sway variability and cognitive functioning illustrated in **Figure 4.12** (a balanced sample of intact and MCI subjects would be recommended to emulate this cohort). All power calculations were performed in G*Power 3.1 [157,158] with a *p*-value set to 0.003 and power set to 80%. In sum, a sample population of at least 56 would be necessary to achieve statistically significant results with Bonferroni-corrected *p*-values.

5.1.2.iv. Is the Cognitive Load Necessary?

Since we found the day-to-day variability in postural sway to be associated with cognitive functioning under both the single- and dual-task condition, and because there was no effect of cognitive status on postural dual-task cost in *Chapter 4* (unlike our cross-sectional findings in *Chapter 3*), an added cognitive load may not be necessary to differentiate between cognitively intact and mildly cognitively impaired older adults. Removing the cognitive dual-task would simplify the experimental design and in turn reduce the amount of time and resources necessary for in-home monitoring of postural sway. But before removing the cognitive dual-task entirely, one must first determine whether or not there was a real difference (quantified by an effect on postural sway) between our single-task condition in our cross-sectional study (simple quiet stance with no added cognitive distraction; *i.e.*, actual baseline measure of postural sway) and that in our

longitudinal study (quiet stance with a potential added cognitive distraction of visual tracking as the progress bar crossed the screen of the tablet; *i.e.*, may not actually be a baseline measure of postural sway). If the "single"-task condition in our longitudinal study is shown to influence postural sway (compared to the true baseline measure in our cross-sectional study), then our longitudinal findings would actually be dependent upon cognitive dual-tasking. Additional research is necessary before we can determine whether or not a cognitive dual-task is necessary to differentiate between cognitive status groups based on daily postural sway.

5.1.3. Comparison of our Longitudinal Findings to the Longitudinal Patterns of other Motor Measures within the ORCATECH Cohort

The variability in time-domain postural sway was higher in older adults who tested lower in cognitive functioning when analyzing across cognitive status groups. These findings are consistent with the literature (discussed previously in *Chapters 1 & 4*) and couple well with findings from other ORCATECH studies.

Dodge *et al.* found in-home gait speeds and variability trajectories to be associated with MCI. Within the framework of ORCATECH's in-home technological platform, we have continuously monitored gait speed for years (the assessment of gait speed and its data validation process are described elsewhere in [159,160]). Dodge and colleagues analyzed weekly means of in-home gait speeds in both cognitively intact and mildly cognitively impaired older adults. The weekly means and week-to-week variability in gait speed was assessed over the course of 182 weeks, or 3.5 years. Latent class trajectory models were used to compare the trajectories of gait speed means and variability between cognitive status groups. Dodge *et al.* found distinct time-course trajectories to be associated with both early and late-stage MCI. They found slower weekly mean gait speeds to be associated with MCI status. They also found higher and lower gait speed variability associated with early and late MCI disease state, respectively. Over the course of the 182-week monitoring period, the early-stage MCI group experienced an increase in gait speed variability, followed elevated variability for some time, followed by an accelerated decrease in variability (a pattern similar to the model shown in **Figure 1.4** in *Chapter 1*). The late-stage MCI group sustained less gait speed variability over the course of 182 weeks

(compared to both the intact and early-stage MCI group). In sum, the MCI groups had distinct time-course trajectories when assessing both the mean and variability of gait speed (a specified motor function measure) on a relatively large time scale [91].

Buracchio *et al.* conducted a similar analysis on an even larger time scale: up to 20 years. The rate of change in both gait and finger-tapping speed (two motor function measures) were significantly different between subjects who developed MCI (converters) and those who did not (nonconverters). Motor decline as indexed by tapping speed accelerated after the clinical onset of MCI. Motor decline as indexed by gait speed accelerated up to 12 years before the clinical onset of MCI and in turn predicted MCI conversion. Buracchio and colleagues concluded that "longitudinal changes in motor function may be useful in the early detection of dementia during preclinical stages when the utility of disease-modifying therapies would be greatest" [92].

Because our longitudinal analysis of postural sway (another motor function measure) was performed on a much smaller time scale, we did not expect the "longitudinal" changes in motor function to be indicative of cognitive functioning. We did, however, predict means and/or variability in postural sway to relate to cognitive functioning. Over the course of our short 30-day, or 4-week, monitoring period we found both mean and variability measures of postural sway to be higher in older adults who tested lower in cognitive functioning. Our findings suggest that monitoring the longitudinal patterns of postural sway over the course of a more extended period of time (*e.g.*, months, years, and even decades) may be of great importance.

Objective measures of postural sway are more descriptive than mean gait speed (and other common clinical motor measures such as finger tapping speed) and may enable a more sophisticated analysis of motor (and specifically, postural) control/decline during the preclinical stages of dementia. As discussed in *Chapter 1*, postural control is a complex motor skill derived from the integration of several neural components including cognitive processing [2]. Maintaining postural stability is a higher-level cognitive process that relies on an intact cerebellum and cortical control [116,161,162]. The interrelationship between cognitive deficits and postural instabilities have been attributed to specific brain networks such as the prefrontoparietal and cingulate areas [163,164]. So by fully characterizing

postural sway (*i.e.*, static postural control) via quantitative time- and frequency-domain measures, one may be able to make stronger inferences about cognitive status and mobility (dis)ability [3] compared to simply acquiring a mean measure such as gait speed since different motor-related brain regions may control distinct aspects of movement (*i.e.* speed *vs.* balance) [164-166]. Tracking longitudinal changes in postural sway may further our understanding of early-stage motor decline and its association with cognitive decline.

5.2. Future Direction

5.2.1. Large-Scale Implementation

As detailed in *Chapter 4*, Section 4.4.5.ii, our current in-home technological setup is unreliable, unsustainable, and not yet suitable for future use. All of our technological issues were attributed to the Nook tablet, a relatively inexpensive, low quality device. If one were to invest a sufficient amount of time and resources into technological development (*i.e.*, more than what was allotted for the purpose of this PhD research) and were willing to dedicate more funds to the purchase of a (higher quality) tablet, we are confident that this in-home technological setup could be successfully developed, implemented and sustained on a large-scale.

