EFFECTS OF FATIGUE ON BALANCE CONTROL

DURING DUAL-TASK WALKING

by

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A DISSERTATION

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DISSERTATION ABSTRACT

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Fatigue is one of the most frequently mentioned symptoms among older adults. Although there were many studies examining effects of fatigue on walking and balance control, the findings were inconclusive due to methodology discrepancy. In addition, the cognitive component is often neglected. Therefore, four studies were conducted in this dissertation to investigate how fatigue affects balance control during dual-task locomotion in older adults using a laboratory fatiguing protocol, and further, how these findings could be applied in real-life settings.

In the first study, we demonstrated the use of a repetitive sit-to-stand protocol by examining changes in inter-joint coordination variability along the course of the protocol. The findings suggested that the knee-ankle coordination variability was higher towards the end of protocol. In the second and the third experiments, such fatiguing protocol was applied. Results from the second study suggested that participants regardless of age walked faster after fatigue when concurrently responding to a working memory test. Moreover, young adults showed a greater and faster mediolateral center of mass sway after fatigue; whereas older adults demonstrated a shorter reaction time from pre- to post-fatigue while maintaining a similar body sway during walking. The results from the third study followed the same trend, in which significantly deteriorated balance control during obstacle-crossing was only found in young adults but not in older adults. Taken together, healthy older adults might have a better adaptation to a fatigued status induced by a repetitive sit-to-stand protocol. In the last study, the connection between findings from laboratory experiments and real-life scenarios was explored through examining the effect of fatigue in three older workers following a day-long of occupational activities. Our results showed that some changes observed after work were in line with that observed in the laboratory, but some were opposite or demonstrated unique fatigue adaptations, such as increased body sway, which was not identified when the results were pooled together. Although conclusive interpretation could not be made given the descriptive nature of the study, it highlights the necessity of subgroup analysis and targets the future recruitment on fatigue-prone population.

This dissertation includes unpublished co-authored material.

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CHAPTER I

INTRODUCTION

Fatigue

Fatigue is not interpreted the same way by the public, clinicians and researchers across disciplines. To the public or clinicians, fatigue could be easily defined as a subjective feeling or symptom of tiredness generally caused by physical or mental stressors. To researchers, fatigue is classified into multiple subcategories such as central fatigue vs. peripheral fatigue, physical or muscle fatigue vs. mental fatigue, to indicate the locus of fatigue. However, according to Enoka and Duchateau (2016), "The word ***fatigue*** should not be preceded by an adjective (e.g., central, mental, muscle, peripheral, and supraspinal) to suggest the locus of the changes responsible for an observed level of fatigue".

Given the difficulty in inducing fatigue at a specific site, nor this is a mechanistic study determining the relative contributions of different fatigues, fatigue in this dissertation is defined as a disabling symptom with two domains, perceived and performance fatigabilities interactively limiting an individual's physical and cognitive functions. Perceived fatigability represents the changes in modulating factors that regulate the integrity of the body, such as homeostasis or psychological state; while performance fatigability is an activity-induced reduction of functions and can be measured by the decline in physiological factors during a period of activity (Enoka & Duchateau, 2016).

Background and Significance

Fatigue is a common symptom in workplace and is often observed in older population. Thirty-eight percent of the U.S. workforce report a feeling of fatigue during work (Ricci, Chee, Lorandeau, & Berger, 2007). The prevalence of fatigue increases significantly with aging with incidence rates reported at 29%, 53%, and 68% for the age of 70, 78, and 85, respectively (Moreh, Jacobs, & Stessman, 2010). With aging, fatigue negatively impacts quality of life and is associated with various functional limitations, such as slower walking, deteriorated mobility or increased disability in activity of daily life (Vestergaard et al., 2009) and mortality (Moreh et al., 2010). In fact, fatigue was reported to predict subsequent functional declines (Simonsick et al., 2016) and future fall risks (Kamitani et al., 2019). Despite robust epidemiological evidence showing its high prevalence and serious consequences in older adults, multifaceted forms of fatigue have posed significant challenges to properly assess its risk.

Numerous researchers have reported a degradation in postural balance after fatigue (Davidson, Madigan, & Nussbaum, 2004; Salavati, Moghadam, Ebrahimi, & Arab, 2007; Vuillerme, Burdet, Isableu, & Demetz, 2006; Yaggie & McGregor, 2002). Decreased joint proprioception (Skinner, Wyatt, Hodgdon, Conard, & Barrack, 1986) and/or variable force steadiness (Missenard, Mottet, & Perrey, 2009) were thought to be the contributing factors. However, very limited studies are available to investigate the functional significance of fatigue on gait balance control during level and perturbed walking, where falls occur most frequently (Berg, Alessio, Mills, & Tong, 1997). **To better understand the connection between fatigue and increasing fall risk in older adults, it is, therefore, important to examine the effects of fatigue on balance control**

during walking and obstacle-crossing and to understand how age plays a role in differentiating these fatigue effects.

Walking and simultaneously performing a cognitive-demanding task may occur concurrently with increased fatigue symptoms toward the end of daily activities or job performance. With a lower fatigue threshold (Schrack, Simonsick, & Ferrucci, 2010), older adults need to exert high level of efforts relative to their maximum capability when performing activities (Hortobágyi, Mizelle, Beam, & DeVita, 2003). A systematic review suggested that fatigue can lead to gait and functional declines in older adults (Helbostad, Leirfall, Moe-Nilssen, & Sletvold, 2007). Moreover, age-related declines in cognitive function may pose an additional threat to older adults as the origin of fatigue stems from the central cerebral cortex to peripheral muscles. In fact, an age-related motor cortical hypo-excitability may exacerbate the insufficient central drive during fatigue (Bhandari et al., 2016). Although previous research has demonstrated independent effects of these factors regarding performance fatigability, the combined effect of fatigue and cognitive demand is rarely taken into consideration. **Therefore, it is critical to investigate to what extent cognitive demand affects fatigue effects on balance control using a dual-task (DT) paradigm.**

Aging and fatigue are both intrinsic factors of fall risk, which could be interfered by unpredicted environmental conditions, such as workplace settings, an extrinsic factor. The percentage of older adults in the American workforce has been increasing. This may be due to changes in Social Security retirement age which requires individuals working longer to receive full benefits (Rogers & Wiatrowksi, 2005). These individuals have the highest frequency and severity of slips, trips and falls. For workers ages 65 and over, the incident rate on same-level falls per 10,000 full-time workers was 36.3 (U.S. Bureau of Labor Statistics, 2016a). This rate was highest among all age groups and causes of occupational injury, suggesting that falls are highly prominent among increasing older population workers. Moreover, injuries suffered from older workers are more severe although older workers encounter similar workplace safety hazards as younger workers. Recovering from workplace injuries for older workers are twice as long as their younger counterparts (U.S. Bureau of Labor Statistics, 2016b). The statistics reflects the necessity for an improved fatigue detection and prevention strategies in order to reduce work-related injuries among older workers. However, the consequence of fatigue is predominantly obtained using a laboratory-based protocol, for example, prolonged muscle contraction or repeated bouts of exercise to a targeted endpoint or exercising to exhaustion (Enoka & Duchateau, 2008). It is unknown whether laboratory-induced fatigue can truly reflect real-life situations in older workers. **Therefore, a study design that compares old worker's balance control under dual-task locomotion before and after their daily job performance is needed.**

Effects of Fatigue on Locomotion

Fatigue has been shown to alter gait temporal-distance characteristics. Many studies have reported increased walking speeds (Barbieri, dos Santos, Vitório, van Dieën, & Gobbi, 2013; Morrison et al., 2016; Santos et al., 2016) and wider steps (Barbieri et al., 2016, 2013; Helbostad et al., 2007; Kao, Pierro, & Booras, 2018; Santos et al., 2016; Vieira, de Sá e Souza, Lehnen, Rodrigues, & Andrade, 2016) after fatigue, while others found the walking speed was unaffected (Barbieri et al., 2016; Helbostad et al., 2007) or the step width became narrow (Tay et al., 2016). Such inconsistency in post-fatigue gait changes could be due to the use of different protocols or measures to induce or quantify fatigue.

Nonetheless, altered gait temporal-distance characteristics only provide limited information on gait balance control. Only two studies have reported gait balance measures, such as the margin of stability, and suggested a declined balance control post-fatigue (Kao et al., 2018; Vieira et al., 2016). Previous studies (Catena, van Donkelaar, & Chou, 2007; Chou, Kaufman, Hahn, & Brey, 2003; Hahn & Chou, 2004) consistently demonstrated that the range of center of mass (CoM) displacement and peak CoM velocity allow for sensitive detection of gait imbalance in older adults as well as patients with mild traumatic brain injury. The CoM motion, thus, can serve better as an indicator of balance control compared to walking characteristics.

Fatiguing Protocol

In literature, the change of performance fatigability was predominantly induced by a repeated single-joint motion (Arvin et al., 2015; Granacher, Wolf, Wehrle, Bridenbaugh, & Kressig, 2010; Kao et al., 2018; Lew & Qu, 2014; Tay et al., 2016) or prolonged walking (Morrison et al., 2016; Nagano, James, Sparrow, & Begg, 2014; Vieira et al., 2016). Fatiguing protocol using repetitive single-joint contractions often consists of high-intensity exercise, leading to a shorter exhaustive time (Paillard, 2012). In addition, most daily activities require physical demands that involve movement from multiple joints whereas no high peak loads are involved in the musculoskeletal system. It remains to be validated to what extent the findings reflect real-life situations. In fact, the central mechanism of fatigue was reported to be fundamentally different between the single-joint and task-based (multiple-joint) exercise paradigms (Sidhu, Cresswell, & Carroll, 2013). Excitability of corticospinal cells were shown to increase during single-joint fatiguing protocol while to reduce during prolonged walking. Therefore, walking exercise is often used as a fatiguing protocol when conducted for a prolonged period on the treadmill, as it yields a whole-body movement. Nevertheless, prolonged walking might result in a transient carry-over effect. For example, Morrison et al. (2016) reported that their participants increased walking speed after walking-induced fatiguing protocol and speculated that this change might result from the fact that participants walked at a faster speed when performing a treadmill fatiguing task.

Sit-to-stand (STS) is a biomechanically challenging task, which requires individuals to transit the whole-body CoM from a low, fully supported three-points base-of-support position to an upright two-foot base. STS is a short and simple movement that most individuals can perform. Therefore, it is commonly adopted as a testing protocol in clinical/research settings. With different time durations or number of repetitions, it is widely used as a mean to assess a range of capabilities. Lower extremity strength has been quantified using the amount of time needed to perform a 10-cycle STS movement (Csuka & McCarty, 1985) or the number of repetitions in a 30-second time period (Jones, Rikli, & Beam, 1999). With advanced biomechanical analysis, timed completion of 5-cycle STS and whole-body CoM acceleration during STS movement were used to distinguish fallers (Doheny et al., 2013) and to identify age-related differences in biomechanical strategies that could lead to a potential detection of older adults at a risk of imbalance (Fujimoto & Chou, 2012).

A repeated STS movement has been used as a laboratory-based fatigue protocol

(Barbieri et al., 2016, 2014, 2013; Hatton, Menant, Lord, Lo, & Sturnieks, 2013; Helbostad et al., 2007; Santos et al., 2016) due to its representation for daily life conditions and easy implementation across populations and facilities. This protocol can induce performance fatigability with a relatively long duration, 6.7- 17.0 minutes for young adults (Barbieri et al., 2013). Despite the widespread application, the strength drop in knee muscles seems to be a sole indicator of fatigue, regardless of the fact that STS movement is a multi-joint exercise. During a multi-joint fatiguing protocol for the upper extremity, motor reorganization or behavioral adaptation was found in order to compensate for the effects of fatigue (Terrier & Forestier, 2009). As the lower extremity is a coupled system, examining inter-joint coordination and movement variability may provide further understanding of how fatigue contributes to changes in dynamic task execution. In fact, studies revealed the inter-joint coordination variability significantly increased with fatigue using continuous relative phase (CRP) method (Yang et al., 2018). CRP provides coordination assessments on both spatial and temporal aspects of two adjacent joints (Hamill, van Emmerik, Heiderscheit, & Li, 1999) so that it can account for individual differences in movement speed during the fatiguing protocol. **Therefore, one of the study aims is to examine changes in inter-joint coordination variability throughout the STS fatiguing protocol.**

Interaction Between Fatigue and Cognition

Declined cognitive function is one of the contributing factors to fall accidents in older adults (Montero-Odasso, Verghese, Beauchet, & Hausdorff, 2012). The fatigue-induced incapacity of force generation is attributable to adjustments along the pathway of force production between the brain and muscles, including insufficient cortical activation

(Gandevia, Allen, Butler, & Taylor, 1996). This indicates the potential interaction between fatigue and cognition. Fatigue induced by challenging performance fatigability may diminish central nervous system sensorimotor control through sensory feedback of group III/IV afferents from a working muscle and/or central depressed motor output (Amann & Dempsey, 2008). The prefrontal cortex, a neural substrate of working memory (Owen, McMillan, Laird, & Bullmore, 2005), appears to be an integration center of fatigue-related feedback and to adjust central command of motor output (Thomas & Stephane, 2008). Brain studies using magnetoencephalographic and functional magnetic resonance imaging both found an increased activation of pre-frontal cortex during sustained fatiguing contraction (Liu et al., 2003; Tanaka, Ishii, & Watanabe, 2013). Thus, it is reasonable to hypothesize additional demands imposed on the prefrontal cortex may lead to deteriorated cognitive performance after fatigue due to central capacity limit (Saults & Cowan, 2007).

Using a dual-task paradigm, researchers have shown interactions between effects of fatigue and cognition through adding concurrent cognitive demands into the tasks (Lorist, Kernell, Meijman, & Zijdewind, 2002; Simoneau, Bégin, & Teasdale, 2006; Vanden Noven et al., 2014; Zijdewind, van Duinen, Zielman, & Lorist, 2006). Force steadiness was more variable during dual-task condition compared to single-task condition, suggesting cognitive resource was needed to compensate for fatigue. The interaction between fatigue and cognitive performance can be further supported through examining population with limited cognitive capacity, in which the disruption in motor performance resulted from dual-tasking interference influences older adults more than young adults (Vanden Noven et al., 2014). Performance fatigability has also been reported to affect activation levels of both cortical and subcortical brain structures (i.e., thalamus and basal ganglia) (Hou et al., 2016), suggesting the effect of fatigue may be moderated by the involvement of cognitive tasks. Therefore, a dual-task walking paradigm may not only provide a unique environment to simultaneously assess different facets of fatigue but also highlight its role in fall prevention especially in the older population (Kressig, Herrmann, Grandjean, Michel, & Beauchet, 2008). As the total available cognitive capacity is limited, the concurrent performance of more than one task would reduce the allocation of working memory resource to each of the tasks (Kahneman, 1973).

Granacher et al. (2010) examined the effect of fatigue on walking characteristics under single and dual-task conditions in young and older adults. They revealed that older adults demonstrated significant increases in gait velocity and stride length when walking while answering an arithmetic task after fatigue. No information, nonetheless, regarding gait balance control after fatigue can be interpreted without proper task conditions and sensitive measurements. In order to increase demand to the integration center of fatigue, namely the pre-frontal cortex, a selection of a secondary cognitive tasks should pertain to working memory. The arithmetic task (serial subtractions by three) used in this study might not be enough to challenge each component lined with working memory, including attention, executive function, short-term memory and a phonological loop (Owen et al., 2005). Math anxiety might also compromise the results (Ashcraft & Krause, 2007). On the other hand, Kao et al. incorporated working memory tests, including both paced auditory serial addition test and modified incongruent color-word Stroop test, to identify the significance of cognitive demand in fatigue-related changes (Kao et al., 2018). Although the findings regarding to what extent the cognitive demand moderates fatigue effects were informative, the study only recruited young participants, and like the aforementioned study, utilized isotonic exercises (leg press and heel raise) as the fatiguing protocol. Thus, this dissertation study would improve the previous experimental protocol and chose a N-back test as the concurrent cognitive task. N-back test is a well-established task for working memory performance (Owen et al., 2005).

Overall Goal and Specific Aims

The overall goal of this dissertation study was to examine effects of fatigue, induced by a laboratory-based fatigue protocol and occupational activities, on gait balance control, cognitive performance and their interaction in young and older adults.

Four specific aims were identified, and two experiments were conducted to address these aims. The first aim targeted on validating the use of whole-body fatigue protocol, the second and the third aims focused on effects of fatigue on locomotion and cognition, and the last aim sought to establish a connection between fatigue-related balance control induced by the laboratory-based protocol and real-life occupational activity.

Aim 1: To demonstrate the use of a repeated sit-to-stand movement by examining the changes in inter-joint coordination throughout the fatiguing protocol.

Aim 2: To investigate effects of fatigue as well as age-related differences on balance control and working memory performance following a repeated sit-to-stand movement during single- and dual-task level walking.

Aim 3: To examine effects of fatigue as well as age-related differences on balance control and working memory performance following a repeated sit-to-stand movement during single- and dual-task obstacle-crossing.

Aim 4: To translate a laboratory-driven experiment to real-life setting by determining effects of fatigue on balance control and working memory performance following occupational activity in older workers.

With the use of sensitive measures of gait balance control and application of working memory, this dissertation project hopes to fill the knowledge gap by investigating the interaction of performance fatigability and cognitive demand on gait balance control. Findings from this study will provide a solid base for future studies to examine how biomechanical screening and assessment may preemptively identify individuals at risk and develop effective strategies to prevent fatigue-related injuries in workplace.

Hypotheses

Hypothesis 1: Inter-joint coordination, indicated by the continuous relative phase, would alter throughout the fatiguing protocol and its variability would also increase.

Hypothesis 2: Balance control during walking would become deteriorated at post-fatigue, and such an effect would be exacerbated during dual-task condition and/or in older adults.

Hypothesis 3: Gait performance and balance control during obstacle-crossing would become deteriorated at post-fatigue, and such an effect would be exacerbated during dual-task condition and/or in older adults.

Hypothesis 4: Changes in gait balance control and working memory performance of older workers before and after their work would follow a similar trend as those induced by a laboratory-driven protocol.

Flow of the Dissertation

This dissertation is structured in a journal format. Chapters II through IV include co-authored material and are prepared for submission to peer-reviewed scientific journals.

Chapter II demonstrates that the use of a repeated sit-to-stand movement as a fatiguing protocol and that the variability of inter-joint coordination increased at the end of protocol. This work has been prepared for submission to a peer-reviewed scientific journal. Li-Shan Chou is a co-author.

Chapter III examines the effects of fatigue on balance control and working memory performance in young and older adults during single- and dual-task level walking. This work has been prepared for submission to a peer-reviewed scientific journal. Li-Shan Chou is a co-author.

Chapter IV investigates the effects of fatigue on balance control and working memory performance in young and older adults during single- and dual-task obstacle-crossing. This work has been prepared for submission to a peer-reviewed scientific journal. Li-Shan Chou is a co-author.

Chapter V establishes the connection between laboratory-driven results and real-life setting on balance control and working memory in older workers after occupational activity.

Chapter VI concludes the findings and provides recommendations for future research.

CHAPTER II

VARIABILITY OF INTER-JOINT COORDINATION DURING A REPETIVE SIT-TO-STAND FATIGUING PROTOCOL

This work has been prepared for publication. Szu-Hua Chen contributed to the concept of the studies, recruited subjects, collected data, wrote analysis software, performed data analysis, and prepared the initial manuscript. Dr. Li-Shan Chou contributed to the concept of the study, provided editorial support, and critically reviewed and revised the manuscript.

