Age-related changes in corticospinal drive during locomotor adaptation

Sumire D. Sato
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Age-related changes in corticospinal drive during locomotor adaptation

A Dissertation Presented

by

SUMIRE D. SATO

Submitted to the Graduate School of the University of Massachusetts in partial fulfillment of the requirements for the degree of

DOCTOR OF PHILOSOPHY

February 2022

Neuroscience and Behavior Program
Age-related changes in corticospinal drive during locomotor adaptation

A Dissertation Presented by
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ABSTRACT
AGE-RELATED CHANGES IN CORTICOSPINAL DRIVE DURING LOCOMOTOR ADAPTATION
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During activities of daily living, locomotor patterns must be continuously adapted according to changes in our body (e.g., bodily injuries, fatigue) and to the changing environment (e.g., walking surface). Plasticity of spinal networks and supraspinal centers, including the cerebellum and cerebral cortex, have been shown to play important roles in human locomotor adaptation. However, the neural control of locomotion and the ability to adapt locomotor patterns are altered in older adults, which may limit activities of daily living and increase fall-related injuries in the elderly population. My dissertation project is focused on understanding the role of corticospinal drive during split-belt treadmill and visuomotor walking adaptation in healthy young and older adults. My central hypothesis is that lower corticospinal drive is associated with reduced kinematic adaptability during locomotion in older adults. In Study 1, I examined the age-related changes in corticospinal control during split-belt locomotor adaptation, which is driven by mismatch of expected and actual proprioceptive input. Older adults adapted step length asymmetry slower, and had lower corticospinal drive compared to younger adults. Higher corticospinal drive to the tibialis anterior was associated to larger step length asymmetry change and
smaller double support asymmetry change, and higher corticospinal drive to the tibialis anterior and smaller corticospinal drive to the plantarflexors were associated smaller early change in double support asymmetry during split-belt adaptation. Study 2 examined the age-related changes in corticospinal control during visuomotor locomotor adaptation, which is driven by mismatch between visual and proprioceptive feedback about foot position. Older adults adapted step time asymmetry slower, and had lower corticospinal drive compared to younger adults. Higher corticospinal drive to the tibialis anterior was related to the overall change in step time asymmetry during visuomotor locomotor adaptation. Across both studies, there were age-group differences in some, but not all kinematic adaptation measures, which may suggest that older adults are able to adapt gait kinematics with both the split-belt and the visuomotor locomotor adaptation, but prioritization may differ between the age groups. Corticospinal drive to the lower extremity musculature was associated with kinematic measures independent of age groups, which suggests that the association do not change with age. These findings provide insight into the importance of corticospinal drive during locomotor adaptation, which may have implications for future development of interventions that promote effective recovery in gait in people with neurological injuries.
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CHAPTER 1

LITERATURE REVIEW


1.1 Introduction

It is estimated that 32% of older adults above the age of 60 years have a gait disorder (e.g., slowness, ataxia; Mahlknecht and others 2013), and of the older adults who have a gait disorder, 29% have recurrent falls (Mahlknecht and others 2013). Falls are a leading cause of injuries in older adults, and the estimated cost of fall-related injuries for individuals older than 65 years was 50 billion USD in 2015 (Bergen, Stevens and Burns 2016; Florence and others 2018). The ability to adapt walking patterns in response to the immediate environment is important for functional mobility, and increased difficulty adjusting to novel terrains is known to contribute to the age-related increase in falls in older adults (Rubenstein 2006; Tinetti, Inouye, Gill and Doucette 1995). However, the neural mechanisms underlying age-related changes in locomotor adaptation are still unclear. Current rehabilitation strategies that have been shown to be effective for reducing fall risks in older adults include exercise interventions to increase muscle strength, home modifications, and multifactorial interventions (Gillespie and others 2012), but these interventions do not specifically target gait adaptability required for walking in challenging novel environments.

A key to advancing gait rehabilitation for older adults is to understand the neural mechanisms that underlie different types of locomotor adaptation. In recent
years, experimental investigations of locomotor adaptation in humans have evolved considerably. This chapter will describe experimental paradigms used to study human locomotor adaptation, outline age-related changes in locomotor adaptation, and summarize age-related changes in the neural mechanisms underlying locomotion that may be responsible for the changes in locomotor adaptation.

1.2 Overview of human locomotor adaptation

Walking is a complex motor task that requires precise timing and scaling of muscle activation across many joints (Figure 1.1). As such, walking patterns must be continuously adapted according to changes in our body (e.g., bodily injuries, fatigue, aging) and to a changing environment (e.g., walking surface). Function of both spinal networks and supraspinal centers, including the cerebellum and cerebral cortex, have been shown to play important roles in human locomotor adaptation. Locomotor adaptations can be categorized into reactive (feedback) or predictive (feedforward) mechanisms (Figure 1.2), and both processes are necessary and important to understand in order to improve rehabilitation strategies for gait impairments.
Figure 1.1. Spatiotemporal walking parameters.
A stride begins when the reference limb (right leg in the figure) hits the ground and ends when the same limb strikes the ground again. Each stride consists of a stance phase (solid line) and a swing phase (dotted line). Double support phase is the time between heel strike and contralateral toe off (light shaded areas) - when both legs are on the ground. There are two double support phases in each stride. At heel-strike, the ankle is at the anterior-most point, and at toe-off the ankle is at the posterior-most point. Step length is defined as the anterior-posterior distance between the two ankles at the heel-strike of the leading limb (i.e., right step length = distance between the left ankle and right ankle at time of right heel-strike). Step time is the time between successive heel-strikes (i.e., right step time = duration from left heel-strike to right heel-strike). During locomotion on the treadmill, the distance traveled by each limb during stance phase is calculated as the stance length. Stance length is sometimes defined as “stride length” in treadmill adaptation literature (Bruijn, Van Impe, Duysens and Swinnen 2012; Reisman, Block and Bastian 2005; Roemmich and others 2014). When both right and left treadmill belts moving at the same speed, these spatiotemporal walk parameters are symmetrical for left and right sides. RHS: right heel-strike; RTO: right toe-off; LHS: left heel-strike; LTO: left toe-off.