As eloquently stated by Hayes *et al.* [167], large-scale research deployment of in-home monitoring is an impressive feat with great potential to facilitate the study of both healthy aging and disease-related processes. This PhD research determined longitudinal monitoring of postural sway feasible within the in-home environment and laid the foundation for large-scale implementation. Since we found the day-to-day variability in postural sway to be associated with cognitive functioning under both the single- and dual-task condition, and because there was not a significant effect of cognitive status on postural dual-task cost, an added cognitive load may not be necessary to differentiate between cognitively intact and mildly cognitively impaired older adults. Simply integrating a WBB into ORCATECH's current technological platform would enable daily extraction of meaningful postural sway measures. Keeping the cognitive dual-task feature may be of interest though since studies have shown that dual-task training reduces the impact of cognitive distractions on postural sway in older adults [94], and substantial gains after dual-

task training are sustained even with new task combinations involving new stimuli [95]: these findings suggest that dual-task skills can be substantially improved in older adults and that cognitive plasticity in attentional control is attainable even in old age [95]. So by simply installing our system (after making the necessary technological improvements detailed above in Section 5.1.2.vi), we could easily implement a dual-task training program to help improve and/or sustain dual-task skills in older adults, which in turn may directly aid in fall prevention. Relatively little time, effort, and resources would be required to implement this system in all homes outfitted with ORCATECH equipment and supported by ORCATECH researchers and staff. A significant amount of gain could be acquired with little additional work and financial support.

5.2.2. Conclusions

Tracking longitudinal changes in postural sway may further our understanding of early-stage postural decline and its association with cognitive decline and may aid in the early detection of dementia during the preclinical stages. Early detection may also yield the development and implementation of therapeutic interventions [49,96]. Timely intervention is integral because treatment during the initial stages of disease state (*e.g.*, MCI) may prevent subsequent neurodegeneration and progressive motor and/or cognitive decline (*e.g.*, progression to dementia).

REFERENCES

1. Buracchio, T.J.; Mattek, N.C.; Dodge, H.H.; Hayes, T.L.; Pavel, M.; Howieson, D.B.; Kaye, J.A. Executive function predicts risk of falls in older adults without balance impairment. *BMC Geriatr* **2011**, *11*, 74.

2. Horak, F.B. Postural orientation and equilibrium: What do we need to know about neural control of balance to prevent falls? *Age Ageing* **2006**, *35 Suppl 2*, 7-11.

3. Segev-Jacubovski, O.; Herman, T.; Yogev-Seligmann, G.; Mirelman, A.; Giladi, N.; Hausdorff, J.M. The interplay between gait, falls and cognition: Can cognitive therapy reduce fall risk? *Expert Rev Neurother* **2011**, *11*, 1057-1075.

4. Tinetti, M.E.; Speechley, M.; Ginter, S.F. Risk factors for falls among elderly persons living in the community. *N Engl J Med* **1988**, *319*, 1701-1707.

5. Montero-Odasso, M.; Wells, J.L.; Borrie, M.J.; Speechley, M. Can cognitive enhancers reduce the risk of falls in older people with mild cognitive impairment? A protocol for a randomised controlled double blind trial. *BMC Neurol* **2009**, *9*, 42.

6. Alexander, B.H.; Rivara, F.P.; Wolf, M.E. The cost and frequency of hospitalization for fall-related injuries in older adults. *Am J Public Health* **1992**, *82*, 1020-1023.

7. Buchman, A.S.; Bennett, D.A. Loss of motor function in preclinical alzheimer's disease. *Expert Rev Neurother* **2011**, *11*, 665-676.

8. Aggarwal, N.T.; Wilson, R.S.; Beck, T.L.; Bienias, J.L.; Bennett, D.A. Motor dysfunction in mild cognitive impairment and the risk of incident alzheimer disease. *Arch Neurol* **2006**, *63*, 1763-1769.

9. Hayes, T.L.; Abendroth, F.; Adami, A.; Pavel, M.; Zitzelberger, T.A.; Kaye, J.A. Unobtrusive assessment of activity patterns associated with mild cognitive impairment. *Alzheimers Dement* **2008**, *4*, 395-405.

10. Buchner, D.M.; Larson, E.B. Transfer bias and the association of cognitive impairment with falls. *Journal of general internal medicine* **1988**, *3*, 254-259.

11. Gleason, C.E.; Gangnon, R.E.; Fischer, B.L.; Mahoney, J.E. Increased risk for falling associated with subtle cognitive impairment: Secondary analysis of a randomized clinical trial. *Dement Geriatr Cogn Disord* **2009**, *27*, 557-563.

12. Liu-Ambrose, T.Y.; Ashe, M.C.; Graf, P.; Beattie, B.L.; Khan, K.M. Increased risk of falling in older community-dwelling women with mild cognitive impairment. *Phys Ther* **2008**, *88*, 1482-1491.

13. Ryan, J.J.; McCloy, C.; Rundquist, P.; Srinivasan, V.; Laird, R. Fall risk assessment among older adults with mild alzheimer disease. *J Geriatr Phys Ther* **2011**, *34*, 19-27.

14. Delbaere, K.; Kochan, N.A.; Close, J.C.; Menant, J.C.; Sturnieks, D.L.; Brodaty, H.; Sachdev, P.S.; Lord, S.R. Mild cognitive impairment as a predictor of falls in community-dwelling older people. *Am J Geriatr Psychiatry* **2012**, *20*, 845-853.

15. Harlein, J.; Dassen, T.; Halfens, R.J.; Heinze, C. Fall risk factors in older people with dementia or cognitive impairment: A systematic review. *J Adv Nurs* **2009**, *65*, 922-933.