Introduction

Sit-to-stand (STS) is a biomechanically challenging task, yet a short and simple movement that most individuals can perform and is widely used by clinicians. From sitting to standing, individuals are required to transit their whole-body center of mass (CoM) from a low and fully stabilized three-points base-of-support position to an upright position with a smaller two-foot base. A repetitive STS movement challenges individuals even more, as it requires eccentric control when sitting back to the chair. STS protocols have been shown to provide additional insights when included in clinical examinations. For example, lower extremity strength could be implicated with the amount of time needed to perform a 10-cycle STS (Csuka & McCarty, 1985) or the number of repetitions in a 30-second time period (Jones et al., 1999). In addition, with further biomechanical analysis, CoM acceleration during STS movement was reported to identify age-related differences in biomechanical strategies that could lead to a potential detection of older adults at a risk of imbalance (Fujimoto & Chou, 2012).

STS movement has also been adopted as a fatiguing protocol for both young and older adults given it is a common daily activity and its easy implementation across populations and facilities (Barbieri et al., 2016, 2014, 2013; Hatton et al., 2013; Helbostad et al., 2007; Santos et al., 2016). During the STS fatiguing protocol, study participants were asked to conduct STS repetitively either at certain pace or as fast as possible until exhaustion or reaching a pre-determined duration. Results from these studies have revealed adaptive lower extremity movement patterns, such as a wider step width during gait (Barbieri et al., 2016), in response to fatigue. Although it is evident that STS protocol could induce fatigue at the end of its application, it remains uncertain at what point of time individuals progressively become fatigued and to what extent individuals are fatigued. In fact, strength loss at post-fatigue has been used as a sole index of fatigue on several studies (Paillard, 2012), and fatiguing effects during STS fatiguing protocol have not been studied yet.

STS is a multi-joint movement, in which segments are coordinated efficiently to displace body position. Investigation on joint coupling has given insights on motor adaptation during fatiguing protocol. Ground work was done in 1997 by Sparto et al. (Sparto, Parnianpour, Reinsel, & Simon, 1997), where inter-joint coordination was derived from phase portrait to indicate the change in movement pattern during a repetitive lifting movement. This method is now known as continuous relative phase (CRP). CRP could be an outcome measure to examine the process of fatiguing as it provides coordination assessments on both spatial and temporal aspects of movement. Trial-to-trial variabilities of both joint position and velocity have been shown to increase after fatigue (Fuller, Fung, &

Côté, 2011). Adoption of CRP could account for changes in joint position or velocity during a fatiguing process as well as reflect changes in joint coordination. In fact, recent work has incorporated the variability measure of CRP and suggested that, after fatigue, segmental coordination variability increased (Yang et al., 2018). It is postulated that the increased variability is an indication of reduced motor control or a result of compensation, where secondary agonists are activated to optimize movement.

To further understanding of how the inter-joint coordination changes during a widely-used STS fatiguing protocol, this study examined changes in variability of hip-knee and knee-ankle CRPs during the STS course. It was hypothesized that decreased motor control as a result of fatigue would be evident by the increasing variability in the coordination dynamics.

Methods

Fifteen young and 15 older adults were recruited in this study (Table 2-1). None of the participant had a history of musculoskeletal injuries with the past six months, diagnosed cardiovascular disease or metabolic disease and any of the following signs or symptoms present: chest discomfort or pain, shortness of breath at rest or with mild exertion dizziness or syncope, orthopnea palpitations or tachycardia, intermittent claudication, known heart murmur, unusual fatigue or shortness of breath with usual activities. Participants who could not perform STS without assistance would be excluded. All participants signed an informed consent approved by the Institutioanl Review Board at the University prior to the beginning of experiment.

Participants were instructed to sit on a standard 46 cm tall wooden chair without armrests and perform STS movement. They were asked to perform repetitive STS movements for 30 minutes at their comfortable paces, defined as the pace they believed they could comfortably perform for an extended period of time. A practice period was provided to determine the pace for each participant. This pace was then set throughout the entire fatiguing protocol using a metronome (https://www.webmetronome.com/). Participants were instructed to keep their feet in place and not to use arm movements to assist STS movement during the entire protocol. The repetitive STS fatiguing protocol was terminated when 1) participants cannot continue due to exhaustion, 2) when the movement frequency fell below prescribed pace after encouragement, or 3) after 30 minutes (Barbieri et al., 2013a). A Borg 15-point scale (6-20) (Borg, 1998) was used to measure each participant's Rating of Perceived Exertion (RPE) at baseline and throughout the fatiguing protocol (Wilkins, Valovich McLeod, Perrin, & Gansneder, 2004). Prior to stopping, the participants were encouraged to perform 10 more STS motions if possible. Maximal joint torque of isokinetic contraction of right knee extensor at 60°/second was recorded using an isokinetic dynamometer (Biodex Medical Systems, Inc., NY) at pre- and post-fatigue

Whole body motion data were collected during each minute of the entire fatiguing protocol. A set of 40 retro-reflective markers placed on bony landmarks, including head (right, left, apex), shoulder, 7th cervical (C7) vertebra, sternum, elbow, medial and lateral wrists, 3rd finger, anterior superior iliac spine (ASIS), posterior superior iliac spine (PSIS), lateral thigh, tibial tuberosity, lateral knee, lateral shank, lateral ankle, toe, 5th metatarsal head, heel (medial, lateral, center) was used with a 12-camera motion system (Motion Analysis Corporation, CA). Marker trajectory data were low-pass filtered with a Butterworth fourth order filter with a cut-off frequency of 10 Hz. The whole-body CoM was calculated as the weighted sum of 15 segmental center of masses using Visual3D (C-Motion, Inc., MD). The CoM velocity was further derived from position data using the cross-validating spline smoothing and differentiation (GCVSPL) method and used to determine STS events. To calculate CRP, sagittal plane joint angles and velocities of ankle, knee and hip were first derived using Visual3D (C-Motion, Inc., MD). Only data from the dominant limb, indicated as the leg used to kick a ball, were analyzed.

Each STS cycle includes both UP and DOWN sections, which were identified by using a zero-crossing of CoM velocity. The UP section (from sitting to standing) was defined from the instant of zero-crossing of horizontal CoM velocity to the start of DOWN section; while the DOWN section (from standing to sitting) was initiated at the instant of zero-crossing of vertical CoM velocity to the start of the next UP section (Figure 2-1). Data from three consecutive STS cycles from every minute of STS fatiguing protocol were extracted, and data in each cycle was normalized to 101 points for further analysis.

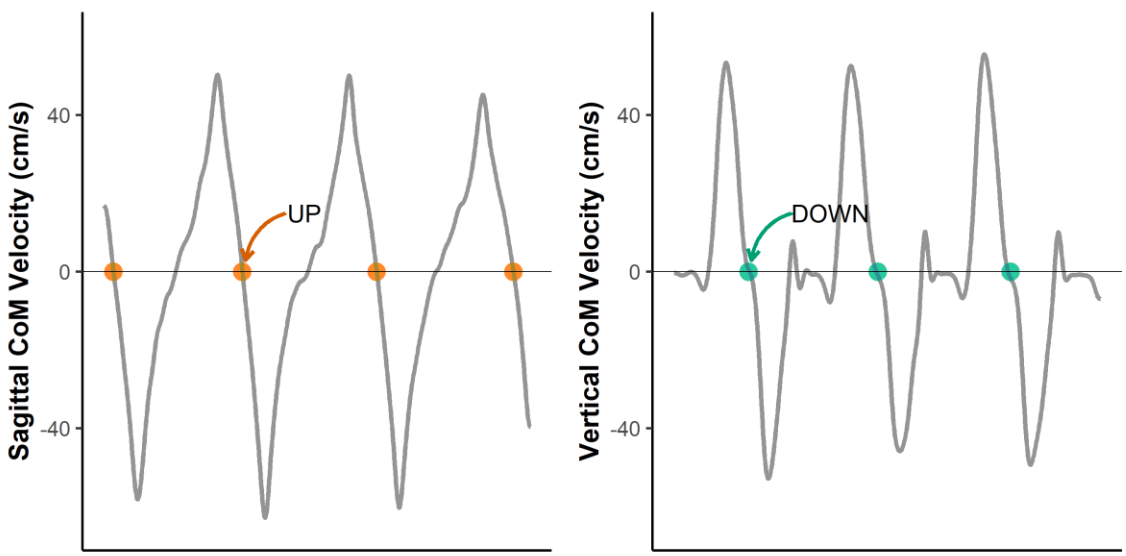

Figure 2-1. Determination of the start of UP (left, orange color) and DOWN (right, green) sections from a representative participant.

Hip-knee and knee-ankle inter-joint coordination during UP and DOWN sections, respectively, were calculated using CRP (Hamill et al., 1999; Sparto et al., 1997). Sagittal plane joint angles and velocities were first normalized using the following equation, where θ_i and ω_i were the angular position and velocity for each data point during UP or DOWN section.

$$\theta_i = \frac{2\times[\theta_i - \min(\theta_i)]}{\max(\theta_i) - \min(\theta_i)} - 1$$

$$\omega_i = \frac{\omega_i}{\max|\omega_i|}$$

Phase portrait, constructed by plotting normalized angular position over normalized velocity, were generated for each cycle (Figure 2-21). Secondly, phase angle(φ) was calculated as $\varphi = \tan^{-1}(\omega/\theta)$ for each data point. Lastly, hip-knee CRP was obtained by subtracting the hip_{φ} from the $knee_{\varphi}$, whereas knee-ankle CRP was calculated the $knee_{\varphi}$ from the $ankle_{\varphi}$ (Figure 2-23). Outcome variable was variability of inter-joint coordination between cycles, namely deviation phase (DP). DP was the average value of all standard deviations calculated from three CRP curves for each 101 point during each minute along STS course (Stergiou, Jensen, Bates, Scholten, & Tzetzis, 2001). A higher DP values indicates a more variable joint coupling.

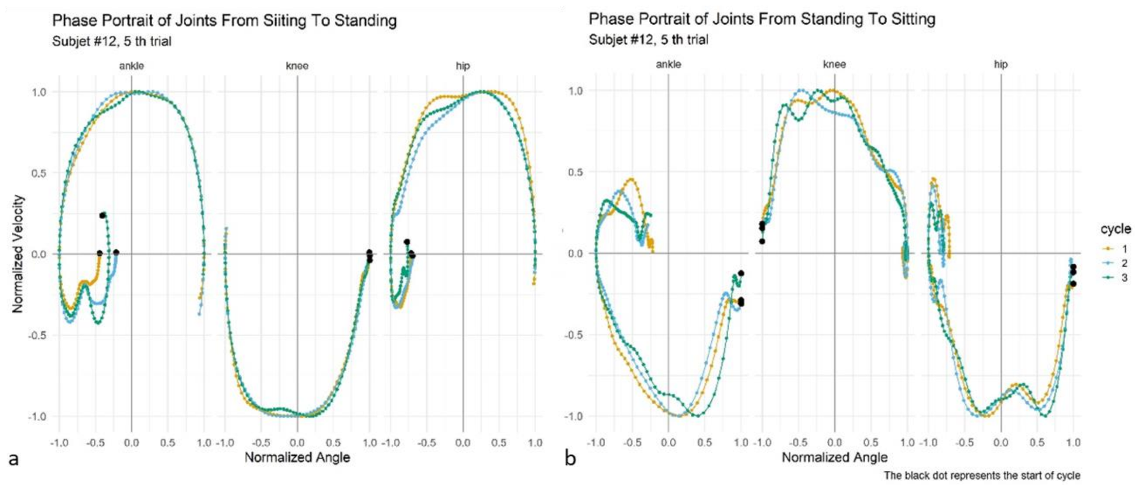

Figure 2-12. Phase portrait during UP (left) and DOWN (right) from a representative participant.

Due to individual differences in exhaustion time of STS fatiguing protocol (STS duration), it resulted in various total numbers of trials being recorded from each participant. Thus, STS trial collected from every minute was time normalized to STS duration and dummy coded as five stages: 0-20%, 20-40%, 40-60%, 60-80% and 80%-100% of fatiguing protocol. Two-way 2*5 mixed-effect ANOVA was used to examine changes in DP during different stages of fatiguing protocol in young and older adults. Tukey's HSD method was applied to adjust *p* value in cases of interaction. Alpha level was set at .05. Statistical analyses were conducted using R and Rstudio software with {lme4}, {lmerTest} and {emmean} packages.

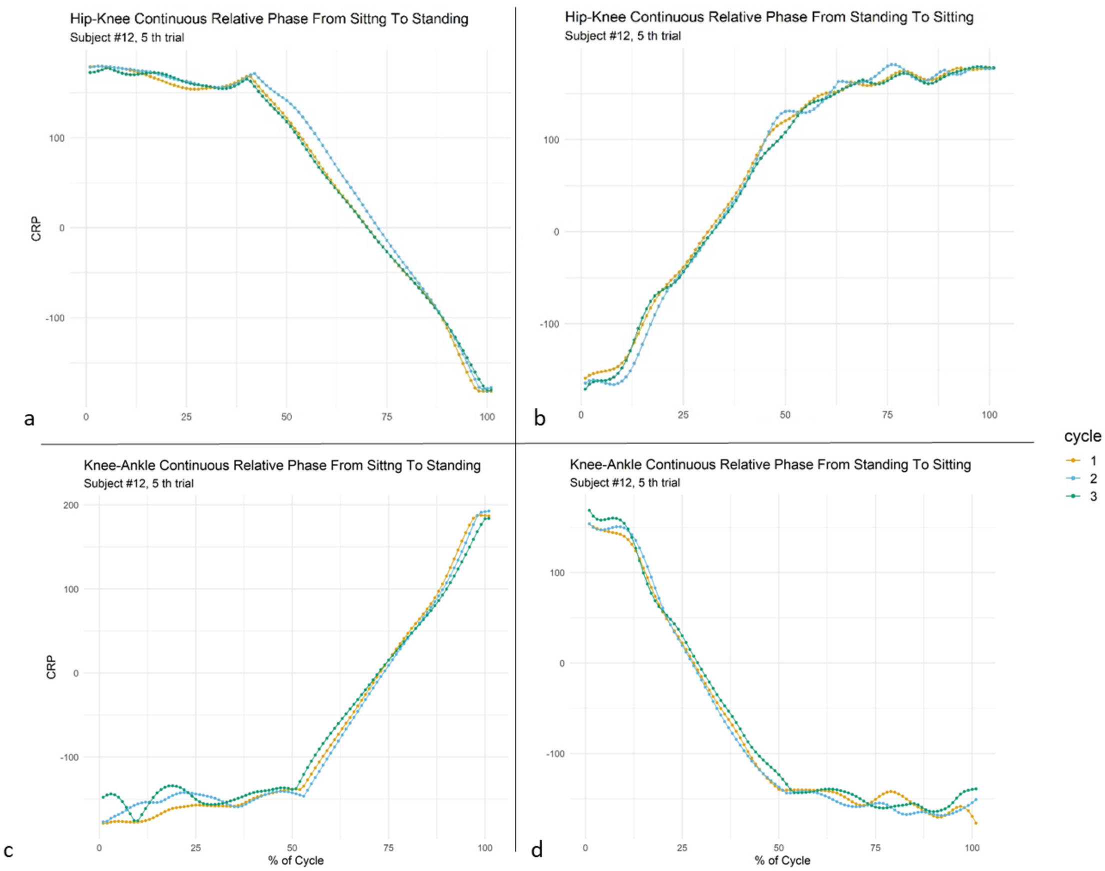

Figure 2-~~2~~3. Hip-knee (a, b) and knee-ankle (c, d) continuous relative phases during UP (a, c) and DOWN (b, d) cycles from a representative participant.

Results

Performance of STS fatiguing protocol is summarized in Table 2-1. Isokinetic strength was significantly decreased at post-fatigue. Older and young adults performed STS protocol to the same degree except for that the pace of STS was slower in older adults.

Table 2-1. Demographic data and STS performance between two age groups

	older	**young**	***p* value**
age [a]	69.3±5.7	26.7±5.8	< .001
sex	9 females, 6 males	9 females, 6 males	n/a
height (cm)	168.3±11.8	169.1±7.3	0.81
weight (kg)	71.7±17.6	69.9±12.8	0.75
RPE			
at pre-fatigue	7.3±1.8	6.9±1.4	0.51
at post-fatigue	17.5±1.4	18.1±1.4	0.25
STS duration (s)	940.2±731.2	1188.9±651.6	0.34
Metronome frequency (bpm) [a]	46.6±8.4	54.8±4.9	0.003
peak torque (N-m) [b]			I: 0.46 G: 0.16, T: < .001
at pre-fatigue	95.5±46.0	135.24±65.69	
at post-fatigue	78.7±42.7	109.71±51.69	

Note. a = significant group difference between older and young adults; b = significant differences across time; I = interaction effect, G = group effect, T = time effect

Deviation phase values for both UP and DOWN sections during STS course were summarized in Table 2-2. No interactions between Age and Time were found in neither hip-knee or knee-ankle coordination variability during UP or DOWN section. From sitting to standing, inter-joint coordination variability of hip-knee and knee-ankle segments did not significantly change along the STS fatiguing protocol ($p = .22$ and p = .24) nor was there an age effect ($p = .91$ and $p = .85$).

Table 2-2. Inter-joint coordination variability during UP and DOWN cycles

	UP		DOWN	
	older	**young**	**older**	**young**
Hip-knee deviation phases				
0-20%	9.1±2.4	9.1±2.5	8.0±2.1	8.7±2.6
20-40%	9.4±2.5	9.0±2.0	9.7±3.0	9.0±2.0
40-60%	9.2±3.0	9.6±2.7	8.9±2.7	10.1±2.4
60-80%	11.1±4.1	9.8±2.9	9.8±3.6	10.7±3.3
80-100%	9.6±3.7	10.2±3.9	9.6±3.4	10.0±4.9
Knee-ankle deviation phases				
0-20%	16.0±8.0	15.2±8.4	14.3±6.4	13.6±5.6
20-40%	16.5±6.3	15.4±5.6	16.3±6.5	14.5±5.2
40-60%	14.0±5.0	16.1±5.0	16.0±6.3	16.8±7.2
60-80%	17.7±7.9	18.0±7.9	16.4±7.2	18.4±7.2
80-100% [a]	18.0±8.2	17.0±5.8	18.9±8.1	17.3±7.0

Note. a = significantly different from 0-20% during DOWN event

On the other hand, changes in knee-ankle variability from standing to sitting was dependent on stages, $F_{(1, 108)} = 3.48$, $p = .01$. Specifically, knee-ankle variability during the late-stage (80-100 %) of fatiguing protocol was higher than that of early-stage (0-20%), Figure 2-~~3~~4. No similar effect was found in hip-knee coordination variability ($p = .12$). Young and older adults seemed to have similar pattern in inter-joint coordination variability of hip-knee ($p = .46$) and knee-ankle ($p = .92$) during DOWN section.