16. Hauer, K.; Pfisterer, M.; Weber, C.; Wezler, N.; Kliegel, M.; Oster, P. Cognitive impairment decreases postural control during dual tasks in geriatric patients with a history of severe falls. *J Am Geriatr Soc* **2003**, *51*, 1638-1644.

17. Allan, L.M.; Ballard, C.G.; Burn, D.J.; Kenny, R.A. Prevalence and severity of gait disorders in alzheimer's and non-alzheimer's dementias. *J Am Geriatr Soc* **2005**, *53*, 1681-1687.

18. Verghese, J.; Lipton, R.B.; Hall, C.B.; Kuslansky, G.; Katz, M.J.; Buschke, H. Abnormality of gait as a predictor of non-alzheimer's dementia. *N Engl J Med* **2002**, *347*, 1761-1768.

19. Camicioli, R.; Bouchard, T.; Licis, L. Dual-tasks and walking fast: Relationship to extra-pyramidal signs in advanced alzheimer disease. *J Neurol Sci* **2006**, *248*, 205-209.

20. Camicioli, R.; Wang, Y.; Powell, C.; Mitnitski, A.; Rockwood, K. Gait and posture impairment, parkinsonism and cognitive decline in older people. *J Neural Transm* **2007**, *114*, 1355-1361.

21. Montero-Odasso, M.; Bergman, H.; Phillips, N.A.; Wong, C.H.; Sourial, N.; Chertkow, H. Dual-tasking and gait in people with mild cognitive impairment. The effect of working memory. *BMC Geriatr* **2009**, *9*, 41.

22. Lopez, O.L.; Jagust, W.J.; DeKosky, S.T.; Becker, J.T.; Fitzpatrick, A.; Dulberg, C.; Breitner, J.; Lyketsos, C.; Jones, B.; Kawas, C., *et al.* Prevalence and classification of mild cognitive impairment in the cardiovascular health study cognition study: Part 1. *Arch Neurol* **2003**, *60*, 1385-1389.

23. Petersen, R.C.; Doody, R.; Kurz, A.; Mohs, R.C.; Morris, J.C.; Rabins, P.V.; Ritchie, K.; Rossor, M.; Thal, L.; Winblad, B. Current concepts in mild cognitive impairment. *Arch Neurol* **2001**, *58*, 1985-1992.

24. Petersen, R.C.; Morris, J.C. Mild cognitive impairment as a clinical entity and treatment target. *Arch Neurol* **2005**, *62*, 1160-1163; discussion 1167.

25. Petersen, R.C. Mild cognitive impairment as a diagnostic entity. *J Intern Med* **2004**, *256*, 183-194.

26. Verghese, J.; Robbins, M.; Holtzer, R.; Zimmerman, M.; Wang, C.; Xue, X.; Lipton, R.B. Gait dysfunction in mild cognitive impairment syndromes. *J Am Geriatr Soc* **2008**, *56*, 1244-1251.

27. Shin, B.M.; Han, S.J.; Jung, J.H.; Kim, J.E.; Fregni, F. Effect of mild cognitive impairment on balance. *J Neurol Sci* **2009**, *305*, 121-125.

28. Franssen, E.H.; Souren, L.E.; Torossian, C.L.; Reisberg, B. Equilibrium and limb coordination in mild cognitive impairment and mild alzheimer's disease. *J Am Geriatr Soc* **1999**, *47*, 463-469.

29. Folstein, M.F.; Folstein, S.E.; McHugh, P.R. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res* **1975**, *12*, 189-198.

30. Nasreddine, Z.S.; Phillips, N.A.; Bedirian, V.; Charbonneau, S.; Whitehead, V.; Collin, I.; Cummings, J.L.; Chertkow, H. The montreal cognitive assessment, moca: A brief screening tool for mild cognitive impairment. *J Am Geriatr Soc* **2005**, *53*, 695-699.

31. Jak, A.J.; Bondi, M.W.; Delano-Wood, L.; Wierenga, C.; Corey-Bloom, J.; Salmon, D.P.; Delis, D.C. Quantification of five neuropsychological approaches to defining mild cognitive impairment. *Am J Geriatr Psychiatry* **2009**, *17*, 368-375.

32. Tinetti, M.E. Performance-oriented assessment of mobility problems in elderly patients. *J Am Geriatr Soc* **1986**, *34*, 119-126.

33. Berg, K.O.; Wood-Dauphinee, S.L.; Williams, J.I.; Maki, B. Measuring balance in the elderly: Validation of an instrument. *Canadian journal of public health = Revue canadienne de sante publique* **1992**, *83 Suppl 2*, S7-11.

34. Hay, L.; Bard, C.; Fleury, M.; Teasdale, N. Availability of visual and proprioceptive afferent messages and postural control in elderly adults. *Exp Brain Res* **1996**, *108*, 129-139.

35. Prieto, T.E.; Myklebust, J.B.; Hoffmann, R.G.; Lovett, E.G.; Myklebust, B.M. Measures of postural steadiness: Differences between healthy young and elderly adults. *IEEE Trans Biomed Eng* **1996**, *43*, 956-966.

36. Pajala, S.; Era, P.; Koskenvuo, M.; Kaprio, J.; Tormakangas, T.; Rantanen, T. Force platform balance measures as predictors of indoor and outdoor falls in community-dwelling women aged 63-76 years. *J Gerontol A Biol Sci Med Sci* **2008**, *63*, 171-178.

37. Mancini, M.; Horak, F.B.; Zampieri, C.; Carlson-Kuhta, P.; Nutt, J.; Chiari, L. Trunk accelerometry reveals postural instability in untreated parkinson's disease. *Parkinsonism Relat Disord* **2011**.

38. Dean, J.C.; Alexander, N.B.; Kuo, A.D. The effect of lateral stabilization on walking in young and old adults. *IEEE Trans Biomed Eng* **2007**, *54*, 1919-1926.

39. Maki, B.E.; McIlroy, W.E. Postural control in the older adult. *Clin Geriatr Med* **1996**, *12*, 635-658.

40. Maki, B.E.; Holliday, P.J.; Topper, A.K. A prospective study of postural balance and risk of falling in an ambulatory and independent elderly population. *J Gerontol* **1994**, *49*, M72-84.

41. Woollacott, M.H. Systems contributing to balance disorders in older adults. *J Gerontol A Biol Sci Med Sci* **2000**, *55*, M424-428.

42. Melzer, I.; Benjuya, N.; Kaplanski, J. Postural stability in the elderly: A comparison between fallers and non-fallers. *Age Ageing* **2004**, *33*, 602-607.

43. Norris, J.A.; Marsh, A.P.; Smith, I.J.; Kohut, R.I.; Miller, M.E. Ability of static and statistical mechanics posturographic measures to distinguish between age and fall risk. *J Biomech* **2005**, *38*, 1263-1272.

44. Leandri, M.; Cammisuli, S.; Cammarata, S.; Baratto, L.; Campbell, J.; Simonini, M.; Tabaton, M. Balance features in alzheimer's disease and amnestic mild cognitive impairment. *J Alzheimers Dis* **2009**, *16*, 113-120.

45. Leandri, M.; Campbell, J.; Molfetta, L.; Barbera, C.; Tabaton, M. Relationship between balance and cognitive performance in older people. *J Alzheimers Dis* **2015**, *45*, 705-707.

46. Deschamps, T.; Beauchet, O.; Annweiler, C.; Cornu, C.; Mignardot, J.B. Postural control and cognitive decline in older adults: Position versus velocity implicit motor strategy. *Gait Posture* **2014**, *39*, 628-630.

47. Jeon, S.Y.; Han, S.J.; Jeong, J.H.; Fregni, F. Effect of exercise on balance in persons with mild cognitive impairment. *NeuroRehabilitation* **2014**, *35*, 271-278.

48. Mignardot, J.B.; Beauchet, O.; Annweiler, C.; Cornu, C.; Deschamps, T. Postural sway, falls, and cognitive status: A cross-sectional study among older adults. *J Alzheimers Dis* **2014**, *41*, 431-439.

49. Kluger, A.; Gianutsos, J.G.; Golomb, J.; Ferris, S.H.; George, A.E.; Franssen, E.; Reisberg, B. Patterns of motor impairement in normal aging, mild cognitive decline, and early alzheimer's disease. *J Gerontol B Psychol Sci Soc Sci* **1997**, *52*, P28-39.

50. Mancini, M.; Horak, F.B. The relevance of clinical balance assessment tools to differentiate balance deficits. *Eur J Phys Rehabil Med* **2010**, *46*, 239-248.

51. Moe-Nilssen, R.; Nordin, E.; Lundin-Olsson, L. Criteria for evaluation of measurement properties of clinical balance measures for use in fall prevention studies. *J Eval Clin Pract* **2008**, *14*, 236-240.

52. Chastan, N.; Debono, B.; Maltete, D.; Weber, J. Discordance between measured postural instability and absence of clinical symptoms in parkinson's disease patients in the early stages of the disease. *Mov Disord* **2008**, *23*, 366-372.

53. Beuter, A.; Hernandez, R.; Rigal, R.; Modolo, J.; Blanchet, P.J. Postural sway and effect of levodopa in early parkinson's disease. *Can J Neurol Sci* **2008**, *35*, 65-68.

54. Mancini, M.; Horak, F.B.; Zampieri, C.; Carlson-Kuhta, P.; Nutt, J.; Chiari, L. Trunk accelerometry reveals postural instability in untreated parkinson's disease. *Parkinsonism Relat Disord* **under revision**.

55. Swanenburg, J.; de Bruin, E.D.; Uebelhart, D.; Mulder, T. Falls prediction in elderly people: A 1-year prospective study. *Gait Posture* **2010**, *31*, 317-321.

56. Keus, S.H.; Nieuwboer, A.; Bloem, B.R.; Borm, G.F.; Munneke, M. Clinimetric analyses of the modified parkinson activity scale. *Parkinsonism Relat Disord* **2009**, *15*, 263-269.

57. Mayagoitia, R.E.; Lotters, J.C.; Veltink, P.H.; Hermens, H. Standing balance evaluation using a triaxial accelerometer. *Gait Posture* **2002**, *16*, 55-59.

58. Moe-Nilssen, R.; Helbostad, J.L. Trunk accelerometry as a measure of balance control during quiet standing. *Gait Posture* **2002**, *16*, 60-68.

59. Moe-Nilssen, R. Test-retest reliability of trunk accelerometry during standing and walking. *Arch Phys Med Rehabil* **1998**, *79*, 1377-1385.

60. Hogan, N.; Sternad, D. Sensitivity of smoothness measures to movement duration, amplitude, and arrests. *J Mot Behav* **2009**, *41*, 529-534.

61. Jacobi, H.; Alfes, J.; Minnerop, M.; Konczak, J.; Klockgether, T.; Timmann, D. Dual task effect on postural control in patients with degenerative cerebellar disorders. *Cerebellum & ataxias* **2015**, *2*, 6.

62. Kelly, V.E.; Johnson, C.O.; McGough, E.L.; Shumway-Cook, A.; Horak, F.B.; Chung, K.A.; Espay, A.J.; Revilla, F.J.; Devoto, J.; Wood-Siverio, C., *et al.* Association of cognitive domains with postural instability/gait disturbance in parkinson's disease. *Parkinsonism Relat Disord* **2015**, *21*, 692-697.

63. Mancini, M.; Salarian, A.; Carlson-Kuhta, P.; Zampieri, C.; King, L.; Chiari, L.; Horak, F.B. Isway: A sensitive, valid and reliable measure of postural control. *J Neuroeng Rehabil* **2012**, *9*, 59.

64. Park, J.H.; Kang, Y.J.; Horak, F.B. What is wrong with balance in parkinson's disease? *Journal of movement disorders* **2015**, *8*, 109-114.