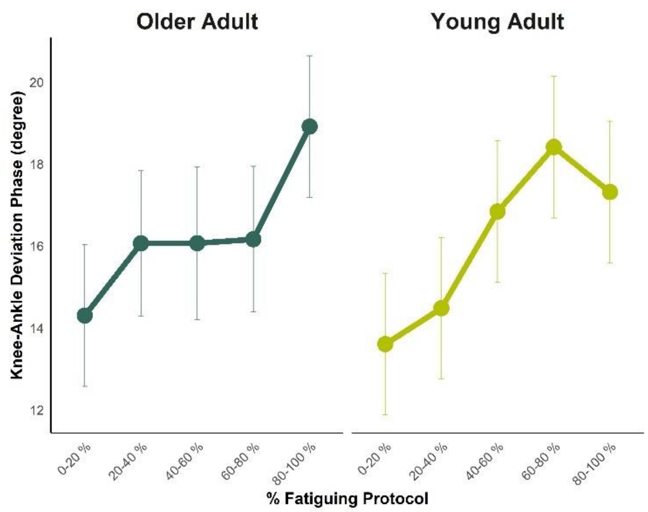

Figure 2-~~3~~4. Variability of inter-joint coordination of knee-ankle segment (mean ± standard error). Time effect was found, $p = .01$, but not age effect.

Discussion

The purpose of the study was to examine inter-joint coordination variability during the STS fatiguing protocol with the hypothesis that the variability would increase along the course. Our data partially supported the hypothesis, in which fatigue resulted in an increased coordination variability, but only in particular joint coupling and only at a certain stage of fatiguing protocol. Specifically, knee-ankle variability from standing to sitting significantly increased during the last stage of fatiguing protocol.

In line with literature, inter-joint coordination became more variant after fatigue (Ferber & Pohl, 2011; Yang et al., 2018). Yang et al. reported a higher shoulder-elbow variability during the last 30-seconds of repetitive pointing task compared to that at the beginning of 30 seconds. Ferber et al. took another approach, in which a set of foot adduction contractions was used as a fatiguing protocol, and increased leg and foot coordinative variabilities were found during walking. In addition, such an increased variability was found not just at certain instant of the movement but during the majority of the cycle. Although there was no quantitative measure on variability during difference intervals of movement as we focused on deviation phase (systemic cycle-to-cycle variability with a cycle) in this study, we did observe qualitatively that the knee-ankle variability during the last stage of STS protocol (80-100%, dark blue in Figure 2-45) was higher during the most of the DOWN section and less distinct from other stages during the mid-point of the section, likely corresponding to the instant right before weight acceptance on the chair.

It is speculated that motor adaptation induced by fatigue is a process of motor learning, where participants exploit new motor strategies to adapt the increasing challenges raised by prolong task execution (Fuller et al., 2011), leading to an increased coordinative variability. Such an adaptation might be achieved by motor reorganization, meaning that spatial changes (e.g. increased range of motion of joints), temporal changes (e.g. early activation of agonist) or combination of the two (e.g. increased variability of fatigued joint) were made to compensate for the deficit at the fatigued site (Bonnard, Sirin, Oddsson, & Thorstensson, 1994; Côté, Mathieu, Levin, & Feldman, 2002; Qin, Lin, Faber, Buchholz, & Xu, 2014). The notion could be further supported by a study that compared coordinative variability between normal STS task and narrow base-of-support STS task using uncontrolled manifold. As task challenge increased, task-equivalent variability also increased in a way that ensured the task variables, such as CoM momentum, to maintain invariant (Reisman, Scholz, & Schöner, 2002). Taken together, it is argued that the central nervous system (CNS) makes efficient use of degree-of-freedom abundance in the human motor system along the course of fatiguing protocol to compensate for deficit and optimize the performance. The overlapping CRP curves at mid-point of DOWN section derived from different stages of fatiguing protocol may further imply that a certain amount of variability is required to ensure individuals to safely sit back to the chair.

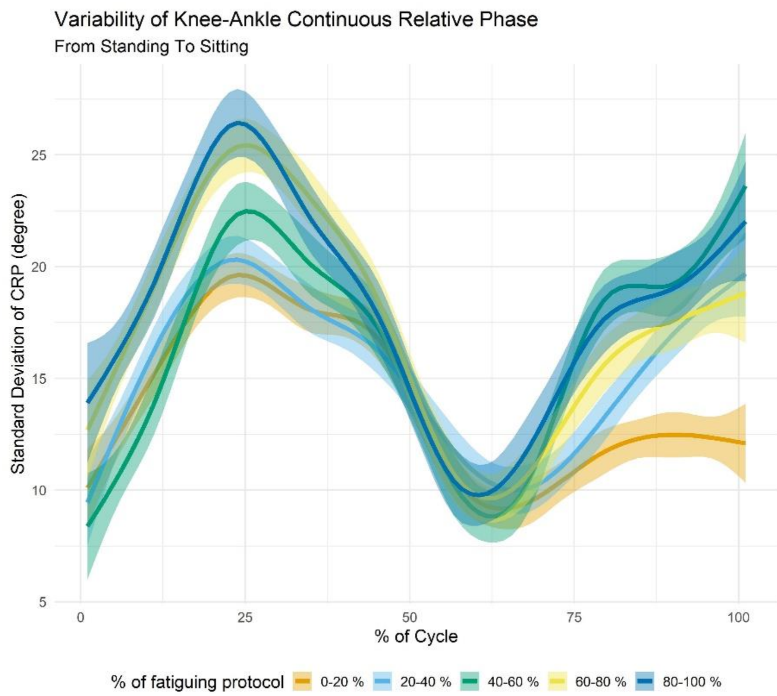

Figure 2-45. Ensemble CRP curve from all participants during DOWN section (mean±standard error)

There exists opposite results or insignificant findings regarding change in coordinative variability after fatiguing protocol or exhaustive exercise (Cowley & Gates, 2017; Hu & Ning, 2015; Miller, Meardon, Derrick, & Gillette, 2008; Samaan, Hoch, Ringleb, Bawab, & Weinhandl, 2015). Direct comparison across studies is not warranted due to discrepancy of fatiguing protocol, segments of interest, task demands and constraints, such as timing or accuracy, as well as methods to derive inter-joint coordination and/or variability measure. Nevertheless, differences in methodology from these studies provided some insights on why the increased variability was only observed in DOWN but not UP section. DOWN section could be viewed as a goal-orientating task, in which participants reached the goal (chair) every time when moving from a standing position back to sitting; whereas during UP section there was no specific target on the movement trajectory. In the fatigue literature using CRP variability, the coordinative variability during the goal-orientating task, such as repetitive pointing task, increased at post-fatigue (Yang et al., 2018); while during non-goal-orientating task, like exhaustive running or lifting, no significant change in coordinative variability was found (Hu & Ning, 2015; Miller et al., 2008). It is possible that effects of fatigue on coordinative variability was adjusted in movement speed during non-goal-orientating tasks. Individuals may slow down by adjusting movement trajectories over time during fatigue, in turn, counteract any effects of fatigue (Gates & Dingwell, 2011). On the contrary, timing error during goal-orientating task was well preserved at the expense of coordinative variability (Yang et al., 2018).

Decreased coordinative variability is representation of repeatable joint coupling, or a rigid control, where CNS reduces motor abundance to improved system stability or resiliency to perturbation. Essentially, a low CRP variability allows individuals to accomplish task within a narrow range of movements. This notion might be evident when muscle weakness induced by the fatiguing protocol was not substantial and/or the task of interest was not long enough to facilitate motor adaptation. For example, strength drop was about 25-30% at post-fatigue in Samaan et al. (2015) and Cowley et al. (2017), which reported a decreased coordinative variability during 5-times of cutting maneuver and 3-

minutes of ratcheting movement, respectively, after localized fatiguing protocol. In contrast, in the case where strength drop was significant (e.g. 67% in Ferber et al.), motor adaptation became necessary to compensate for the significant deficit as a result of fatigue, leading to an increased variability.

Future studies are needed to investigate the potential positive correlation between change in muscle weakness and change in coordinative variability. In our study, strength drop was considered minimal (18%), but the prolonged task of interest may provide participants enough time to gradually adapt for fatigue. It is worth noting that such an adaptation was prominent at the site away from the fatigued muscle. Hip and knee extensors were the most affected muscle group during STS fatiguing protocol (Yoshioka, Nagano, Hay, & Fukashiro, 2012), thus it is speculated that change in hip-knee variability was limited due to motor deficit, while contribution of less involved muscles or joints resulted in more variant movement pattern as a part of motor reorganization. That is, this distal change may be additive in contributing motor adaptation in a way that can efficiently compensate for fatigue toward the end of fatiguing course.

To our knowledge, studies investigating age-related changes in coordinative variability during or after fatiguing protocol have not been researched yet. In our study, no age effects were found during any stage of fatiguing protocol; both groups demonstrated increased knee-ankle variability at last-stage of fatiguing protocol. This is in accordance with literature that motor adaptation strategies in response to fatigue, indicated by changes in joint variability, were similar among older and young adults (Qin et al., 2014). In addition, we did not find any differences in isokinetic strength drop between two age group, as suggested by a systematic review suggested that older adults would develop greater fatigue during dynamic contraction (Christie, Snook, & Kent-Braun, 2011). The insignificant findings on age effect could be attributed to, in part, the healthy volunteer phenomenon, in which fatigue study tended to recruit participants with greater fatigue resistance. Applying the STS fatiguing protocol and the CRP variability measure on fatigue-prone population in the future would help elucidate how individual factors moderate effects of fatigue.

In conclusion, the impact of fatigue during repetitive sit-to-stand protocol is not only limited to a decline in force production but also manifested as increased knee-ankle variability when moving from standing to sitting. Future studies using sit-to-stand movement as a fatiguing protocol could adopt knee-ankle deviation phase as the index of fatigue.

Bridge

Chapter II validated the use of STS fatiguing protocol. In the next chapter, we applied this protocol and effects of fatigue on balance control, working memory and their interaction during unobstructed walking using dual-task paradigm.

CHAPTER III

GAIT BALANCE CONTROL DURING WALKING AFTER FATIGUE: EFFECTS OF AGE AND COGNITIVE DEMAND

This work has been prepared for publication. Szu-Hua Chen contributed to the concept of the studies, recruited subjects, collected data, wrote analysis software, performed data analysis, and prepared the initial manuscript. Dr. Li-Shan Chou contributed to the concept of the study, provided editorial support, and critically reviewed and revised the manuscript.

Introduction

Fatigue is prevalent in older adults. About one-third of people at the age of 70 reported feeling fatigue, and this number could reach as high as 68% at the age of 85 (Moreh et al., 2010). Perceived fatigability is a key indicator of declines in functional performance. Indeed, the severity of self-reported fatigue has been shown to be associated with risks of falling (Kamitani et al., 2019). On the other hand, in laboratory settings, researchers have adopted a fatigue protocol to reveal a correlation between performance fatigability and fall risks in older adults (Morrison et al., 2016). As accidental falls are a common problem among older adults, attention should be drawn to investigate changes in balance control during gait, when most falls occur, after fatigue in this population.

Fatigue has been shown to alter gait temporal-distance characteristics. Many studies have reported increased walking speeds (Barbieri et al., 2013; Morrison et al., 2016; Santos et al., 2016) and wider steps (Barbieri et al., 2016; Helbostad et al., 2007; Santos et al., 2016; Vieira et al., 2016) after fatigue, while others found the walking speed was unaffected (Barbieri et al., 2016; Helbostad et al., 2007) or the step width became narrow (Tay et al., 2016). Such inconsistency in post-fatigue gait changes could be due to the use of different fatigue protocols or outcome measures. Nonetheless, altered gait temporal-distance characteristics only provide limited insight to changes in balance control. Only one study reported gait balance measures, the margin of stability, and suggested a declined balance control post-fatigue (Vieira et al., 2016).

Distracted walking is also commonly observed during our daily life and can happen with the presence of fatigue, especially at the end of work or sport activity. The effect of fatigue on gait balance control may be exacerbated when concurrent cognitive demands increase. The ability to maintain a steady force production is reported to deteriorate after fatigue, and such deterioration is significantly worsen when performing a cognitive task concurrently (Lorist et al., 2002; Vanden Noven et al., 2014). It is speculated that a reduced amount of cognitive resource is available for optimized motor performance when additional cognitive demands are imposed (Gandevia, 2001). In addition, disruption in motor performance from dual-tasking interference was found to influence older adults more than young adults (Vanden Noven et al., 2014). In dynamic movements, a cognitive cost is also found necessary for motor reorganization or behavioral adaptation in order to compensate for the effects of fatigue (Simoneau et al., 2006; Terrier & Forestier, 2009).

Despite many findings on gait balance control or cognitive interference, only one study has examined how fatigue and cognitive demand interact to affect gait using a dual-task paradigm and compared the effects between young and older adults (Granacher et al., 2010). Furthermore, improvements in methodology are still needed to enrich the current fatigue literature. First, a single-joint isokinetic or isotonic protocol is widely used to induce fatigue. Findings derived from such protocol need to be interpreted with caution as the majority of daily activities impose physical demands with movements from more than one joint. Indeed, the systemic impacts of fatigue, such as corticospinal excitability, is different between whole-body and single-joint movements (Sidhu et al., 2013). Second, the concurrent cognitive task used as an interference needs to be selected carefully. Given that fatigue signal is dynamically integrated at prefrontal cortex (Tanaka et al., 2013), the selection of cognitive tasks should closely target this area, such as working memory tests (Owen et al., 2005), rather than a simple backward serial subtraction.

To address these gaps, this study is sought to examine how fatigue, induced by a whole-body movement, affects walking balance control in young and older adults with and without performing a concurrent cognitive task. Specifically, we adopted a well-established gait balance measure, medial-lateral motion of the whole-body center of mass (M-L CoM) (Chou, Kaufman, Walker-Rabatin, Brey, & Basford, 2004), as well as one of the most widely used working memory paradigms, the N-back test, to examine the effects of fatigue, induced by a repetitive sit-to-stand fatigue protocol, and age-related differences. We hypothesized gait balance control would become deteriorated at post-fatigue, and such an effect would be exacerbated during the dual-task condition and/or in older adults.

Methods

Participants with age ranges of 18-45 and 60-90 years, respectively, with normal hearing and able to walk on level ground without an assistive device were recruited. Exclusion criteria included 1) any history of neurological disease or head trauma that leads to impaired cognition, 2) diagnosed cardiovascular disease or metabolic disease, 3) impairments involved with bones, muscles, or joints within the past six months, 4) any of the following signs or symptoms present: chest discomfort or pain, shortness of breath at rest or with mild exertion dizziness or syncope, orthopnea palpitations or tachycardia, intermittent claudication, known heart murmur, unusual fatigue or shortness of breath with usual activities, 5) persistent symptoms of dizziness, lightheadedness, unsteadiness, or any other medical condition that may affect your ability to walk over ground, 6) any strenuous activity 24 hours prior to the examination that may affect walking and sit-to-stand ability, and 7) any out-of-routine consumption of alcohol or caffeine 24 hours prior to the examination that may affect energy level and/or balance control. All participants signed an informed consent approved by the local ethics committee after they were informed of study procedures and potential risks.

Study participants visited the laboratory twice, no more than a week apart, a familiarization session for the first visit and a testing session during the second visit. During the first visit, participant's anthropometric data, health history, perceived fatigue level, physical activity level, and cognitive ability were measured. The fatigue level was assessed using the Pittsburgh Fatigability Scale (Glynn et al., 2015) while the physical activity was measured using the Modified Baecke Questionnaire (Baecke, Burema, & Frijters, 1982). The higher score represents more fatigue and more active, respectively. The Mini-cog test was used to screen for cognitive deficits (Borson, Scanlan, Brush, Vitaliano, & Dokmak, 2000). The participant recalled zero of the 3 items or if the participant recalled 1-2 of the items and had an abnormal clock drawing were excluded in the participation. In addition, the gait task and cognitive test to be conducted during the second visit were introduced to participants for practice.

During the second visit, participants were asked to perform three tasks in random order: 1) single-task walking, 2) working memory test and 3) dual-task walking. In the single-task walking, participants were asked to walk continuously with a self-selected speed for 2 minutes along an oval shape loop, which includes a 15-m straight walkway for motion data collection. During the working memory test, participants performed a 3-back cognitive task while seated. The 3-back task lasted for two-minute and consisted of a sequence of random numbers played from a wireless headset (Blue Tiger USA) every two seconds. Participants were required to identify repeated numbers that were presented three digits before in the sequence. A total of 8 sets of random numbers were pre-programmed using Superlab 5 (Cedrus, CA) and randomly assigned to each testing for each participant. During dual-task walking, participants were instructed to walk and concurrently perform the 3-back task without prioritization to either task. All three tasks were performed again immediately after finishing a fatigue protocol.

A repetitive sit-to-stand (STS) task was selected as the fatiguing protocol. Participants were asked to sit on a standard wooden chair without armrests. A couple of repetitive sit-to-stand movements were performed as a warm-up trial. Participants were instructed to keep their feet in place and not to use arm movements to assist sit-to-stand movement during the entire protocol. The task was guided by a metronome set at a comfortable pace for each individual. Participants continued the task until 1) they were too fatigued to continue, 2) when the movement frequency fell below the set pace after encouragement, or 3) after 30 minutes (Barbieri et al., 2013). A Borg 15-point scale (6-20) (Borg, 1998) was used to measure each participant's Rating of Perceived Exertion (RPE) at baseline and throughout the fatiguing protocol as an indicator of perceived fatigability (Wilkins, Valovich McLeod, Perrin, & Gansneder, 2004).

Maximal isokinetic contraction of right knee extensor at 60°/second was measured with a dynamometer (Biodex Medical Systems, Inc., NY) during the following three time points: 1) before fatigue (pre-fatigue), 2) at the termination of fatigue protocol (post-fatigue), and 3) at the completion of the study (end) as an indicator of performance fatigability. Participants were given practice trials before performing the test. A total of three trials were conducted at each time point and the peak torque was recorded for further analysis.

A 12-camera motion analysis system (Motion Analysis Corporation, CA) with a set of 40 markers was used to record the whole-body movement during walking. Marker data from a total of five trials of each task were labeled using Cortex (Motion Analysis Corporation, CA) software before exported as .c3d file and processed using Visual3D (C-Motion, Inc., MD). Kinematic data were low-pass filtered with Butterworth fourth order filter at the cut-off frequency of 10 Hz. The whole-body center of mass (CoM) was calculated as a weighted sum of segmental center of masses. Outcome variables included 1) the range of M-L CoM displacement, 2) the peak M-L CoM velocity, 3) gait velocity, 4) stride width during a gait cycle and 5) 3-back test accuracy. Gait velocity was normalized to participant's body height, whereas the width of the anterior superior iliac spine (ASIS) was used to normalize stride width, M-L CoM displacement and velocity. One gait cycle was defined from a heel strike to the next heel strike of the same leg. The M-L CoM velocity was derived from position data using cross-validatory spline smoothing and differentiation (GCVSPL) method. The 3-back test accuracy was calculated as the percentage of correct responses to total numbers of stimuli. Reaction time of correct responses was also registered through wireless headset using SuperLab 5 program (Cedrus, CA) for further analysis.

Demographics, RPE, physical activity, general fatigue level and performance of the fatiguing protocol were analyzed using an independent *t* test for examining group differences in older and young adults. A one-way ANOVA was used to analyze differences in peak torque at pre-fatigue, post-fatigue and at the completion of the study between two age groups. For gait and balance measures as well as 3-back test accuracies (omission rate and commission rate), 2X2X2 three-way ANOVA were used with Age (young and older adults), Fatigue (pre-fatigue and post-fatigue), and Task (single-task walking, working memory test and dual-task walking) as factors. To account for random missing data due to missing target during the 3-back test, a linear mixed-effects model was established to examine changes in reaction time using Age, Fatigue and Task as fixed effects and Subject as random effect. For the pairwise comparison, Tukey method was applied to adjust *p* value. The correlation between changes in parameters was indicated by Pearson correlation. Alpha level was set at .05. Statistical analyses were conducted using R and Rstudio software with {afex}, {lme4}, {lmerTest} and {emmean} packages.