65. Woollacott, M.; Shumway-Cook, A. Attention and the control of posture and gait: A review of an emerging area of research. *Gait Posture* **2002**, *16*, 1-14.

66. Horak, F.B.; Dimitrova, D.; Nutt, J.G. Direction-specific postural instability in subjects with parkinson's disease. *Experimental neurology* **2005**, *193*, 504-521.

67. Horak, F.B.; Nutt, J.G.; Nashner, L.M. Postural inflexibility in parkinsonian subjects. *J Neurol Sci* **1992**, *111*, 46-58.

68. Mancini, M.; Carlson-Kuhta, P.; Zampieri, C.; Nutt, J.G.; Chiari, L.; Horak, F.B. Postural sway as a marker of progression in parkinson's disease: A pilot longitudinal study. *Gait Posture* **2012**, *36*, 471-476.

69. Rocchi, L.; Chiari, L.; Cappello, A.; Horak, F.B. Identification of distinct characteristics of postural sway in parkinson's disease: A feature selection procedure based on principal component analysis. *Neurosci Lett* **2006**, *394*, 140-145.

70. Gago, M.F.; Fernandes, V.; Ferreira, J.; Silva, H.; Rocha, L.; Bicho, E.; Sousa, N. Postural stability analysis with inertial measurement units in alzheimer's disease. *Dementia and geriatric cognitive disorders extra* **2014**, *4*, 22-30.

71. Nakamura, T.; Meguro, K.; Yamazaki, H.; Okuzumi, H.; Tanaka, A.; Horikawa, A.; Yamaguchi, K.; Katsuyama, N.; Nakano, M.; Arai, H., *et al.* Postural and gait disturbance correlated with decreased frontal cerebral blood flow in alzheimer disease. *Alzheimer Dis Assoc Disord* **1997**, *11*, 132-139.

72. Chong, R.K.; Horak, F.B.; Frank, J.; Kaye, J. Sensory organization for balance: Specific deficits in alzheimer's but not in parkinson's disease. *J Gerontol A Biol Sci Med Sci* **1999**, *54*, M122-128.

73. Sidorovich, E.; Likhachev, S.; Klishevskaya, N.; Dimkovskaya, M.; Naumovskaya, N.; Bogdanova, L. Subclinical postural instability detected by stabiloplatform examination in the patients with vascular mild cognitive impairment--part 1. *Wiadomosci lekarskie* **2014**, *67*, 64-70.

74. Huxhold, O.; Li, S.C.; Schmiedek, F.; Lindenberger, U. Dual-tasking postural control: Aging and the effects of cognitive demand in conjunction with focus of attention. *Brain research bulletin* **2006**, *69*, 294-305.

75. Dault, M.C.; Yardley, L.; Frank, J.S. Does articulation contribute to modifications of postural control during dual-task paradigms? *Brain research. Cognitive brain research* **2003**, *16*, 434-440.

76. Pellecchia, G.L. Postural sway increases with attentional demands of concurrent cognitive task. *Gait Posture* **2003**, *18*, 29-34.

77. Granacher, U.; Bridenbaugh, S.A.; Muehlbauer, T.; Wehrle, A.; Kressig, R.W. Age-related effects on postural control under multi-task conditions. *Gerontology* **2010**, *57*, 247-255.

78. Shumway-Cook, A.; Woollacott, M. Attentional demands and postural control: The effect of sensory context. *J Gerontol A Biol Sci Med Sci* **2000**, *55*, M10-16.

79. Holtzer, R.; Stern, Y.; Rakitin, B.C. Predicting age-related dual-task effects with individual differences on neuropsychological tests. *Neuropsychology* **2005**, *19*, 18-27.

80. Pichierri, G.; Wolf, P.; Murer, K.; de Bruin, E.D. Cognitive and cognitive-motor interventions affecting physical functioning: A systematic review. *BMC Geriatr* **2011**, *11*, 29.

81. Silsupadol, P.; Shumway-Cook, A.; Lugade, V.; van Donkelaar, P.; Chou, L.S.; Mayr, U.; Woollacott, M.H. Effects of single-task versus dual-task training on balance performance in older adults: A double-blind, randomized controlled trial. *Arch Phys Med Rehabil* **2009**, *90*, 381-387.

82. Kang, H.G.; Lipsitz, L.A. Stiffness control of balance during quiet standing and dual task in older adults: The mobilize boston study. *J Neurophysiol* **2010**, *104*, 3510-3517.

83. Herath, P.; Klingberg, T.; Young, J.; Amunts, K.; Roland, P. Neural correlates of dual task interference can be dissociated from those of divided attention: An fmri study. *Cereb Cortex* **2001**, *11*, 796-805.

84. Melzer, I.; Benjuya, N.; Kaplanski, J. Age-related changes of postural control: Effect of cognitive tasks. *Gerontology* **2001**, *47*, 189-194.

85. van Iersel, M.B.; Ribbers, H.; Munneke, M.; Borm, G.F.; Rikkert, M.G. The effect of cognitive dual tasks on balance during walking in physically fit elderly people. *Arch Phys Med Rehabil* **2007**, *88*, 187-191.

86. Kaye, J.A.; Maxwell, S.A.; Mattek, N.; Hayes, T.L.; Dodge, H.; Pavel, M.; Jimison, H.B.; Wild, K.; Boise, L.; Zitzelberger, T.A. Intelligent systems for assessing aging changes: Home-based, unobtrusive, and continuous assessment of aging. *J Gerontol B Psychol Sci Soc Sci* **2011**, *66 Suppl 1*, i180-190.

87. Li, S.; Aggen, S.H.; Nesselroade, J.R.; Baltes, P.B. Short-term fluctuations in elderly people's sensorimotor functioning predict text and spatial memory performance: The macarthur successful aging studies. *Gerontology* **2001**, *47*, 100-116.

88. Pickering, T.G.; Gerin, W.; Schwartz, A.R. What is the white-coat effect and how should it be measured? *Blood pressure monitoring* **2002**, *7*, 293-300.

89. Wang, L.; Larson, E.B.; Bowen, J.D.; van Belle, G. Performance-based physical function and future dementia in older people. *Arch Intern Med* **2006**, *166*, 1115-1120.

90. MacDonald, S.W.; Nyberg, L.; Backman, L. Intra-individual variability in behavior: Links to brain structure, neurotransmission and neuronal activity. *Trends Neurosci* **2006**, *29*, 474-480.

91. Dodge, H.H.; Mattek, N.; Austin, D.; Hayes, T.L. In-home walking speeds and variability trajectories associated with mild cognitive impairment. *PMC Journal in Process* **2012**.

92. Buracchio, T.; Dodge, H.H.; Howieson, D.; Wasserman, D.; Kaye, J. The trajectory of gait speed preceding mild cognitive impairment. *Arch Neurol* **2010**, *67*, 980-986.

93. SMARTRISK.CA. The economic burden of injury in canada.

94. Pellecchia, G.L. Dual-task training reduces impact of cognitive task on postural sway. *J Mot Behav* **2005**, *37*, 239-246.

95. Bherer, L.; Kramer, A.F.; Peterson, M.S.; Colcombe, S.; Erickson, K.; Becic, E. Transfer effects in task-set cost and dual-task cost after dual-task training in older and younger adults: Further evidence for cognitive plasticity in attentional control in late adulthood. *Exp Aging Res* **2008**, *34*, 188-219.

96. Christofoletti, G.; Oliani, M.M.; Gobbi, S.; Stella, F.; Bucken Gobbi, L.T.; Renato Canineu, P. A controlled clinical trial on the effects of motor intervention on balance and cognition in institutionalized elderly patients with dementia. *Clin Rehabil* **2008**, *22*, 618-626.

97. Maki, B.E.; Holliday, P.J.; Fernie, G.R. Aging and postural control. A comparison of spontaneous- and induced-sway balance tests. *J Am Geriatr Soc* **1990**, *38*, 1-9.

98. Clark, R.A.; Bryant, A.L.; Pua, Y.; McCrory, P.; Bennell, K.; Hunt, M. Validity and reliability of the nintendo wii balance board for assessment of standing balance. *Gait Posture* **2010**, *31*, 307-310.

99. Huurnink, A.; Fransz, D.P.; Kingma, I.; van Dieen, J.H. Comparison of a laboratory grade force platform with a nintendo wii balance board on measurement of postural control in single-leg stance balance tasks. *J Biomech* **2013**, *46*, 1392-1395.

100. Young, W.; Ferguson, S.; Brault, S.; Craig, C. Assessing and training standing balance in older adults: A novel approach using the 'nintendo wii' balance board. *Gait Posture* **2010**, *33*, 303-305.

101. Jorgensen, M.G.; Laessoe, U.; Hendriksen, C.; Nielsen, O.B.; Aagaard, P. Intra-rater reproducibility and validity of nintendo wii balance testing in community-dwelling older adults. *J Aging Phys Act* **2013**.

102. Holmes, J.D.; Jenkins, M.E.; Johnson, A.M.; Hunt, M.A.; Clark, R.A. Validity of the nintendo wii(r) balance board for the assessment of standing balance in parkinson's disease. *Clin Rehabil* **2012**, *27*, 361-366.

103. Bartlett, H.L.; Ting, L.H.; Bingham, J.T. Accuracy of force and center of pressure measures of the wii balance board. *Gait Posture* **2014**, *39*, 224-228.

104. Pagnacco, G.; Oggero, E.; Wright, C.H. Biomedical instruments versus toys: A preliminary comparison of force platforms and the nintendo wii balance board - biomed 2011. *Biomed Sci Instrum* **2011**, *47*, 12-17.

105. Pagnacco, G.; Bundle, M.W.; Carrick, F.R.; Wright, C.H.; Oggero, E. Letter to the editor: On "validity and reliability of the nintendo wii balance board for assessment of standing balance" by r.A. Clark et al. [gait & posture 31 (2010) 307-310]: Are the conclusions stated by the authors justified? *Gait Posture* **2014**, *39*, 1150-1151.

106. Hubbard, B.; Pothier, D.; Hughes, C.; Rutka, J. A portable, low-cost system for posturography: A platform for longitudinal balance telemetry. *Journal of otolaryngology - head & neck surgery = Le Journal d'oto-rhino-laryngologie et de chirurgie cervico-faciale* **2012**, *41 Suppl 1*, S31-35.

107. Fox, Z.G.; Mihalik, J.P.; Blackburn, J.T.; Battaglini, C.L.; Guskiewicz, K.M. Return of postural control to baseline after anaerobic and aerobic exercise protocols. *Journal of athletic training* **2008**, *43*, 456-463.

108. Hof, A.L.; Gazendam, M.G.; Sinke, W.E. The condition for dynamic stability. *J Biomech* **2005**, *38*, 1-8.

109. NASA. Anthropometry and biomechanics. msis.jsc.nasa.gov/sections/section03.htm (September 9 2013),

110. Scoppa, F.; Capra, R.; Gallamini, M.; Shiffer, R. Clinical stabilometry standardization: Basic definitions--acquisition interval--sampling frequency. *Gait Posture* **2013**, *37*, 290-292.

111. Hayes, M.H. *Statistical digital signal processing and modeling*. 1st ed.; John Wiley & Sons, Inc.: New York, 1996.

112. Winter, D.A. *Biomechanics of human movement*. 3rd ed.; John Wiley & Sons, Inc.: New York, 2004.

113. Horak, F.B. Clincal assessment of balance disorders. In *Gait Posture*, 1997; Vol. 6, pp 76-84.

114. McClellan, J.H.; Schafer, R.W.; Yoder, M.A. *Signal processing first*. Pearson Education, Inc.: Upper Sadle River, NJ 07458, 2003; p 489.