Results

A total of 46 participants were recruited. Only participants with RPE greater than 15 (hard) at post-fatigue were analyzed to reduce potential within-group variability (Susco, Valovich McLeod, Gansneder, & Shultz, 2004). This yielded to 17 young (9 females) and 17 older (9 females) adults for further analysis (Table 3-1). There were no significant differences in anthropometric data or subjective fatigue levels between older and young adults. However, older adults were more active than young adults as indicated by the Modified Baecke Questionnaire. Both groups performed the fatiguing protocol for a similar duration with 8 older adults and 9 young adults finishing the entire 30-minutes task. Older adults performed STS task with a slower pace than young adults (p=0.003). There was a significant strength drop from pre-fatigue to post-fatigue for both groups ($p < .001$). Although strength did recover at the completion of study ($p = .01$), the strength drop was still significant from pre-fatigue ($p = .02$).

Table 3-1. Demographic data and STS performance between two age groups

	older	**young**	***p* value**
age [a]	69.5±5.4	26.0±5.8	< 0.001
height (cm)	168.9±11.5	170.8±8.5	0.58
weight (kg)	71.5±16.9	72.4±14.9	0.86
physical activity level [a]	10.1±1.6	8.8±1.4	0.02
general fatigue level			
physical	16.7±4.9	19.2±8.2	0.28
mental	14.9±7.1	19.1±9.2	0.14
RPE			
at baseline	7.3±1.8	6.9±1.3	0.45
at post-fatigue	17.6±1.4	18.1±1.5	0.34
STS duration (s)	1041.4±756.0	1260.8±656.0	0.37
Metronome frequency (bpm) [a]	46.2±8.7	54.2±5.3	0.003
peak torque (N-m) [b]			
at pre-fatigue	97.0±43.3	135.3±65.7	I: 0.54
at post-fatigue	79.4±40.3	109.7±51.7	G: 0.05,
at completion of study	88.1±42.9	121.6±58.4	T: < .001

Note. a = significant group difference between older and young adults; b = significant differences across time; I = interaction effect, G = group effect, T = time effect

Gait velocity showed a Fatigue X Task interaction effect, $F_{(1, 32)} = 5.19$, $p = .03$. At both pre-fatigue and post-fatigue conditions, participants of both age groups walked slower when answering the 3-back test concurrently than just walking, $p < .001$. These results verified that the concurrent 3-back testing interference could be generally observed in this study. From pre- to post-fatigue, an increased gait velocity was only observed during dual-task walking regardless of age, $p = 0.02$. (Figure 3-1). Neither interaction or main effect of Age, Task or Fatigue factors was revealed for stride width.

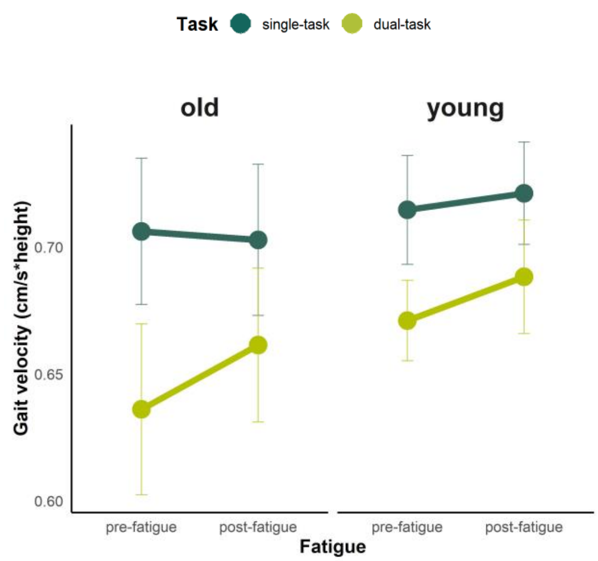

Figure 3-1. Changes in gait velocity from pre-fatigue to post-fatigue among two age groups. Significant Fatigue X Task interaction effect was observed, $p = .03$.

M-L CoM displacement and peak velocity showed a similar changing pattern, in which a Group X Fatigue effect was found (displacement: $F_{(1, 32)} = 6.14$, $p = .02$; velocity: $F_{(1, 32)} = 8.00$, $p < .01$). Regardless of task condition, young adults demonstrated a greater and faster M-L CoM movement at post-fatigue when compared to pre-fatigue; while such changes were not observed in older adults. (Figure 3-2)

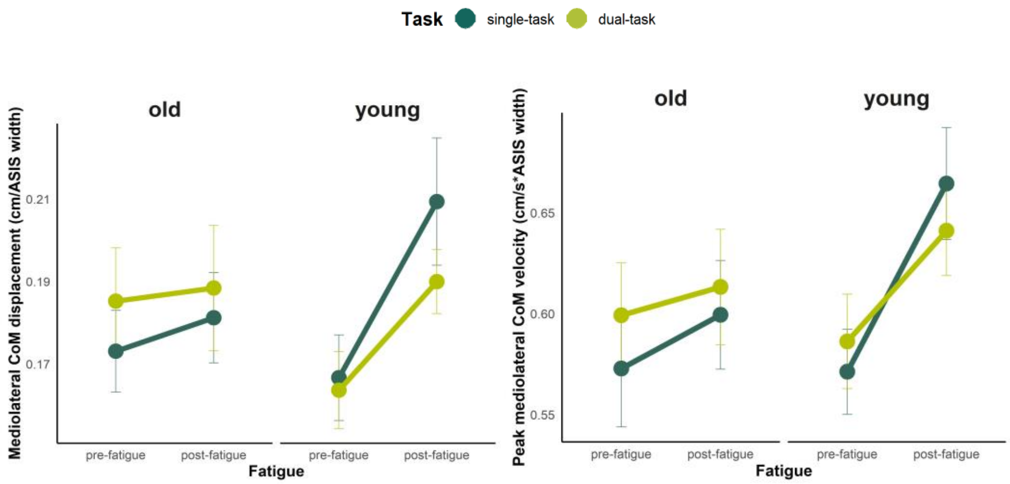

Figure 3-2. Changes in M-L CoM displacement (left) and peak velocity (right) of a gait cycle from pre-fatigue to post-fatigue among two age groups. Significant Group X Fatigue interaction effects were observed, $p = .02$ and $< .01$.

Further correlation analyses between changes in gait and balance measures were conducted to explore the gait adaptation in response to fatigue under different task conditions. One significant correlation was revealed, in which post-fatigue changes in gait velocity was negatively and moderately correlated with changes in M-L CoM displacement, suggesting that a greater increase in gait velocity is associated with a smaller increase in mediolateral sway. Such effect, however, was diminished during dual-task walking. (Figure 3-3)

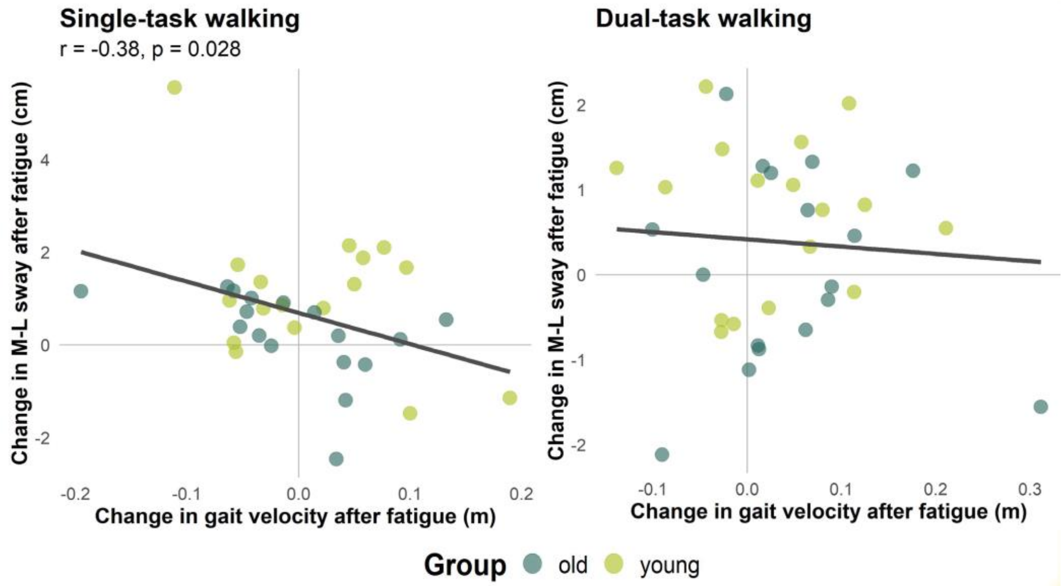

Figure 3-3. Correlation between changes in gait velocity and changes in M-L CoM displacement during single-task (left) and dual-task (right) walking.

The accuracies of 3-back test were not affected by age, task condition, or fatigue. However, a linear mixed-effects model revealed that older adults shortened their reaction time from pre-fatigue to post-fatigue ($p < .001$) while no significant change was found in young adults. In addition, at both pre-fatigue ($p = .02$) and single-task condition ($p = .01$), reaction time was faster in young adults than older adults (Figure 3-4).

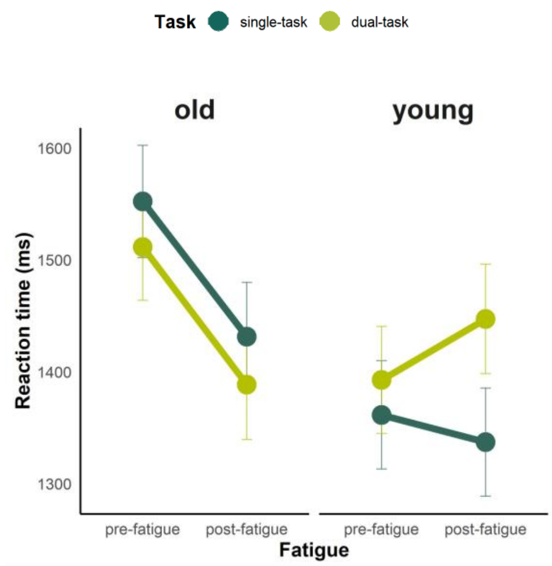

Figure 3-4. Changes in reaction time during 3-back test from pre-fatigue to post-fatigue among two age groups. Significant Fatigue X Group and Task X Group interaction effects were observed, $p < .01$ and $p = .02$.

Discussion

The purpose of the study was to investigate the effects of fatigue on gait balance control and working memory using a dual-task paradigm and to examine age-related changes in response to fatigue with the following hypothesis: 1) Balance control would become deteriorated at post-fatigue, and 2) fatigue effects would be exacerbated during dual-task condition and/or in older adults. The study hypotheses were only partially supported by our data. Balance control, as measured by M-L CoM motion, became deteriorated after fatigue. Such a result, nevertheless, was observed only in young adults, not in older adults. The increased cognitive demand during dual-task walking seemed to negatively affect gait adaptation after fatigue as indicated by the diminished correlation between changes in gait velocity and CoM sway. Although we hypothesized aging as an exacerbating factor to fatigue effects, the analysis showed an opposite result, in which older adults improved reaction time from pre-fatigue to post-fatigue while maintaining the mediolateral body sway.

Using the dual-task paradigm, Granacher et al. (2010) have shown differential age-related changes in gait velocity, in which young adults decreased their velocity in single-task walking while older adults increased theirs during dual-task walking after fatigue. In the present study, we did not observe a similar finding. In fact, there was a task-related change rather an age-related change. Although perceived fatigability was comparable in both studies (RPE: young- 16.9±1.5 vs. 18.1±1.5; old- 16.1±1.8 vs. 17.6±1.4), the protocol to induce performance fatigability were quite different. The fatigue criteria in their study was three consecutive knee extensor contractions below 50% of maximum after repetitive isokinetic contractions, while in our study the average strength drop of knee extensor in both groups was about 18%, not to mention there were more than one muscle groups were involved. A great amount of strength loss may result in an immediate compensation, as argued by Granacher et al. (2010), young adults adopt a conservative gait after fatigue, whereas older adults compensated such decreases by increasing hip power or simply tried to overcome feelings of physical discomfort as quickly as possible given the test was conducted during a short walk. Conversely, we used a multi-joint fatiguing protocol with small amount of strength drop induced, thus no obvious change in gait characteristics were expected. In addition, the gait parameter was measured during a 2-minute walk. Participants may not be able to keep up the faster speed the entire time if they strategically increase the gait velocity in order to end the test early.

Since balance control is flexibly regulated among different motor systems (e.g.

visual, cognitive or proprioception), it is speculated that healthy participants could maintain the optimal motor output (stable gait velocity) even with the presence of neuromuscular disturbance (fatigue) through a behavioral adaptation (Mulder, Zijlstra, & Geurts, 2002). The compensation, however, may require cognitive demand be allocated to active control task (Simoneau et al., 2006). Once the costs of compensation exceed an individual's capacity, such as during dual-task walking, an optimal gait velocity may be no longer reached. In fact, the correlation between CoM motion and gait velocity during dual-task condition was not evident anymore in our study, suggesting the strategy used to tightly regulate the gait was compromised as a result of increased cognitive demand. The increased gait velocity during dual-task walking after fatigue may be also postulated as a strategy to improve stability. The gait stability was shown reaching the best when walking at 100-110% of regular velocity (Jordan, Challis, & Newell, 2007). Our results fit within the range with an average speed increased to 103% during dual-task walking. Since there was no control group in the study, we cannot rule out the possibility of learning effect. Granacher et al. (2010) has shown that the older adults did not continue increasing dual-task walking velocity during a re-test at 5-minutes post-fatigue, suggesting the leaning effect only plays a minor role in the findings. Our effort to reduce the impact of the learning effect was to include several practice sessions during participant’s first visit and to give another practice session before data collection.

Unlike the finding of gait velocity, we found an age-related change in mediolateral CoM motion. Young adults demonstrated a faster and greater CoM motion after fatigue, indicating a disturbance to gait balance control (Chou et al., 2004), while older adults maintained theirs. Such a result in young adults is in agreement with our prior study as well as previous literature, in which fatigue-induced deterioration was indicated by the decreased margin of stability and decreased stability of trunk motion (Vieira et al., 2016). Although Nagano et al. have found age-related differences in minimum toe clearance during walking (Nagano et al., 2014), suggesting older adults may increase tripping risks due to a smaller clearance height after fatigue, Granacher et al. (2010) have demonstrated the opposite results, showing older adults decreased step length variability and perhaps improved gait stability after fatigue. Yet, there is no study, to our knowledge, investigating the effects of fatigue on balance control in older adults. The insignificant changes in CoM motion in our older participants could be explained by several factors. First, our older participants may have developed adaptability to fatigue. Although older adults have been known to have deficits in several systems that regulate dynamic stability (muscle properties, proprioception, cognitive function, etc.), the natural history of aging may lead to an adapted motor pattern, such as distal-to-proximal redistribution (DeVita & Hortobagyi, 2000), in which older adults predominantly rely on hip musculature for power generation not at the knee or ankle. Thus, older adults in our study were less susceptible to the STS fatiguing protocol, and in turn, demonstrated less changes in CoM motion than young adults.

Second, our findings may be representative of healthy volunteer effect, in which fatigue study most likely recruits participants with relatively high fatigue-resistance. In fact, our older adults reported higher physical activity level compared to the young adults. Nevertheless, according to Barbieri et al.'s investigation on how physical activity level modulates effects of fatigue, fatigue-induced changes in gait kinematics and kinetics were not dependent on individual's physical activity level (Barbieri et al., 2013). Lastly, it is reasonable to assume that our healthy older adults walked with the frontal plane CoM motion closer to their maximum capacity, thus perturbation could not be manifested in the form of CoM displacement or velocity after fatigue. The instantaneous velocity of CoM and its location are two key components of feasible stability region, which predicts whether the balance control could be maintained (Pai & Patton, 1997). Older adults may have fallen once the changes in the CoM motion exceed the stability region. It is still unclear, however, at what expense the older adults used to maintain the resultant body sway.

In contrast to our hypothesis, older adults but not young adults demonstrated improved cognitive function, indicated by a faster reaction time, from pre- to post-fatigue. Findings from young adults were in line with previous literature, in which fatigue did not affect cognitive performance but walking balance control (Kao et al., 2018); whereas findings from older adults were in accordance with a similar result that showed soldiers enhanced reaction time while maintaining their balance at shooting position after fatigue (Bermejo, García-Massó, Paillard, & Noé, 2018). Although individuals may benefit from the acute physiological responses to the exercise (e.g. endorphins, serotonin, dopamine), a meta-analysis suggests that all aspects of memory, including what we tested here- working memory, are not improved by acute exercise (Chang, Labban, Gapin, & Etnier, 2012). The observed result might be attributed, in part, to learning effect. Although we have given a practice session on a separate day and several practice trials prior to testing, we cannot fully rule the possibility that participant learned from this two-minute 3-back test and carried this learning to the post-fatigue testing.

While it is unclear what specific mechanism is responsible for the improved working memory after fatigue, the differential changes between older and young adults may be speculated from studies on brain function. The dorsolateral prefrontal cortex (DLPFC) has been suggested as an important neural substrate that regulates fatigue feedback and adjusts central drive for the ongoing task (Tanaka et al., 2013). Thus, it is reasonable to hypothesize that an additional demand from the working memory test imposed on the same region may lead to a deteriorated cognitive performance due to central capacity limit (Saults & Cowan, 2007). Although the exercise-elicited cortical activation is most marked over the left DLPFC in young adults (Yanagisawa et al., 2010); older adults dominantly recruit right frontopolar area (FPA) after an acute bout of exercise (Hyodo et al., 2012). In fact, the DLPFC takes an inhibitory control while FPA is responsible for an excitatory control during cognitive performance (Medalla & Barbas, 2010). The different neural substrates for activity-elicited activation between older and young adults may explain the observed findings of reaction time in our study.

One of our study limitations is that we did not include an additional testing session to examine to what extent the time and/or recovery factors play roles in these fatigue-induced findings. Previous studies have shown that 20-minutes post-fatigue interval was not enough to reach a full recovery (Barbieri et al., 2016; Vieira et al., 2016). Thus, the duration of the experiment was tightly controlled in our study to ensure the entire data collection finished within 20 minutes after completion of fatiguing protocol. Lack of inclusion of control group is another limitation. Yet, a well-controlled activity as opposed to STS fatiguing protocol may not exist. Moreover, if experimental and control studies were done on the same day, individual differences of fatigue recovery may become a confounding factor; while day-to-day fluctuation of fatigue status may also lead to mixed results if studies were done on separate days. We believe, with the current standardized protocol, we reduced the impact of learning effect at our best by giving enough practice sessions to participants.

In conclusion, an increased frontal plane CoM motion was observed at post-fatigue in young adults but not older adults, fatigue effects were not exacerbated during dual-task walking, and older adults demonstrated a shorter reaction time from pre- to post-fatigue while maintaining a similar mediolateral body sway. Older adults may have a better adaptation and response to a fatigued condition. These results may serve as a scientific evidence and point out another prospective when it comes to prevention of falling accidents in workers whose job requires high physical and/or cognitive demand. Nevertheless, it is still unknown if such finding remains true if the primary locomotion task requires a high-level attention, such as crossing an obstacle, which is also a common scenario where older adults fall.

Bridge

Chapter III examined effects of fatigue on balance control, working memory and their interaction during unobstructed walking using dual-task paradigm. In the next chapter, we applied the same study paradigm and investigated the effects of fatigue during obstructed walking, in which falling accidents frequently happen.