115. van Iersel, M.B.; Kessels, R.P.; Bloem, B.R.; Verbeek, A.L.; Olde Rikkert, M.G. Executive functions are associated with gait and balance in community-living elderly people. *J Gerontol A Biol Sci Med Sci* **2008**, *63*, 1344-1349.

116. Yogev-Seligmann, G.; Hausdorff, J.M.; Giladi, N. The role of executive function and attention in gait. *Mov Disord* **2008**, *23*, 329-342; quiz 472.

117. Hausdorff, J.M.; Yogev, G.; Springer, S.; Simon, E.S.; Giladi, N. Walking is more like catching than tapping: Gait in the elderly as a complex cognitive task. *Exp Brain Res* **2005**, *164*, 541-548.

118. Springer, S.; Giladi, N.; Peretz, C.; Yogev, G.; Simon, E.S.; Hausdorff, J.M. Dual-tasking effects on gait variability: The role of aging, falls, and executive function. *Mov Disord* **2006**, *21*, 950-957.

119. Lezak, M.D.; Howieson, D.B.; Loring, D.W.; Hannay, H.J.; Fischer, J.S. *Neuropsychological assessment*. 4th ed.; Oxford University Press: New York, 2004.

120. Grigsby, J.; Kaye, K. Alphanumeric sequencing and cognitive impairment among elderly persons. *Percept Mot Skills* **1995**, *80*, 732-734.

121. Brandt, J., Benedict, R. Hopkins verbal learning test-revisied. *Professional Manual* **2001**.

122. Simon, J.R. Reactions towarsd the source of stimulation. *Journal of Experimental Psychology* **1969**, *81*, 174-176.

123. Simon, J.R.; Craft, J.L.; Webster, J.B. Reactions toward the stimulus source: Analysis of correct responses and errors over a five-day period. *J Exp Psychol* **1973**, *101*, 175-178.

124. Simon, J.R.; Agens, R.M. Retrieval time in a monaural learning task. *Cortex; a journal devoted to the study of the nervous system and behavior* **1980**, *16*, 231-238.

125. Simon, J.R.; Acosta, E., Jr. Effect of irrelevant information on the processing of relevant information: Facilitation and/or interference? The influence of experimental design. *Perception & psychophysics* **1982**, *31*, 383-388.

126. Maurer, C.; Peterka, R.J. A new interpretation of spontaneous sway measures based on a simple model of human postural control. *J Neurophysiol* **2005**, *93*, 189-200.

127. Rocchi, L.; Chiari, L.; Cappello, A. Feature selection of stabilometric parameters based on principal component analysis. *Med Biol Eng Comput* **2004**, *42*, 71-79.

128. Camicioli, R.; Majumdar, S.R. Relationship between mild cognitive impairment and falls in older people with and without parkinson's disease: 1-year prospective cohort study. *Gait Posture* **2010**, *32*, 87-91.

129. Delignieres, D.; Torre, K.; Bernard, P.-L. Transition from persistent to anti-persistent correlations in postural sway indicates velocity-based control. *PLoS Comput Biol* **2011**, *7*.

130. Andersson, G.; Hagman, J.; Talianzadeh, R.; Svedberg, A.; Larsen, H.C. Effect of cognitive load on postural control. *Brain research bulletin* **2002**, *58*, 135-139.

131. Bloem, B.R.; Grimbergen, Y.A.; van Dijk, J.G.; Munneke, M. The "posture second" strategy: A review of wrong priorities in parkinson's disease. *J Neurol Sci* **2006**, *248*, 196-204.

132. Beauchet, O.; Dubost, V.; Aminian, K.; Gonthier, R.; Kressig, R.W. Dual-task-related gait changes in the elderly: Does the type of cognitive task matter? *J Mot Behav* **2005**, *37*, 259-264.

133. Camicioli, R.; Howieson, D.; Lehman, S.; Kaye, J. Talking while walking: The effect of a dual task in aging and alzheimer's disease. *Neurology* **1997**, *48*, 955-958.

134. Pettersson, A.F.; Olsson, E.; Wahlund, L.O. Effect of divided attention on gait in subjects with and without cognitive impairment. *J Geriatr Psychiatry Neurol* **2007**, *20*, 58-62.

135. McNevin, N.H.; Shea, C.H.; Wulf, G. Increasing the distance of an external focus of attention enhances learning. *Psychological research* **2003**, *67*, 22-29.

136. Wulf, G.; McNevin, N.; Shea, C.H. The automaticity of complex motor skill learning as a function of attentional focus. *Q J Exp Psychol A* **2001**, *54*, 1143-1154.

137. Polskaia, N.; Richer, N.; Dionne, E.; Lajoie, Y. Continuous cognitive task promotes greater postural stability than an internal or external focus of attention. *Gait Posture* **2015**, *41*, 454-458.

138. McGrath, D.; Greene, B.R.; Sheehan, K.; Walsh, L.; Kenny, R.A.; Caulfield, B. Stability of daily home-based measures of postural control over an 8-week period in highly functioning older adults. *European journal of applied physiology* **2015**, *115*, 437-449.

139. Parmelee, P.A.; Thuras, P.D.; Katz, I.R.; Lawton, M.P. Validation of the cumulative illness rating scale in a geriatric residential population. *J Am Geriatr Soc* **1995**, *43*, 130-137.

140. Sheikh, J.I., Yesavage, J.A. Geriatric depression scale (gds): Recent evidence and development of a shorter version. *Clincal Geronotolgy* **1986**, *5*, 165-173.

141. Kopke, S.; Meyer, G. The tinetti test: Babylon in geriatric assessment. *Z Gerontol Geriatr* **2006**, *39*, 288-291.