CHAPTER IV

GAIT BALANCE CONTROL DURING OBSTACLE-CROSSING AFTER FATIGUE: EFFECTS OF AGE AND COGNITIVE DEMAND

This work has been prepared for publication. Szu-Hua Chen contributed to the concept of the studies, recruited subjects, collected data, wrote analysis software, performed data analysis, and prepared the initial manuscript. Dr. Li-Shan Chou contributed to the concept of the study, provided editorial support, and critically reviewed and revised the manuscript.

Introduction

Fatigue is a frequently mentioned symptom in older adults (Moreh et al., 2010). Although it is underappreciated in research and undertreated in clinics (Yu, Lee, & Man, 2010), fatigue and fatigability (performance-induced fatigue symptom) can represent a physiologic warning sign to mobility and mortality. Previous studies have shown a significant association of fatigue with mortality, functional status (Moreh et al., 2010) and decline in walking speed (Mänty et al., 2012). Moreover, fatigability induced by prolonged walking activity increases the risk of falling accidents in older adults (Morrison et al., 2016). In fact, a two-year follow-up study found that severity of fatigue increases the likelihood of future falling accidents (Kamitani et al., 2019). Thus, attention should be made on fatigue-related gait imbalance in older adults.

A greater gait variability was reported post-fatigue in healthy young adults (Kao et al., 2018; Vieira et al., 2016). However, the margin of stability was found to increase in one but decease in the other study. Such inconsistency may stem from the use of different fatiguing protocols (isotonic exercises versus prolonged walking). In fact, pathways of fatigue effect could vary depending on the fatiguing protocol. Whole-body exercise was shown to reduce corticospinal excitability, while movement with loading on the local joints was reported to increase it (Sidhu et al., 2013). Given most daily activities involve multi-joint movement, such fatiguing protocol may be more clinically relevant. However, little is known on how a multi-joint fatiguing protocol affects older adult’s balance control during locomotion.

Cognition-gait interaction with aging has been well-documented (Al-Yahya et al., 2011; Montero-Odasso et al., 2012). Researchers have identified parallel decline of gait and cognition in older adults (Watson et al., 2010). Using a dual-task paradigm (e.g. walking while preforming a cognition-demanding task concurrently), gait imbalance and falls could be results of such interference (dual-task cost). Given that the integration center of fatigue feedback is located predominately at the pre-frontal cortex (Thomas & Stephane, 2008), this cognition-gait interaction would be affected by fatigue (Granacher et al., 2010). Older adults were reported to exhibit a reduced gait variability and faster gait speed after fatigue during dual-task walking, which is in accordance with the results in chapter II of this dissertation. Although increasing the gait velocity may be a strategy to optimize the dynamic balance (Jordan et al., 2007), time to acquire visuospatial information for proper movement planning is reduced.

Obstacle-crossing is a well-validated task to pose the visuospatial demand when studying balance control during walking. Mediolateral center of mass (CoM) movement during obstacle crossing was reported to distinguish older fallers from non-fallers (Chou et al., 2003). Similarly, increasing visuospatial demand, such as texting while walking, was shown to perturb CoM control on the frontal plane along with a closer leading foot placement to the obstacle (Chen, Lo, Kay, & Chou, 2018). Therefore, this study sought to investigate how fatigue, induced by a repeated multi-joint movement, interferes with older adult's balance control and crossing characteristics during single- and dual-task obstacle-crossing. We hypothesized that 1) older adults would demonstrate an increased frontal plane CoM movement, decreased leading foot placement and cognitive performance to a greater degree at post-fatigue compared to young adults and 2) a concurrent cognitive demand during obstacle-crossing would exacerbate the effects of fatigue.

Methods

Participants

Due to a lack of study with a similar experiment design, a priori power analysis, with a two-tails alpha error of .05 and 90% power, was conducted using the dual-task cost (e.g. reduction of performance under dual-task relative to the single-task condition) in gait velocity during level walking previously reported in the literature (Granacher et al., 2010) and indicated a minimum of 30 participants were required. A total of 46 participants were recruited, but only data from participants who reported the Rating of Perceived Exertion (RPE) greater than 15 (hard) on a Borg 15-point scale (6-20) at post-fatigue were analyzed (Susco et al., 2004). Therefore, seventeen older (9 females) and seventeen young (9 females) healthy adults were included in the study.

All participants reported no histories of neurological disease, diagnosed cardiovascular disease, impairments involved with bones, muscles, or joints within the past six months, or any of the following signs or symptoms: chest discomfort or pain, shortness of breath at rest or with mild exertion dizziness or syncope, orthopnea palpitations or tachycardia, intermittent claudication, known heart murmur, unusual fatigue or shortness of breath with usual activities, persistent symptoms of dizziness, lightheadedness, unsteadiness or any other medical condition that may affect their ability to walk. In addition, they were refrained from any strenuous activity or any out-of-routine consumption of alcohol or caffeine 24 hours prior to the experiment. All participants signed the informed consent form after they were informed of the study protocol, which was approved by the Institutional Review Board of the university.

Procedure

The study protocol consisted of two visits, no more than a week apart. The first visit was a familiarization session, in which participants were asked to practice gait and cognitive tasks to be used during the second visit. In addition, participant's anthropometric data, health history, trait fatigue level, physical activity level, and cognitive ability were measured. The fatigue level was measured using the Pittsburgh Fatigability Scale (Glynn et al., 2015) with a higher score indicating a more fatigued trait. The physical activity was measured using the Modified Baecke Questionnaire (Baecke et al., 1982) with a higher score representing a more active status. The Mini-cog test was used to screen for cognitive deficits (Borson et al., 2000). The participant recalled zero of the 3 items or if the participant recalled 1-2 of the items and had an abnormal clock drawing were excluded in the participation.

During the second visit, each participant performed three tasks at pre- and at post-fatigue, respectively, in a random order: single-task obstacle-crossing (SO), dual-task obstacle-crossing (DO) and working memory test (WM). In the SO condition, participants were instructed to walk toward an obstacle placed in the middle of a 15-m walkway and circle an oval shape loop (Figue 4-1) at their self-selected speed and manner for 2 minutes. The obstacle was made of a plastic pipe with a diameter of 1.3 cm and a length of 1.3m, which was placed on two adjustable metal stands at 10% of participant's body height. In the WM condition, a 3-back cognitive test were employed. The 3-back test consisted of a sequence of numbers played from a wireless headset (Blue Tiger USA) every two seconds for 2 minutes. Participants were required to identify the repeated numbers that were presented 3 numbers before in the sequence. Different sets of 3-back test were pre-programmed using Superlab 5 (Cedrus, CA) and randomly assigned to participants. In the DO condition, participants performed SO and WM simultaneously without prioritization to either task (Figure 4-1).

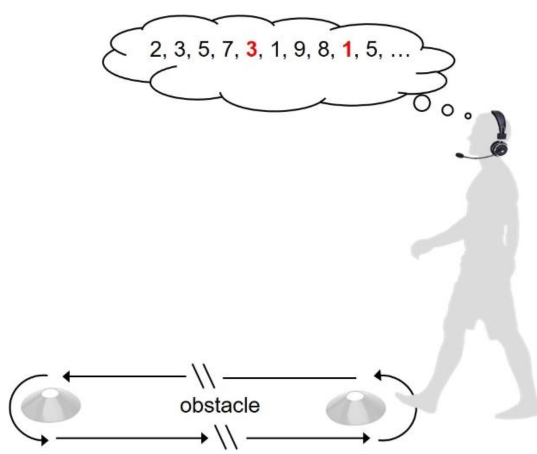

Figure 4-1. Illustration of dual-task obstacle-crossing (DO), which equals to single-task obstacle-crossing (SO) + working memory task (WM).

Fatiguing protocol was a repetitive sit-to-stand task (Barbieri et al., 2013). Participants were instructed to sit and stand from a standard wooden chair without armrests at their comfortable pace (Figure 4-2). The pace was then fixed throughout the protocol and guided by a metronome. In addition, during the protocol, participants had to keep their feet in place and not to use arm movements to assist sit-to-stand movement. A couple of practice trials were performed as a warm-up prior to the protocol. Participants continued the fatiguing protocol until 1) they were unable to continue, 2) when the movement frequency fell below prescribed pace after encouragement, or 3) after 30. A Borg 15-point scale (Borg, 1998) was used to measure each participant's RPE at pre-fatigue and throughout the fatiguing protocol as an indicator of perceived fatigability (Wilkins et al., 2004).

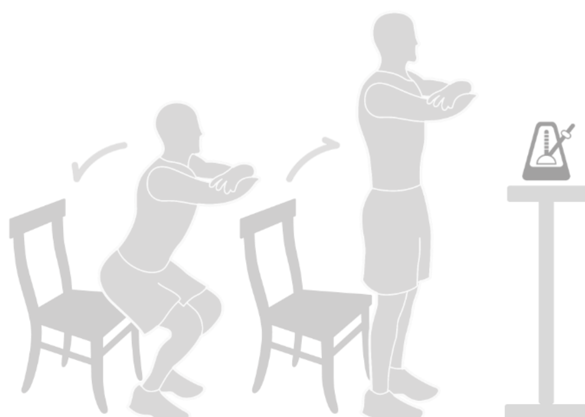

Figure 4-2. Illustration of the repetitive sit-to-stand fatiguing protocol

A 12-camera motion capture system (Motion Analysis Corp., Santa Rosa, CA) was used to collet kinematic data of the whole-body when walking along the 15-m walkway and stepping over the obstacle at a sampling frequency of 100 Hz. A set of 40 retro-reflective markers was place on bony landmarks, including top of head, ears, shoulders, C7, sternum, right scapula, elbows, medial and lateral wrists, middle metacarpals, anterior superior iliac spines (ASIS), posterior superior iliac spines (PSIS), mid-thighs, lateral knees, tibial tuberosities, lateral shanks, lateral ankles, toes, 5^{th} metatarsals, 5^{th} tuberosities, heels, medial heels. Two additional markers were affixed at both ends of the obstacle. To indicate performance fatigability, the maximal isokinetic torque knee extensor torque at 60°/second was recorded using a dynamometer (Biodex Medical Systems, Inc., NY) at pre-fatigue, post-fatigue and the completion of the study (end). Participants were given practice trials before performing the test. A total of three trials were conducted at each time point and the peak torque was recorded for further analysis.

Data analysis

Marker trajectory data from five trials of each walking task were labeled using Cortex software (Motion Analysis Corporation, CA) before exported as .c3d file and processed using Visual3D (C-Motion, Inc., MD). Kinematic data were low-pass filtered with a Butterworth fourth order filter at the cut-off frequency of 10 Hz. All dependent variables were then calculated using R (R Foundation for Statistical Computing, Vienna, Austria) and Rstudio software (RStudio, Inc., Boston, MA). Obstacle-crossing was characterized with the toe-obstacle clearances and foot placements of trailing and leading limbs (Figure 4-3). Leading limb was referred to the limb that crossed the obstacle first while the trailing limb crossed the obstacle the after. Toe-obstacle clearances was calculated as the vertical distance between the obstacle and the toe marker when the toe marker was directly above the obstacle. Foot placement of trailing limb was determined as the horizontal distance between the obstacle and the toe marker prior to crossing, whereas immediately after crossing the distance between the obstacle and heel marker was called foot placement of leading limb.

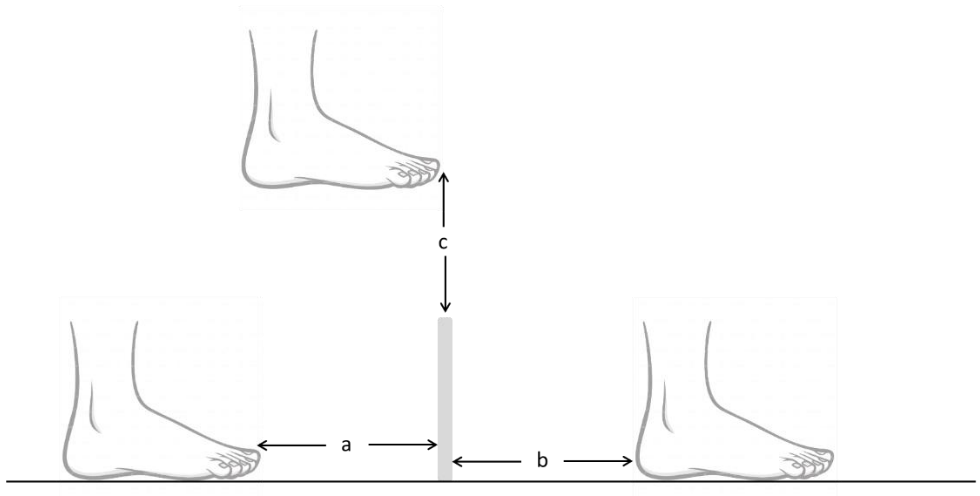

Figure 4-3. Illustration of obstacle-crossing characteristics. (a) foot placement of trailing limb, (b) foot placement of leading limb, and (c) toe-obstacle clearance.

Gait balance control was examined using a whole-body CoM movement, which was calculated as a sum of the weighted center of masses using Visual3D. The velocity of CoM was then derived from position data using a cross-validatory spline smoothing and differentiation (GCVSPL) method. Outcome variables included the range of mediolateral CoM (M-L CoM) displacement, the peak M-L CoM velocity, and the average anteroposterior CoM velocity (gait velocity) during the crossing stride, defined as the gait cycle between heel strikes of the trailing limb immediately before and after obstacle-crossing. Additionally, the crossing step width was determined as the mediolateral distance between the trailing heel marker before crossing and the leading heel markers after crossing. Gait velocity was normalized to participant's body height whereas the width of

ASISs was used to normalize step width, M-L CoM displacement and velocity. As for cognitive performance, accuracy of the 3-back was calculated as the percentage of correct responses to total numbers of stimuli. Reaction time of correct responses was also registered through the wireless headset using SuperLab 5 for further analysis.

Statistical analysis

Anthropometric measures, RPE, physical activity, general fatigue level and performance of the fatiguing protocol were analyzed using independent *t* tests to examining group differences in older and young adults. Data greater than three standard deviation was deemed as outliers and tossed from the analysis. A one-way ANOVA was used to analyze differences in peak torque at pre-fatigue, post-fatigue and at the end between two age groups. For gait and balance measures as well as 3-back test accuracy, 2X2X2 three-way ANOVAs were used with Age (young and older adults), Fatigue (pre-fatigue and post-fatigue), and Task (single-task and dual-task) as factors. To account for random missing data due to missing targets during the 3-back test, a linear mixed-effects model was established to examine changes in reaction time using Age, Fatigue and Task as fixed effects and Subject as random effect. For the pairwise comparison, Tukey method was applied to adjust *p* values. Alpha level was set at .05. Statistical analyses were conducted using R and Rstudio software with {afex}, {lme4}, {lmerTest} and {emmean} packages.

Results

Data from 17 older adults (age: 69.5±5.4) and 17 young adults (age: 25.9±5.8) were analyzed. There were no significant group differences in body height, body weight and general fatigue level, and baseline RPE (older: 7.3±1.8; young: 6.9±1.3). Older adults, nevertheless, reported a higher activity level (10.1±1.6) than young adults (8.8±1.4). Both groups seemed to perform the fatiguing protocol to the same extent, in which no significant group differences were found in RPE at post-fatigue (older: 17.6±1.4; young: 18.1±1.5), strength drop (older: 18.1±7.0%; young: 18.9±21.3%) and time-to-task failure (older: 1041.4±756.0 s; young: 1260.8±656.0 s). There was a significant fatigue effect in strength regardless of age ($p < .001$). Although strength did recover at the completion of study when compared to post-fatigue ($p = .01$), the strength drop was still significant from pre-fatigue ($p = .02$). Eight older adults and 9 young adults ended up finishing the 30 minutes task, with older adults performed task with a slower pace (46.2±8.7 bpm) than young adults (54.2±5.3 bpm).

From the 3-way ANOVA analysis using fatigue, task and group as factors, participants crossed the obstacle faster in the single-task compared to dual-task condition, $F_{(1, 32)} = 20.86$, $p < .001$. (Figure 4-4)

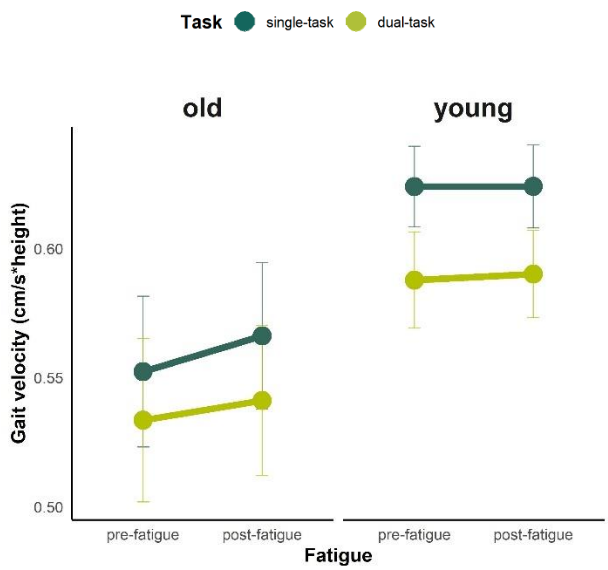

Figure 4-4. Changes in gait velocity from pre-fatigue to post-fatigue among two age groups. Significant Task main effect was observed, $p < .001$.

Similar task main effects were also found in M-L CoM displacement and peak velocity, step widths, leading limb foot placement and toe-obstacle clearance. Regardless of age or fatigue, participants swayed more ($F_{(1, 32)}= 8.44$, $p = .007$) and faster ($F_{(1, 32)}= 6.38$, $p = .02$), had a wider step width ($F_{(1, 32)}= 4.90$, $p = .03$), lifted the leg higher ($F_{(1, 32)}= 13.75$, $p < .001$), and placed foot closer to the obstacle after crossing ($F_{(1, 32)}= 7.88$, $p = .008$) during dual-task condition in comparison to single-task condition.

M-L CoM displacement and peak velocity showed a similar changing pattern, in which a Group X Fatigue effect was found (displacement: $F_{(1, 32)}= 8.12$, $p = .008$; velocity: $F_{(1, 32)}= 4.44$, $p = .04$). Pairwise comparison revealed that young adults had a more and faster mediolateral sway from pre-fatigue to post-fatigue. Such an effect was not found in older adults. Additionally, older adults demonstrated a greater sway compared to young adults at pre-fatigue. (Figure 4-5)

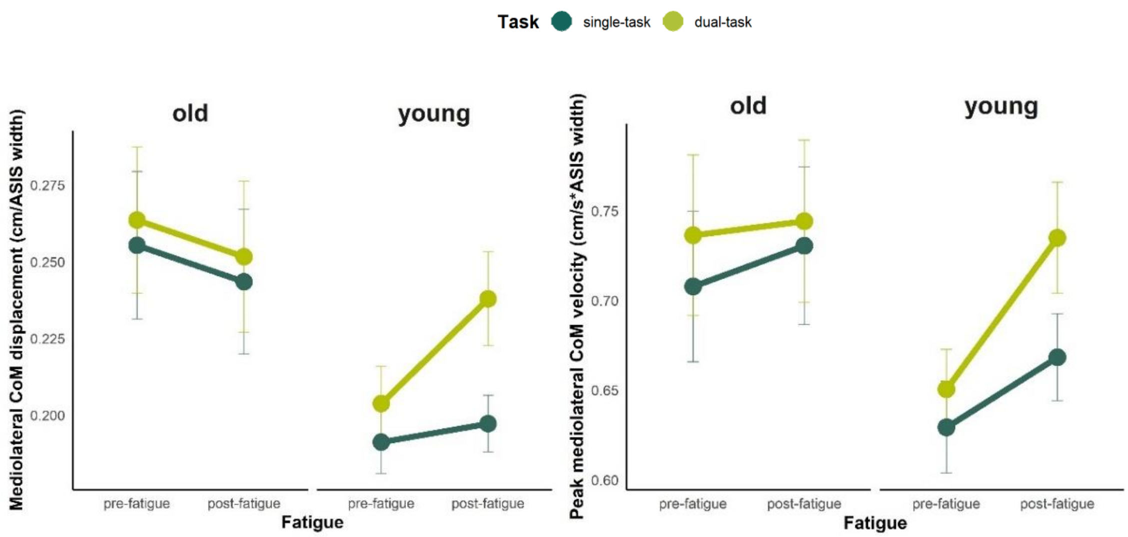

Figure 4-5. Changes in M-L CoM displacement (left) and peak velocity (right) of a crossing gait cycle from pre-fatigue to post-fatigue among two age groups. Significant Group X Fatigue interaction effects were observed, *p* = .008 and = .04.

For crossing characteristics, after fatigue participants increased their step width during the crossing step, $F_{(1, 32)}$= 8.59, *p* = .006. At pre-fatigue, toe-obstacle clearance of trailing limb was higher when crossing the obstacle while answering the 3-back test, $F_{(1, 32)}$= 6.03, *p* = .02, suggesting the difference between dual-task and single-task (dual-task cost) was diminished at post-fatigue. Similarly, a 3-way interaction revealed that young adults demonstrated a higher leading toe-obstacle clearance during dual-task condition than single-task condition at pre-fatigue, $F_{(1, 32)}$= 4.76, *p* = .04. As for foot placement, older adults were found placing their foot closer to the obstacle after crossing compared to young adults, $F_{(1, 32)}$= 8.33, *p* = .007. No effects were found in trailing limb placement. (Figure 4-6)

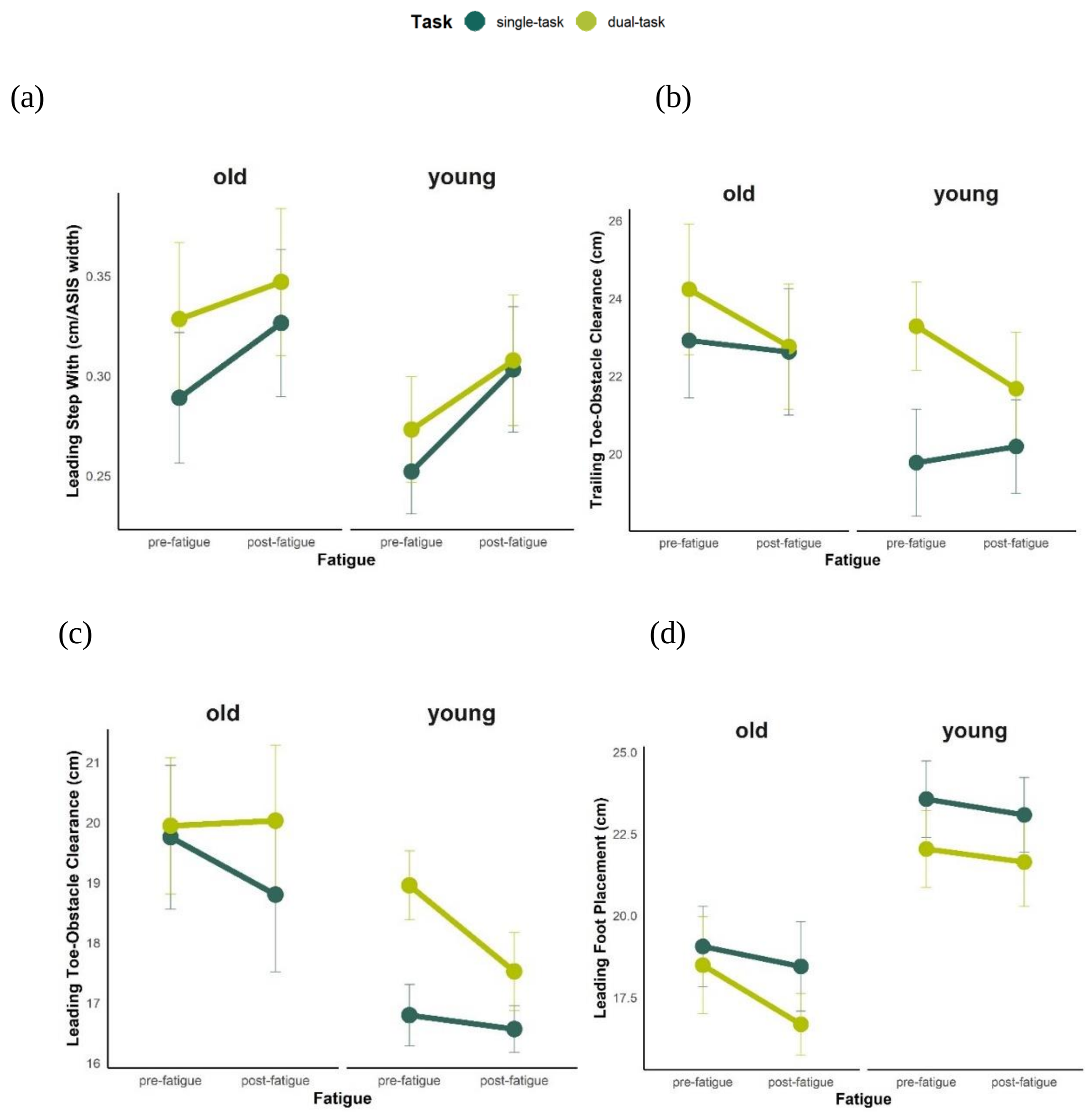

Figure 4-6. Changes in crossing characteristics of a crossing gait cycle from pre-fatigue to post-fatigue among two age groups. (a: step width, b: trailing toe-obstacle clearance, c: leading toe-obstacle clearance, d: leading foot placement). Task main effect was found in step width, toe-obstacle clearance and foot placement. Step width also shows a Fatigue main effect, $p = .006$. Leading foot placement also shows a Group main effect, $p = .007$

Accuracy of 3-back test was increased after fatigue regardless of age groups and task conditions, $F_{(1, 32)}$= 4.72, p = .04. Reaction time follows the similar trend, in which participants answered 3-back task faster at post-fatigue than pre-fatigue, $F_{(1, 779)}$= 14.77, p < .001. The shorter reaction time was also found during single-task versus dual-task, $F_{(1, 768)}$= 6.03, p = .01, as well as in young adults versus older adults, $F_{(1, 32)}$= 5.09, p = .03. (Figure 4-7)

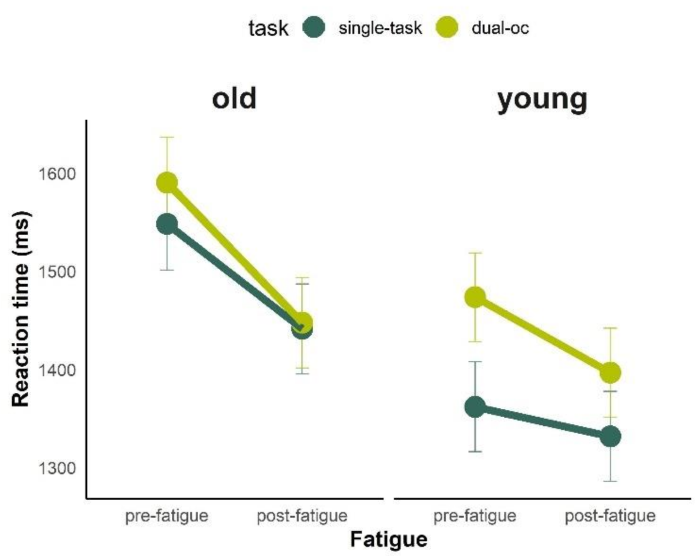

Figure 4-7. Changes in reaction time when performing 3-back test from pre-fatigue to post-fatigue among two age groups. Significant Group, Task and Fatigue main effects were observed.

Discussion

This study aimed to investigate how fatigue induced by a repetitive sit-to-stand movement affects obstacle-crossing characteristics and balance control in older and young adults with the following hypotheses: 1) participants would deteriorate mediolateral balance control and adapts crossing characteristics after fatigue, 2) cognitive demand would exacerbate the effects of fatigue, and 3) effects of fatigue would be more prominent in older adults. The current data analyzed from 34 participants did not support the hypotheses. Mediolateral CoM did increase its displacement and peak velocity after fatigue, but such an effect was only observed in young adults. Additionally, accuracy and reaction time of the 3-back test improved regardless of age after fatigue.

In studies investigating effects of fatigue during walking, including our findings reported in chapter III, a faster gait velocity was reported post-fatigue (Granacher et al., 2010). A faster gait velocity may be a strategy to minimize balance perturbation, but it may result in reduced time to acquire visuospatial information about the environment. previous study reported the similar result during obstacle-crossing (Barbieri et al., 2014). Nevertheless, we did not find any fatigue-induced change in gait velocity during obstacle-crossing. Participants maintained the same walking speed from pre-fatigue to post-fatigue. The inconsistent findings may be originated from the pre-determined pace used during repetitive STS protocol. Barbieri et al. (2014) applied a pace of 60 bpm on all participants, while our participants chose their comfortable pace and were guided by this pace throughout the protocol. As a result, the time to task failure (endurance time) in our study was much longer. It is speculated that participants were able to accommodate the fatigue effect and slowed down before the obstacle to ensure proper crossing. The consistent gait velocity may also explain why several crossing characteristics, such as toe-obstacle clearance and foot placement, were not affected by fatigue. Step width appeared to be a sole gait characteristic that increased from pre-fatigue to post-fatigue. In line with literature, the increased step width facilitated the balance control in the mediolateral direction (Barbieri et al., 2014).

Mediolateral CoM sway and peak velocity post-fatigue were increased in young adults but not in older adults. The finding was consistent with chapter III regarding effects of fatigue during unobstructed walking. The increased mediolateral CoM motion in young adults was similar to the amount of motion been observed in individual with gait imbalance (Chou et al., 2003), suggesting that fatigue induced by a repetitive fatiguing protocol could perturb gait balance control. Although there were no group differences in perceived and performance fatigability, older adults failed to demonstrate the similar change in CoM motion. There were three possible reasons, as discussed in chapter III, that may explain such insignificant change in older adults. First, older adults may have developed different movement patterns that help them become less susceptible to the fatiguing protocol. For example, a well-known distal-to-proximal redistribution mentions that older adults predominantly rely on hip musculature for power generation (DeVita & Hortobagyi, 2000), indicating they may be less responsive to STS protocol. Additionally, the way of obstacle-crossing developed by a nature history of aging may help them easily adapt any perturbation. Compared to young adults, older adults placed their leading limb closer to the obstacle. In fact, placing the leading limb closer to the obstacle was a compensatory strategy to reduce the mediolateral body sway (Chen et al., 2018). A faster placement of the leading limb on the ground after crossing helps to establish a larger base of support for a better stabilization, therefore the CoM motion becomes less vulnerable. Second, given the healthy volunteer effect, the older adults recruited in the study reported a higher physical activity level compared to the young adults. Although a previous study has shown that effects of fatigue was not dependent of the physical activity level (Barbieri et al., 2013), the older adults may have experienced more fatigued episodes and developed an adapted motor control through daily physical activities. Lastly, it is speculated that older adults already sway their CoM motion close to their limit of balance control. Any further increased of sway or velocity may result in falling accident.

It is worth noting that the difference in toe-obstacle clearance between dual-task and single-task condition disappeared at post-fatigue. The increased toe-obstacle clearance while answering the 3-back test concurrently might be accounted for the fact that participants were alerted with the cognitive interference and adopted a safe crossing strategy to avoid tripping. After fatigue, this conservative strategy seems to be diminished. It was possibly attributed to the improved cognition, indicated by greater accuracy and faster reaction time during the 3-back test, at post-fatigue. Since the cognitive interference decreased, the interference-induced increase in toe-obstacle clearance became diminished. One the other hand, a previous study has reported that healthy individuals were able maintain movement pattern at the expense of cognitive performance while crossing an obstacle and attending an attention demand task concurrently (Lo, van Donkelaar, & Chou, 2015). After fatigue, the opposite trend was found, in which participants improved their cognition at expense of conservative crossing strategy. This may be an important indication in terms of tripping prevention.

It remains unclear what contributes to a better cognitive performance after fatigue. There is a possible learning effect as the tasks were given repeatedly and a learning curve may distort the results. We have addressed this issue by allowing participants to practice tasks during a familiarization session and before the study. Granacher et al. (2010) have shown the similar results and suggests that participants allocated a greater portion of central resources to the cognitive task than balance task after fatigue. Our data only partially support this explanation as no impaired balance control was detected in the older adults. It is possible that task-based fatiguing protocol induced other brain region in older adults, such as right frontopolar area (Hyodo et al., 2012), instead of pre-frontal cortex as we hypothesized. Thus, older adults were free from the central capacity limit; while young adults activate and overload the same region (pre-frontal cortex) when answering the 3-back task, when acquiring visuospatial information during crossing, and when fatigued. It is also possible that we happened to capture the "sweet phase" of fatiguing process. A previous study has reported that oxygenation of pre-frontal cortex would increase at first during the fatiguing protocol and decrease toward the exhaustion (Thomas & Stephane, 2008). As future study goes, neuroimaging techniques, such as near-infrared spectroscopy, would help probe the underlying mechanism of fatigue. Moreover, a longer and self-paced fatiguing session (e.g. occupational activity) should be examined so that compensatory period would be taken into consideration.

In conclusion, the current findings suggest that older adults did not demonstrate the effects of fatigue to a greater extent than young adults. In contrast, young adults showed a greater frontal plane CoM motion after fatigue while older adults remained theirs the same. Regardless of age, participants improved their cognition after fatigue, thus dual-task condition was not an exacerbating factor of fatigue.

Bridge

Chapter IV examined how the laboratory-based fatiguing protocol impacted individual's balance control and working memory during obstructed walking. In the next chapter, we used the occupational activity as the fatiguing protocol and investigated how older worker’s balance control and working memory were affected after fatigue.

CHAPTER V

GAIT BALANCE CONTROL AND WORKING MEMORY PEFFORMANCE AFTER OCCUPATIONAL ACTIVITY IN OLDER WORKERS: A PRELIMINARY STUDY

Introduction

Labor force is aging, as its median age was 37.7 years and had steadily increased to 41.9 in 2014 (Toossi,Mitra, 2015). Although there is only a 3-year difference, the age distribution has dramatically shifted with increasing older workers (Figure 5-1). An older worker is referred to those who are ages 55 and older, as defined by the Bureau of Labor Statistics. It is projected that, by 2024, one in every four workers who are employed or actively seeking employment, will be an older worker.

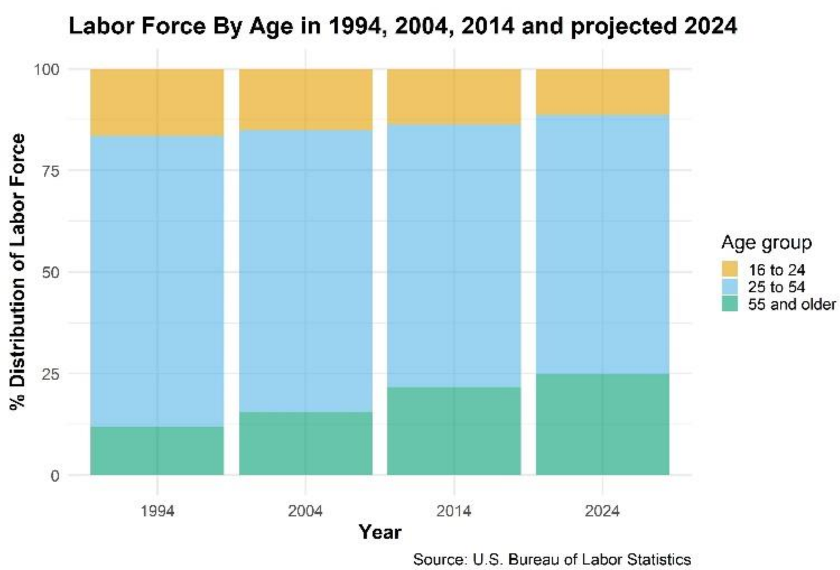

Figure 5-1. Distribution of labor force by age from 1994-2024.

Labor force participation rate of older adults in the American workforce has been increasing since 1995 as the baby boomers gradually moved into the 55-and-older group (Lacey, Toossi, Dubina, & Gensler, 2017). In fact, only older adults demonstrated positive change in labor force participation rate since 1994 (Figure 5-2). Higher participation rate could be attributed to an aging population. Since 1960, life expectancy has been increasing 8.7 years in the United States (World Bank, 1960). From an individual aspect, higher participation rate could also be a result of changes in Social Security retirement age, which requires individuals working longer to receive full benefits (Rogers & Wiatrowksi, 2005).

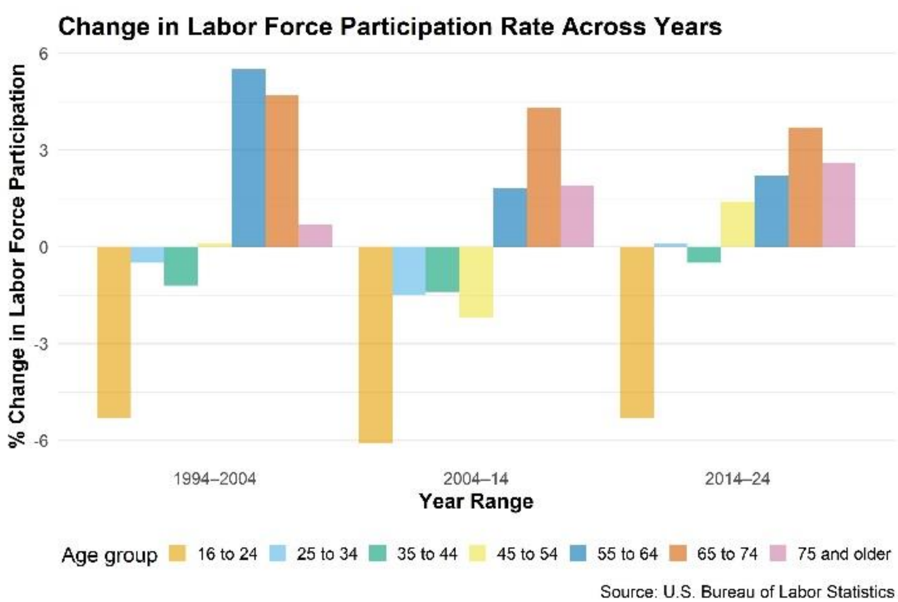

Figure 5-2. Changes in labor force participation rate by age over 30 years

Older workers have the highest frequency and severity of slips, trips and falls. For workers aged 65 and over, the incident rate on same-level falls per 10,000 full-time workers was 36.3 (U.S. Bureau of Labor Statistics, 2016a). This rate was highest among all age groups and leading events, suggesting that falls are highly prominent among increasing older population workers. Moreover, injuries suffered from older workers are more severe even though they encounter similar workplace safety hazards as younger workers. Recovering from workplace injuries for older workers takes twice as long compared to their younger counterparts. The median day away from work is 6 day in workers age between 25-34; while this value doubles up at the age of 45-54 (U.S. Bureau of Labor Statistics, 2016b). Fatigue symptoms and the need to recuperate from work have been found to be risk factors of occupational injuries (Swaen, Amelsvoort, Bültmann, & Kant, 2003). Workers who reported higher level of fatigue had a relative risk of 1.75 of being injured compared to non-fatigued workers. Although studies investigating associated between fatigue and fall in older adults were still lacking, these reports and statistics necessity the need to examine balance control among older workers.