142. Bondi, M.W.; Edmonds, E.C.; Jak, A.J.; Clark, L.R.; Delano-Wood, L.; McDonald, C.R.; Nation, D.A.; Libon, D.J.; Au, R.; Galasko, D., *et al.* Neuropsychological criteria for mild cognitive impairment improves diagnostic precision, biomarker associations, and progression rates. *J Alzheimers Dis* **2014**, *42*, 275-289.

143. Shrout, P.E.; Fleiss, J.L. Intraclass correlations: Uses in assessing rater reliability. *Psychological bulletin* **1979**, *86*, 420-428.

144. McGraw, K.O., Wong, S. P. Forming inferences about some intraclass correlation coefficients. *Psychological Methods* **1996**, *1*, 30-46.

145. Weir, J.P. Quantifying test-retest reliability using the intraclass correlation coefficient and the sem. *Journal of strength and conditioning research / National Strength & Conditioning Association* **2005**, *19*, 231-240.

146. Shumway, R.H., Stoffer, D.S. *Time series analysis and its application*. Third edition ed.; Springer: New York, NY, 2011; p 596.

147. Bouisset, S.; Duchene, J.L. Is body balance more perturbed by respiration in seating than in standing posture? *Neuroreport* **1994**, *5*, 957-960.

148. Bravo, G.; Potvin, L. Estimating the reliability of continuous measures with cronbach's alpha or the intraclass correlation coefficient: Toward the integration of two traditions. *Journal of clinical epidemiology* **1991**, *44*, 381-390.

149. Brach, J.S.; Berlin, J.E.; VanSwearingen, J.M.; Newman, A.B.; Studenski, S.A. Too much or too little step width variability is associated with a fall history in older persons who walk at or near normal gait speed. *J Neuroeng Rehabil* **2005**, *2*, 21.

150. Lange, F.; Seer, C.; Muller, D.; Kopp, B. Cognitive caching promotes flexibility in task switching: Evidence from event-related potentials. *Scientific reports* **2015**, *5*, 17502.

151. Taillan, J.; Ardiale, E.; Lemaire, P. Relationships between strategy switching and strategy switch costs in young and older adults: A study in arithmetic problem solving. *Exp Aging Res* **2015**, *41*, 136-156.

152. Pusswald, G.; Tropper, E.; Kryspin-Exner, I.; Moser, D.; Klug, S.; Auff, E.; Dal-Bianco, P.; Lehrner, J. Health-related quality of life in patients with subjective cognitive decline and mild cognitive impairment and its relation to activities of daily living. *J Alzheimers Dis* **2015**, *47*, 479-486.

153. Andersson, G.; Yardley, L.; Luxon, L. A dual-task study of interference between mental activity and control of balance. *The American journal of otology* **1998**, *19*, 632-637.

154. Yardley, L.; Gardner, M.; Leadbetter, A.; Lavie, N. Effect of articulatory and mental tasks on postural control. *Neuroreport* **1999**, *10*, 215-219.

155. Yardley, L.; Papo, D.; Bronstein, A.; Gresty, M.; Gardner, M.; Lavie, N.; Luxon, L. Attentional demands of continuously monitoring orientation using vestibular information. *Neuropsychologia* **2002**, *40*, 373-383.

156. Bergamin, M.; Gobbo, S.; Zanotto, T.; Sieverdes, J.C.; Alberton, C.L.; Zaccaria, M.; Ermolao, A. Influence of age on postural sway during different dual-task conditions. *Frontiers in aging neuroscience* **2014**, *6*, 271.

157. Faul, F.; Erdfelder, E.; Buchner, A.; Lang, A.G. Statistical power analyses using g*power 3.1: Tests for correlation and regression analyses. *Behavior research methods* **2009**, *41*, 1149-1160.

158. Faul, F.; Erdfelder, E.; Lang, A.G.; Buchner, A. G*power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behavior research methods* **2007**, *39*, 175-191.

159. Kaye, J.; Mattek, N.; Dodge, H.; Buracchio, T.; Austin, D.; Hagler, S.; Pavel, M.; Hayes, T. One walk a year to 1000 within a year: Continuous in-home unobtrusive gait assessment of older adults. *Gait Posture* **2012**, *35*, 197-202.

160. Hagler, S.; Austin, D.; Hayes, T.L.; Kaye, J.; Pavel, M. Unobtrusive and ubiquitous in-home monitoring: A methodology for continuous assessment of gait velocity in elders. *IEEE Trans Biomed Eng* **2010**, *57*, 813-820.

161. Kandel, E.R., Schwartz, J.H., Jessell, T.M. *Principles of neural science*. 4th ed. ed.; McGraw-Hill, Health Professions Division: New York, 2000.

162. Takakusaki, K. Neurophysiology of gait: From the spinal cord to the frontal lobe. *Mov Disord* **2013**, *28*, 1483-1491.

163. Montero-Odasso, M.; Verghese, J.; Beauchet, O.; Hausdorff, J.M. Gait and cognition: A complementary approach to understanding brain function and the risk of falling. *J Am Geriatr Soc* **2012**, *60*, 2127-2136.

164. Rosano, C.; Brach, J.; Longstreth Jr, W.T.; Newman, A.B. Quantitative measures of gait characteristics indicate prevalence of underlying subclinical structural brain abnormalities in high-functioning older adults. *Neuroepidemiology* **2006**, *26*, 52-60.

165. Rosano, C.; Aizenstein, H.J.; Studenski, S.; Newman, A.B. A regions-of-interest volumetric analysis of mobility limitations in community-dwelling older adults. *J Gerontol A Biol Sci Med Sci* **2007**, *62*, 1048-1055.

166. Rosano, C.; Brach, J.; Studenski, S.; Longstreth, W.T., Jr.; Newman, A.B. Gait variability is associated with subclinical brain vascular abnormalities in high-functioning older adults. *Neuroepidemiology* **2007**, *29*, 193-200.

167. Hayes, T.L., Pavel, M., Kaye, J.A. Gathering the evidence: Supportinve large-scale research deployments. *Intel Technology Journal* **2009**, *13*, 148-167.