In chapters III and IV, we have investigated how laboratory-induced fatigue affected older adults' balance control and working memory. In brief, we found that older adults demonstrated a shorter reaction time during a working memory test from pre- to post-fatigue while maintaining a similar mediolateral body sway during walking. During obstacle-crossing, older adults demonstrated similar findings as that in unobstructed walking, while increased their step width when crossing at post-fatigue. In order to establish the connection between laboratory-driven results and real-life setting on balance control and working memory, the purpose of this pilot study is to examine effects of fatigue following occupational activity in older workers.

Methods

Participants

Older workers targeted for recruitment in this study were those participating in occupational activities that require moderate to high physical demands and commonly cause occupational injuries. The top twenty occupations that have the most fall injuries are shown in Figure 5-3.

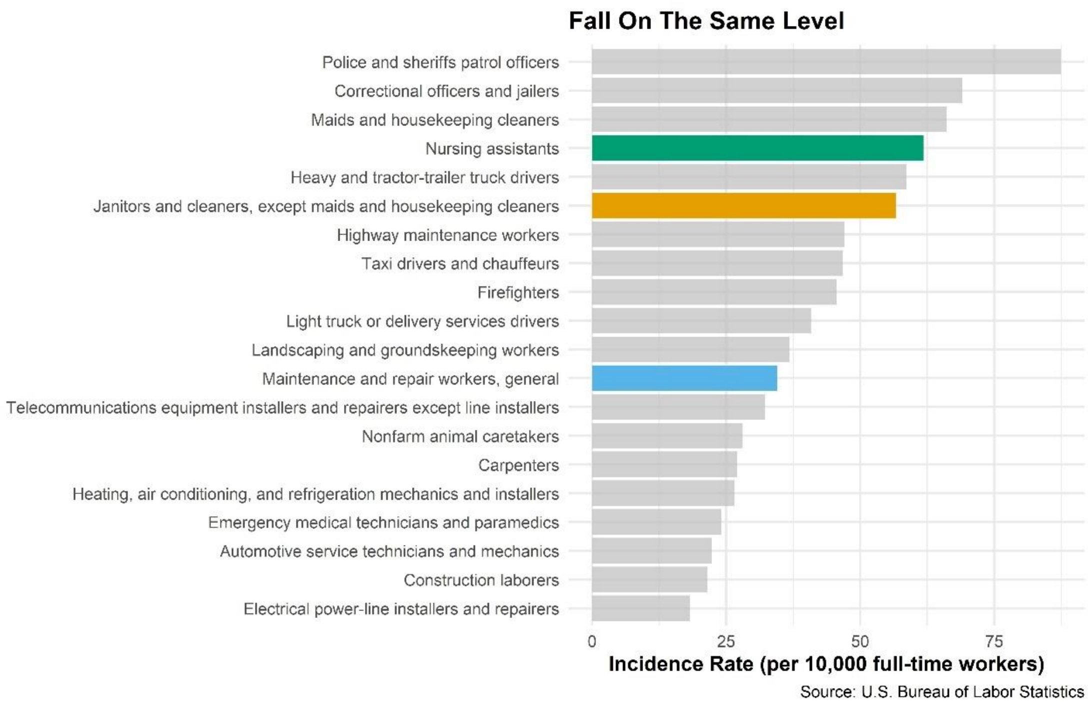

Figure 5-3. Top 20 occupations with highest incidence rate of fall on the same level. Occupations included in this pilot study were highlighted.

We recruited 1 interim coordinator of facilities (referred as A), 1 certified nursing assistant (referred as B) and 1 custodian (referred as C) in this pilot study. Mr. A is a 63-year-old interim coordinator. Mr. A’s job is to perform building maintenance and repair, mainly including sanitary operation but also including air conditioning and heating systems, building automatic control systems, water distribution, fire protection and electrical distribution. Mr. A reported that at work he sometimes sits, sometimes stands, sometimes walks, and sometimes lifts heavy loads. Mr. A also claimed that his job requires heavier physical demand compared to individuals of his own age. Mrs. B is a 62-year-old certified nursing assistant. Her job is to perform basic nursing procedures. On a daily basis, Mrs. B needs to pull or reposition patients in bed, take vital signs, lift supplies, stock equipment, push hospital beds, wheelchairs, and stretchers throughout the unit and the hospital. She reported that at work she walks all the time with an average of 18,000 steps a day. Mr. C is a 72-year-old custodian, and his job is to keep the building interior clean and orderly. Some examples of Mr. C's daily job activities are to 1) gather and empty trash, 2) sweep, mop, or vacuum building floors, 3) clean restrooms and stock supplies, and 4) clean spills and other hazards with appropriate equipment. Mr. C reported that he always walks at work and seldom sits. After working, he often feels tired.

All three participants were free of neurological diseases, cardiovascular diseases, impairments involved with bones, muscles, or joints within the past six months and any persistent symptoms of dizziness, lightheadedness, unsteadiness, or any other medical condition that may affect their ability to walk over ground. They have signed an informed consent approved by the Research Compliance Services at the University in the beginning of the experiment.

Procedures

Participants visited the laboratory 5 days across a span of three working weeks. On each testing day they were tested twice, once before work and once after work. They came in on the first and last working day of each week. For example, if participants work from Monday to Friday and rest on the weekends, they would come in on Mondays and Fridays. Prior to the experiment, participants attended a familiarization session to practice the tasks that they would perform during data collection.

During each laboratory visit, participants were asked to perform three tasks in a random order: 1) single-task walking, 2) working memory test and 3) dual-task walking. In the single-task walking task, participants were asked to walk continuously with a self-selected speed for 2 minutes along an oval shape loop, which includes a 15-m straight walkway for motion data collection. During the working memory test, participants performed a 3-back cognitive task while seated. The 3-back task lasted for two minutes and consisted of a sequence of random numbers played from a wireless headset every two seconds. Participants were required to identify repeated numbers that were presented three digits before in the sequence. During dual-task walking, participants were instructed to walk and concurrently perform the 3-back task without prioritization to either task.

To indicate perceived fatigability, participants were required to rate their feeling of fatigue and how much the fatigue interfered with their activities using the Brief Fatigue Inventory (Mendoza et al., 1999). A higher number represents higher perceived fatigability. Maximal isokinetic contraction of knee extensor at 60°/second was measured with a dynamometer (Biodex Medical Systems, Inc., NY) as an indicator of performance fatigability. Participants were given practice trials before performing the test. A total of three trials were conducted and the peak torque was recorded for further analysis.

Data Reduction

A 12-camera motion analysis system (Motion Analysis Corporation, CA) with a set of 40 markers was used to record the whole-body movement during walking. Marker data from a total of five trials of each task were labeled using Cortex (Motion Analysis Corporation, CA) software before exported as .c3d files and processed using Visual3D (C-Motion, Inc., MD). Kinematic data were low-pass filtered with Butterworth fourth order filter at the cut-off frequency of 10 Hz. The whole-body center of mass (CoM) was calculated as a weighted sum of segmental center of masses. Outcome variables included 1) the range of M-L CoM displacement, 2) gait velocity, 3) step width during a gait cycle and 4) 3-back test accuracy and 5) reaction time. One gait cycle is defined as a heel strike to the next heel strike of the same foot. The 3-back test accuracy was calculated as the percentage of correct responses to total numbers of stimuli. Reaction time of correct responses was also registered through a wireless headset using SuperLab 5 program (Cedrus, CA) for further analysis.

Results and Discussion

Given the descriptive nature of the study design, findings in this pilot study are presented here with discussion to better interpret the results.

Did older workers feel fatigued after their occupational activity?

Results of Brief Fatigue Inventory could be found in Figure 5-4. Mr. A reported the highest level of fatigue on day 1 after work. There were not many differences in perceived fatigability before and after work on days 2, 4, and 5. On the other hand, both Mrs. B and Mr. C reported a higher fatigability after work compared to that before work on most days. Individual differences may be explained by the amount of physical demand required by their jobs, in which Mrs. B and Mr. C walked all the time at work, while Mr. A periodically got to sit.

Given the study design of testing day selection, a “W” pattern might be expected in perceived fatigability before work, as participants experienced the most fatigue on day 1, 3, 5 and were less fatigued on day 2 and 4 after resting over the weekend. However, our results did not match this pattern, which, in part, could be due to that participants did not refrain themselves from physical activities although they did take days off from work. For example, Mr. A reported that he usually performed repair work on his house during his off-day, and such work required heavier physical demand than his paid work, leading to an “M” pattern in perceived fatigability. Nevertheless, it might be worth of paying a close attention to those days when the worker reported the highest fatigue level (Mr. A on day 1) or with the greatest increase in fatigability after work (Mrs. B and Mr. C on day 4).

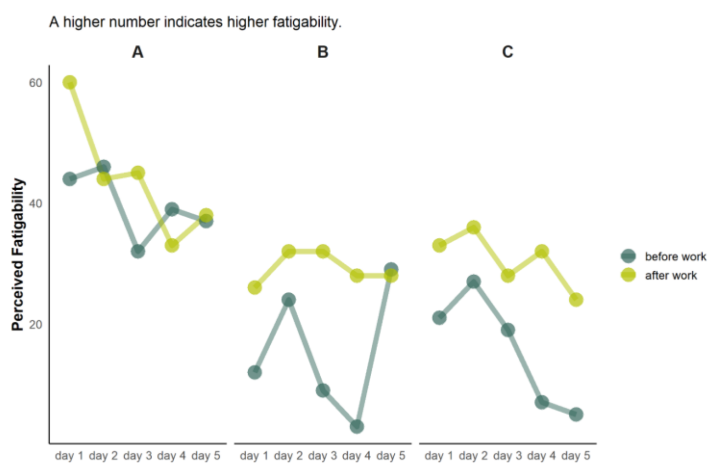

Figure 5-4. Perceived fatigability from worker A, B and C before and after occupational activity.

Did older workers decrease muscle strength after their occupational activity?

After work, Mr. A demonstrated a deceased muscle strength by an average of 11.4%. Similarly, Mrs. B had less muscle strength after work with the average strength drop of 10.2%, although such a reduction became minimal towards day 5. In contrast, no obvious changing pattern was found in Mr. C. (Figure 5-5)

In chapter III and IV, the average strength drop was 18% in older adults after conducting a repetitive sit-to-stand fatiguing protocol guided by a metronome. It is expected that the occupational activity resulted in a less change in strength, as older adults would pace the level of their activity to maintain fatigue within a tolerable range (Eldadah, 2010). Therefore, it is advised that the strength drop should not be a sole indicator of fatigability when conducting fatigue studies in workplace settings. Individuals without any strength drop could still be in a fatigued status.

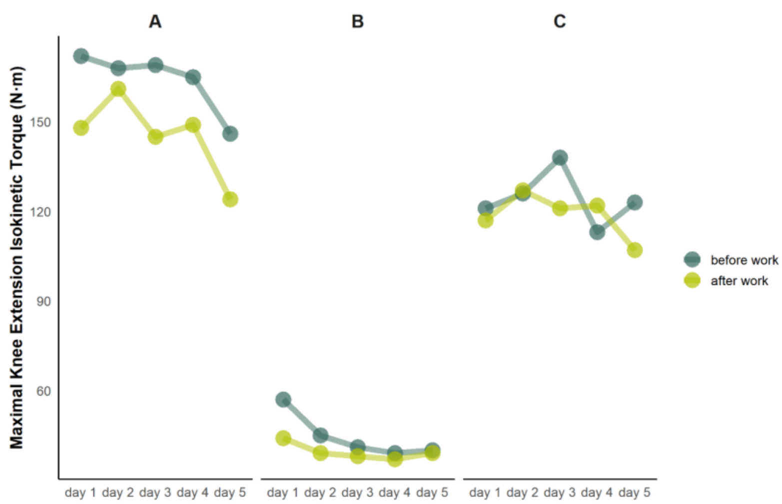

Figure 5-5. Maximal strength from worker A, B and C before and after occupational activity.

What are the changes in gait spatiotemporal characteristics in older workers after their occupational activity? Are these changes dependent on the task condition (single-task versus dual-task)?

There were no consistent patterns observed in gait velocity changes after work (Figure 5-6), as older workers sometimes walked faster or sometimes walked slower after their occupational activities. This result did not agree with the finding reported in chapter III, in which older adults slightly increased their walking speeds during dual-task walking after fatigue. It is speculated that the increased gait might be a strategy to improve balance control, as gait stability was shown reaching its best when walking at 100-110% of regular velocity (Jordan et al., 2007). The discrepant results obtained from laboratory-driven and real-life setting might be attributed to the severity of fatigability. Walking speed is a highly regulated measure and known as the sixth vital sign (Fritz & Lusardi, 2009). In the cases where a good amount of strength loss was induced (e.g. after a repetitive sit-to-stand fatiguing protocol), individuals might need to take an immediate adaptation through changes in gait velocity to maintain optimal balance control.

For the step width, Mrs. B consistently walked with a wider step width after work than that before work. Such a finding does not depend on the task condition. Occupation-induced change in step width seemed random in Mr. A and C. It is speculated different individuals may have different strategies to cope with a fatigued status.

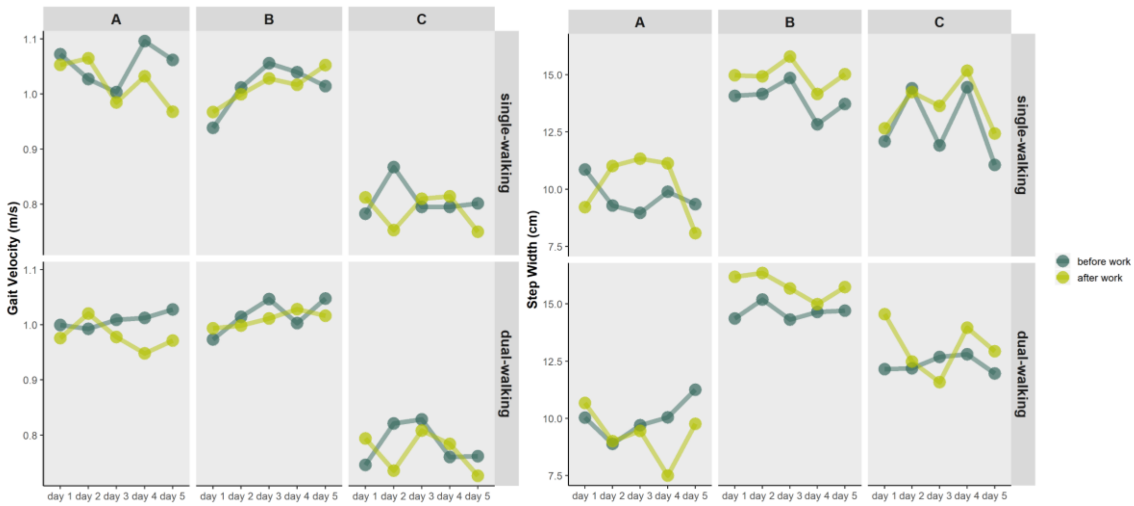

Figure 5-6. Gait velocity and step width from worker A, B and C before and after occupational activity.

What are the changes in CoM movement in the frontal plane in older workers after their occupational activity? Are these changes dependent on the task condition (single-task versus dual-task)?

Results in the mediolateral CoM sway are shown in Figure 5-7. The changes in CoM sway during dual-task walking seemed not to be dependent on fatigability nor associated with any gait measures. On the other hand, Mrs. B seemed to slightly decrease mediolateral sway during single-task walking after work. The decreased sway might be due to, in part, the improved stability adapted from the increased step width after work. On the contrary, Mr. C increased the CoM sway on day 1, 3, and 5 during single-task walking from pre-work to post-work. Day 2 and day 4 were the days when Mr. C possessed a wider step width compared to other days. Although it remains unclear why such adaptation existed, it is possible that the interaction between fatigue status and adapted gait characteristic together determine the changes in CoM sway. There was no significant changing pattern observed in Mr. A. Nevertheless, it is worth noting that his CoM sway increased the most after work on day 1 of investigation, when he reported the highest perceived fatigability. There might exist a certain threshold of fatigability to induce the changes in CoM sway. Future studies are warranted to validate such a notion.

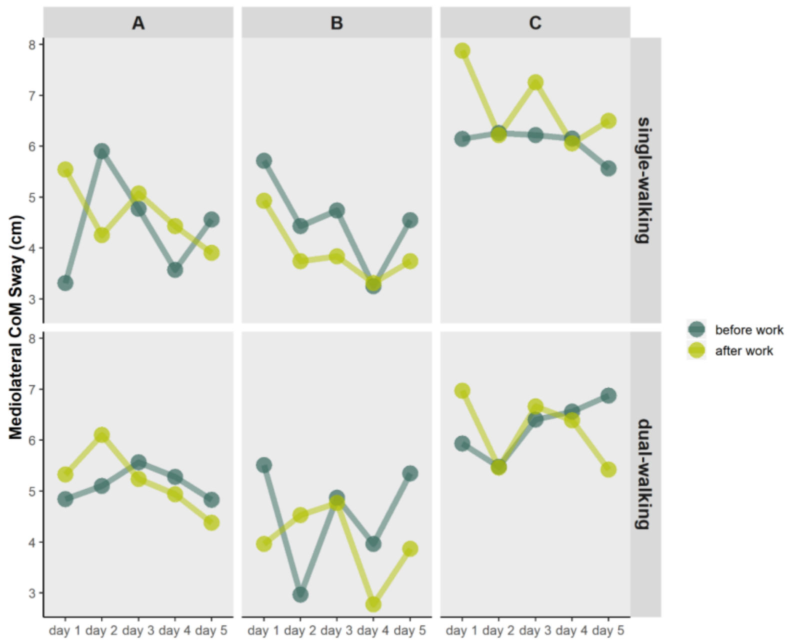

Figure 5-7. Mediolateral CoM sway from worker A, B, and C before and after occupational activity.

In chapters III and IV, older adults were found to maintain CoM sway after fatigue regardless of task condition. We proposed several reasons explaining the findings, including the healthy volunteer preponement, the ceiling effect of CoM sway control, and the fatigue-resistance developed through the natural aging process. Inspired by this pilot study, we wanted to propose another possibility- within group variability. The overall results from the pooled data may be camouflaged by the individual differences in response to fatigue. We revisited and re-ploted the findings of CoM sway of chapter IV in Figure 5-8 as an example. Although most of the young adults had positive change in CoM sway after fatigue, indicating an increased body sway and deteriorated balance control, only half of the older adults increased their sway. As a result, insignificant finding of CoM sway in older adults was statistically generated. From a prevention perspective, attention should still be paid to those who demonstrated fatigue-induced CoM sway despite the overall insignificant findings. Individuals who failed to increase their body sway may also respond to fatigue in different manners. Therefore, future studies might consider taking subgroup analysis in order to identify types of fatigue adaptation.

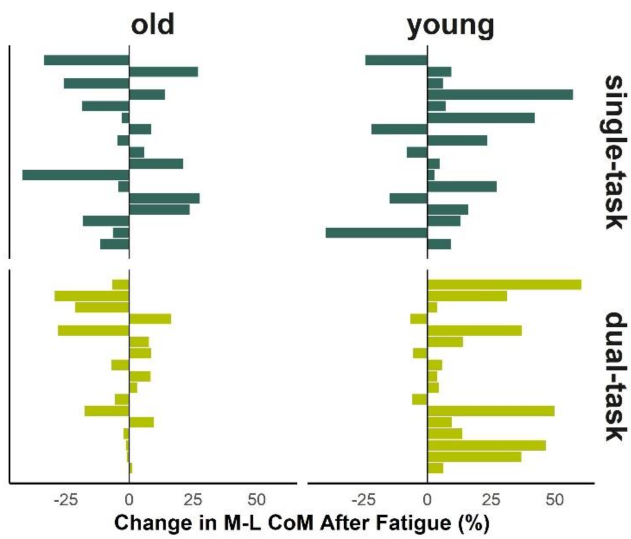

Figure 5-8. Changes in mediolateral CoM sway during obstacle-crossing after fatigue.

What are the changes in working memory in older workers after their occupational activity? Are these changes dependent on the task condition (single-task versus dual-task)?

Mrs. B demonstrated a higher accuracy of the 3-back test after work, although such a finding was only observed in the single-task condition. A high accuracy of the 3-back test indicated an improved working memory, which is in line with the findings in chapters III and IV. In this pilot study, older workers were required to take the 3-back test before and after work, with at least 8 hours washout period. Thus, the observed findings might not necessarily attribute to the learning effect. A previous study found that older adults dominantly recruited right frontopolar area (FPA) after an acute bout of exercise (Hyodo et al., 2012), and such region was found responsible for an excitatory control during cognitive performance (Medalla & Barbas, 2010). It is argued that Mrs. B's cognition might benefit from her work through the similar mechanism. On the other hand, such a benefit might serve at the expense of balance control during dual-task walking.

The fatigue-induced change in working memory was manifested on reaction time, in which Mr. A consistently increased the reaction time during dual-task walking after work. It is possible that Mr. A belongs to a subgroup who maintain the gait characteristics and balance control at the expense of cognition.

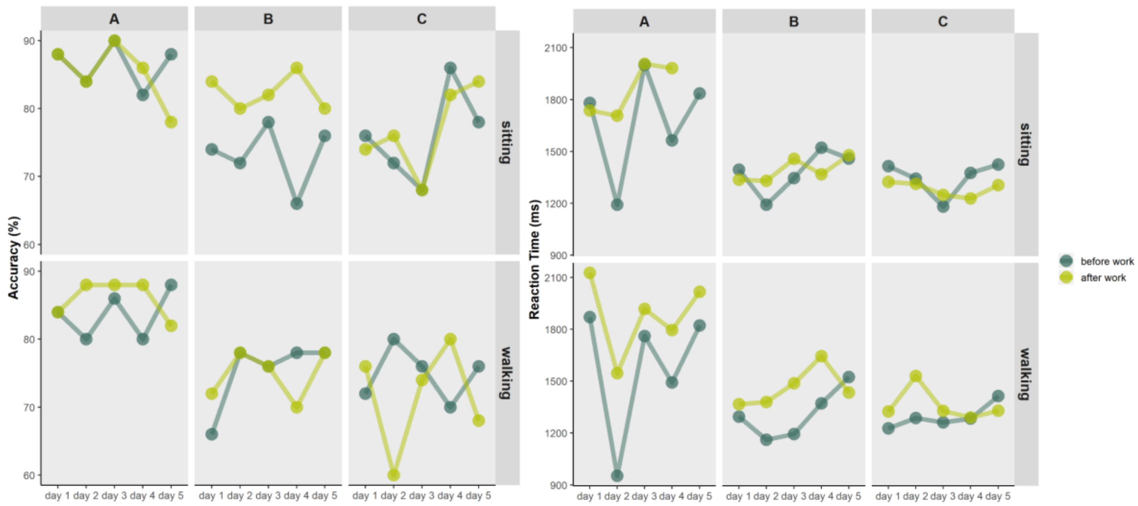

Figure 5-9. Working memory performance (left: accuracy and right: reaction time) from worker A, B, and C before and after occupational activity.

<u>Conclusion</u>

The purpose of this pilot study was to explore the changes in balance control and working memory in older workers after occupational activity and to establish the connection between laboratory-driven results and real-life setting. Several previous studies, including chapters III and IV of this dissertation, were designed to examine effects of fatigue in the laboratory through a combination of self-report measures with performance of physical or cognitive activities, in which the work of the activity can be standardized. Although this method can minimize the impact of self-pacing and allow meaningful comparisons across populations and between studies, it might result in a disconnection from the real-life application. Some findings observed from three workers were in line with laboratory-driven results (e.g. improved accuracy), some were opposite (e.g. longer reaction time), and some might represent unique fatigue adaptations that failed to be identified once the results were pooled together with other participants. It is advised that more fatigue studies employed in the real-life settings is necessary to further inform any fatigue-related intervention and policy changes.

CHAPTER VI

CONCLUSION

Findings Summary

This dissertation study investigated how fatigue affects gait balance control and working memory in young and older adults and explored how these functions would be affected by fatigue induced in real-life job scenarios. Two approaches were conducted to achieve the proposed aims. The first approach employed a repetitive sit-to-stand fatiguing protocol to examine the effect of fatigue on walking and obstacle-crossing, where most fall accidents happen. The second approach explored the connection between laboratory results and real-life scenarios by examining gait balance control and working memory before and after a day-long of occupational activity in older workers.

In the first study, the use of repetitive sit-to-stand (STS) fatiguing protocol was validated. Participants were instructed to perform a repetitive STS movement at their comfortable pace, predetermined and used to guide the movement through a metronome. The whole-body motion data was collected during each minute of the entire fatiguing protocol to generate the calculation of continuous relative phase (CPR), indicating inter-joint coordination. The results showed that from standing to sitting, variability of knee-ankle CRP during late-stage of fatiguing protocol was significantly higher than that of early-stage. The findings suggested that participants exploit new motor strategies to adapt the increasing challenges raised by prolong task execution, and such an adaption was prominent at the site away from the fatigued muscle. The study demonstrated that the impact of fatigue during repetitive STS protocol was not only limited to a decline in force production but also manifested as changes in motor control, thus providing a feasible approach to further apply the observed results to the real-life settings.

In the second study, we examined how fatigue, induced by aforementioned STS protocol, affected balance control and working memory during walking. Participants performed 1) single-task walking, 2) a working memory test and 3) dual-task walking (walking while answering a working memory test) in a random, once before conducting the STS protocol and once after fatigue. The results showed that participants walked faster after fatigue during dual-task condition. Moreover, the balance control, as measured by mediolateral center of mass (CoM) motion, became deteriorated after fatigue regardless of task conditions. Such a result, however, was observed only in young adults, not in older adults. The insignificant changes in balance control in older adults could be explained by 1) pre-existed motor adaptation caused by natural history of aging, such as distal-to-proximal redistribution, leading to less susceptibility to the STS fatiguing protocol, 2) the health volunteer phenomenon, in which a fatigue study most likely recruited participants with high fatigue-resistance, and 3) the ceiling effect, as older adults already walked with the frontal plane CoM motion closer to their maximum capacity. Nevertheless, such findings might not be reproducible if the primary locomotion task required a high-level of attention, such as obstacle-crossing, as time to acquire visuospatial information for proper movement planning was reduced as a result of faster gait speed.

Therefore, in the third study, effects of fatigue on balance control and working memory were investigated during obstacle-crossing. Similar study designed was employed except that participants were asked to cross an obstacle with 10% of body height instead of unobstructed walking. The results showed that participants maintained the same walking speed from pre-fatigue to post-fatigue regardless of age. Given that participants were aware of the obstacle placed in the middle walkway prior to crossing, they were able to accommodate the fatigue effects and slowed down before the obstacle to ensure proper crossing, like car drivers slowing down before the stop sign. The consistent gait velocity may also explain why several crossing characteristics, such as toe-obstacle clearance and foot placement, were not affected by fatigue in this study. Similarly, the changes in balance control was in line with the previous study, in which a greater and faster mediolateral CoM motion was found at post-fatigue in young adults but not in older adults. On the other hand, older adults demonstrated a better cognitive performance after fatigue in both walking and obstacle-crossing studies. A learning effect might be attributed to the findings as the working memory task were given repeatedly and a learning curve might distort the results. It is also possible that task-based fatiguing protocol induced other brain region that takes an excitatory control in older adults, such as right frontopolar area; or only the “sweet phase” as a result of compensation during the fatiguing process was captured. Applying the study in the real-life setting with occupational activity being a fatiguing protocol would help elucidate the effects of fatigue, as the learning effects and compensatory period would be taken into consideration through a longer and self-paced fatiguing session.

In the fourth study, the connection between laboratory-driven results and real-life setting on balance control and working memory was explored through examining effects of fatigue following occupational activity in older workers. Three older workers whose occupational activity required moderate to high physical demands and commonly caused occupational injuries were recruited. Using the same tasks as in the second study, the results showed that some findings observed from three workers were in line with laboratory-driven results (e.g. improved accuracy after work), some were opposite (e.g. longer reaction time after work), and some might represent unique fatigue adaptations that failed to be identified once the results were pooled together (e.g. wider step width or increased body sway after work). Although conclusive interpretation could not be made given the descriptive nature of the pilot study, it highlighted the necessity to look effects of fatigue into the individual level and advised that more fatigue studies employed in the real-life settings is warranted to further inform any fatigue-related intervention and policy changes.

Future research

The dissertation demonstrated the changes in balance control and working memory in healthy older adults. Studies targeting the fatigue-prone population, such as frail older adults or individual participating in high physical-demanding work are in high demand to generate an informative conclusion. Subgroup analyses from a larger study are also necessary to identify and categorize potentially different adaptations towards fatigue. Although in the dissertation, there existed no immediate concern regarding balance control in older adults after fatigue, effects of fatigue should not be underestimated and need to be further examined. In particular, we should identify participants at risk and/or employ tasks with high balance threat, like tripping, to obtain the worst possible effects of fatigue. Neuroimaging techniques, such as near-infrared spectroscopy, would also help examine neural substrates for activity-elicited activation and probe the underlying mechanism of fatigue during dual-task walking.

APPENDIX A

INFORMED CONSENT FORM: EFFECTS OF FATIGUE ON DUAL-TASKING WALKING

UNIVERSITY OF OREGON

Consent for Research Participation

Title:	Effects of Fatigue on Dual-Tasking Walking in Older Adults
Researcher(s):	Szu-Hua Chen, University of Oregon
	Dr. Li-Shan Chou, University of Oregon
Researcher Contact Info:	541-887-0482
	szuhuac@uoregon.edu

You are being asked to participate in a research study. The box below highlights key information about this research for you to consider when making a decision whether or not to participate. Carefully consider this information and the more detailed information provided below the box. Please ask questions about any of the information you do not understand before you decide whether to participate.

Key Information for You to Consider

- **Voluntary Consent.** You are being asked to volunteer for a research study. It is up to you whether you choose to participate or not. There will be no penalty or loss of benefits to which you are otherwise entitled if you choose not to participate or discontinue participation.
- **Purpose.** The purpose of this research is to investigate effects of lower extremity fatigue on dynamic balance control and neuromuscular adaptations during dual-task walking and to suggest any age-related differences in the effects of fatigue.
- **Duration.** If you participate Part A of the study, it is expected that your participation will last 1.5 hours during first visit and 3.5 hours during second visit. Two visits are with no more than a week apart. If you participate Part B of the study, it is expected that you visit the laboratory for a total of 11 times each for 1.5 hours.
- **Procedures and Activities.** Information provided in the health history questionnaire you completed over the phone will be used for research purposes.

  There are two parts of study, Part A and Part B. Two parts of studies are independent. Investigator will inform you which part of study you will be participating.

  Part A
  The study includes two testing visits with no more than a week apart. During the first visit, you will be asked to complete either computer tests or questionnaires about your mental status, fall history, physical activity level, and subjective fatigue level. Additionally, your walking velocity, cognitive ability, and anthropometric data will be measured using electronic carpet, computerized battery, and scale and caliper, respectively. During the second visit, you will be performing five pre-fatigue tasks, including two walking tasks (walking in a loop and crossing an obstacle at 10% of your height), one cognitive task and two dual tasks (walk+ cognitive task). Each task takes approximately 5 minutes. The same five tasks will be conducted again as post-fatigue measurements after you indicate you are fatigued after accomplishing a neuromuscular fatigue protocol, in which you will conduct a sit-to-stand movement repeatedly guided by a metronome. At the completion of fatigue protocol, you will be asked to rate the level of work load. The knee power assessment, where you will sit on a testing chair with limbs fixed by straps and be instructed to forcefully contract knee muscles, will be performed before and

immediately after the fatigue protocol as well as at the completion of five post-fatigue tasks. Walking and sit-to-stand motions will be analyzed with camera-based motion analysis using small reflective markers attached to your body. Ground reaction force will be recorded using in ground force plates. Additionally, surface electromyography (EMG) electrodes will be taped to the surface of your skin over several muscles on your legs. These sensors are used to record electrical activity from your muscle. You will be asked to wear provided compression shorts and shirt and will be performing walking trials barefoot to assist with motion analysis accuracy.

Part B

The study includes 11 testing visits across two weeks. The first visit is a familiarization session. For the second to eleventh sessions, you will need to come in before you go to work (the second, forth, sixth, eighth, tenth sessions) and after you finish working (the third, fifth, seventh, ninth, eleventh sessions). During the first visit, you will be asked to complete either computer tests or questionnaires about your mental status, fall history, physical activity level, and subjective fatigue level. Additionally, your walking velocity, cognitive ability, and anthropometric data will be measured using electronic carpet, computerized battery, and scale and caliper, respectively. During the second to eleventh visit, you will be performing five tasks, including two walking tasks (walking in a loop and crossing an obstacle at 10% of your height), one cognitive task and two dual tasks (walk+ cognitive task). Each task takes approximately 5 minutes. The knee power assessment, where you will sit on a testing chair with limbs fixed by straps and be instructed to forcefully contract knee muscles, will be performed. Walking motions will be analyzed with camera-based motion analysis using small reflective markers attached to your body. Ground reaction force will be recorded using in ground force plates. You will be asked to wear provided compression shorts and shirt and will be performing walking trials barefoot to assist with motion analysis accuracy.

- **Risks.** Some of the foreseeable risks or discomforts of your participation include: skin irritation from double sided adhesive used to adhere reflective markers and sensors to skin, stumbling/tripping during normal walking and muscle soreness caused by the neuromuscular fatigue protocol (only in Part A). To minimize risk of injury during the study, you will complete a 5 minute warm up session at beginning of second visit. During the testing, you will be instructed to take breaks during testing as needed. Examiners will be standing close to you and consistently asking your physical conditions. After the completion of study, you will be asked to rest in the laboratory until no severe signs of fatigue are observed. The potential discomfort or risks of unstable walking induced by the fatigue protocol should be ameliorated when an adequate rest time is provided.

- **Benefits.** There are no direct benefits to the subject from this research study. However, knowledge gained from this study will increase our understanding of balance control strategies after fatigue. This knowledge may not only advance the intervention toward a fall-risk prevention in older adults but also allow for a more realistic replication of fatigue studies on dynamic balance control in fatigue-prone population

- **Alternatives.** Participation is voluntary and the only alternative is to not participate.

What happens to the information collected for this research?

Information collected for this research will be used in professional conference research presentations and scientific peer reviewed research manuscripts. We may publish/present the results of this research in professional conferences and peer reviewed scientific journals; however, we will keep your name and other identifying information confidential.

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How will my privacy and data confidentiality be protected?

We will take measures to protect your privacy including performance of all data collection in a sterile laboratory environment with access limited to study personnel. Furthermore, we will take measures to protect the security of all your personal information. Your information will be coded for the study using subject pseudonyms. Your names will be replaced by code numbers. The code numbers matching particular data sets to individual subjects will be stored in a hard copy that will be kept in a locked filing cabinet separated from the data itself and only the principal investigator and co-investigators involved in this project will have access. All computer files will be coded and secured using a password protected file. All laboratory notes will be archived in coded form in a locked filing cabinet in the security regulated Motion Analysis Laboratory (B52, Gerlinger Annex). At the completion of the study and after the results have been published, the list of participants' names will be destroyed. Despite these precautions to protect your privacy and the confidentiality of your information, we can never fully guarantee confidentiality of all study information.

Individuals and organization that conduct or monitor this research may be permitted access to and inspect the research records. This may include access to your private information and data collection forms. These individuals and organizations include: the University of Oregon Institutional Review Board that reviewed this research.

What if I want to stop participating in this research?

Taking part in this research study is your decision. Your participation in this study is voluntary. You do not have to take part in this study, but if you do, you can stop at any time. You have the right to choose not to participate in any study activity or completely withdraw from continued participation at any point in this study without penalty or loss of benefits to which you are otherwise entitled. Your decision whether or not to participate will not affect your relationship with the researchers or the University of Oregon.

What if I am injured because of participating in this research?

There is very little risk of physical injury due to the simple tasks utilized. However, if you are injured or get sick because of being in this research, call the researchers immediately. If you sustain an injury while participating in this study the researchers will assist you in obtaining appropriate medical treatment. All expenses related to that treatment will be covered by you and/or your insurance company. If you are a University of Oregon student or employee and are covered by a University of Oregon medical plan, the plan might have terms that apply to your injury.

If you experience harm because of the project, you can ask the State of Oregon to pay you. If you have been harmed, there are two University representatives you need to contact. Here are their addresses and phone numbers:

General Counsel/ Office of the President
1226 University of Oregon
Eugene, OR 97403-1226
(541) 346-3082

Research Compliance Services
5237 University of Oregon
Eugene, OR 97403-5237
(541) 346-2510

A law called the Oregon Tort Claims Act may limit the amount of money you can receive from the State of Oregon if you are harmed.

Will I be paid for participating in this research?

For taking part A in this research, you may be paid a total of $50 [check]. For taking part B in this research, you may be paid a total of $220 [check]. Your compensation is based on a $10 per hour rate. In the event you choose to discontinue the study after data collection has commenced, you will receive a partial compensation with prorated amount of $10/hour. Payment will occur at the termination of the study or at the end of data collection (second visit of Part A or eleventh visit of Part B).

Who can answer my questions about this research?

If you have questions, concerns, or have experienced a research related injury, contact the research team at:

Szu-Hua (Teresa) Chen
Phone number: 541-887-0482
Email: szuhuac@uoregon.edu

An Institutional Review Board ("IRB") is overseeing this research. An IRB is a group of people who perform independent review of research studies to ensure the rights and welfare of participants are protected. UO Research Compliance Services is the office that supports the IRB. If you have questions about your rights or wish to speak with someone other than the research team, you may contact:

Research Compliance Services
5237 University of Oregon
Eugene, OR 97403-5237
(541) 346-2510

STATEMENT OF CONSENT

I have had the opportunity to read and consider the information in this form. I have asked any questions necessary to make a decision about my participation. I understand that I can ask additional questions throughout my participation.

I understand that by signing below, I volunteer to participate in this research. I understand that I am not waiving any legal rights. I have been provided with a copy of this consent form. I understand that if my ability to consent or assent for myself changes, either I or my legal representative may be asked to re-consent prior to my continued participation in this study.

I consent to participate in this study.

Name of Adult Participant	Signature of Adult Participant	Date

Researcher Signature (to be completed at time of informed consent)

I have explained the research to the participant and answered all of his/her questions. I believe that he/she understands the information described in this consent form and freely consents to participate.

Name of Research Team Member	Signature of Research Team Member	Date

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