Reactive feedback adaptation involves fast adjustments in movement to accommodate unexpected perturbations. When first exposed to a novel environment, sensory feedback information is sent to a “controller (a theorized nervous system network or structure that is responsible for generating motor
commands for movement)” resulting in fast, reactive adjustments during the ongoing, goal-directed movement (Shadmehr, Smith and Krakauer 2010). Reactive adaptation serves as an initial safety net to aid in the completion of the movement goal during times of sudden, unexpected perturbations. However, due to the variability and delay in the motor command which depend on feedback information through sensory afferents, the execution of the reactive feedback adjustments is inaccurate and delayed.

Predictive feedforward adaptation involves trial-and-error motor learning through repeated training, prolonged exposure to a novel environment, or long-term alterations in sensory input due to changes in the body (e.g., neural damage, aging). In predictive adaptation, the “controller” is updated with each repetition of the movement based on the mismatch between the expected and actual sensory information (i.e., “error”) to form a predictive internal model, which helps to execute movements with better accuracy and without delay (Shadmehr et al. 2010). Predictive-feedforward adaptation can be confirmed by the presence of aftereffects in the movement pattern when placed back in the original environment, where individuals must de-adapt to achieve the accurate movement pattern best for the “original” state (Bastian 2008).
Figure 1.2. Principles of motor adaptation. Predictive-feedforward and reactive-feedback adaptation both occur when people walk on a split-belt treadmill where two legs move at different speeds. Initially, there are rapid changes in stance time (the slow leg spending more time in stance and the fast leg spending less time in stance) and stance length that are necessary to accommodate the differing belts speeds (Choi and Bastian 2007; Reisman, Block and Bastian 2005). These spatial and temporal adjustments persist throughout split-belt walking and then immediately reverses when the belts are returned to normal treadmill conditions (a-b). Secondly, interlimb parameters such as double support time and step length symmetry behave like “error” signals (Malone, Bastian and Torres-Oviedo 2012), which are slowly corrected back towards symmetry during adaptation through predictive mechanisms, and show the opposite errors (negative aftereffect) post-adaptation (c-d). Double support time and step length symmetry adapt at different rates during split-belt walking (Malone and Bastian 2010), are associated with different neural markers (Sato and Choi 2019), and likely reflect distinct neural mechanisms for spatial and temporal control during walking that are differently impacted with aging.

Evidence from neurologically impaired populations (cerebellar lesion, post-stroke) suggests that spinal and supraspinal structures play different roles during locomotor adaptation (Hinton, Conradsson and Paquette 2020). Studies of infant
walking adaptation suggest that the spinal cord plays an important role in integrating sensory afferents with central pattern generators which allows for quick reactive adjustments during walking (Yang, Lamont and Pang 2005). The cerebellum receives sensory information from the limbs and efferent information from the spinal cord about the intended movement pattern, and adjusts walking patterns via cerebellar-brainstem pathways. Damage to the cerebellum has been shown to impair predictive locomotor adaptation in severely ataxic patients (Morton and Bastian 2006), while interlimb adaptation was preserved in mildly ataxic patients (Hoogkamer and others 2015). The cerebral cortex is critical for translating visual information for planning and execution of visually guided walking (Drew and Marigold 2015; Jensen and others 2018). Disruption of cortical input has also been shown to influence the extent and rate of predictive locomotor adaptations (Choi, Bouyer and Nielsen 2015; Choi, Vining, Reisman and Bastian 2009).

For this narrative review chapter, I establish a framework where age-related changes in human locomotor adaptation can be summarized in terms of reactive feedback and predictive feedforward control that can be driven by proprioceptive and visual feedback during walking. However, it is important to keep in mind that these are not the only locomotor adaptation paradigms. For example, other studies have demonstrated that older adults are able to improve stability with treadmill-based slip or trip perturbations (Epro and others 2018; McCrum, Gerards, Karamanidis, Zijlstra and Meijer 2017), but reactive balance responses are diminished in older adults with neuropathology (Karamanidis, Epro, McCrum and Konig 2020). Instead of a full systematic review, I focused on studies using the split-belt treadmill and visuomotor locomotor adaptation paradigms as the effects of age on these paradigms have not been reviewed before. This chapter summarizes the age-related effects on (1) split-
belt locomotor adaptation, (2) visuomotor locomotor adaptation, and (3) neural control of locomotion, and hypothesize a differential effect of age on neural circuits which may influence locomotor adaptation.

1.3 Proprioception-driven locomotor adaptation

Over the past 15 years, there has been a growing interest in the study of human locomotor adaptation using a split-belt treadmill that can control the walking speed of each leg independently (see review: Hinton, Conradsson and Paquette 2020). The split-belt treadmill allows the left and right treadmill belts to be set at the same speed resembling a normal treadmill (i.e., “tied-belt” condition), or at different speeds with one side moving faster than the other (i.e., “split-belt” condition). At the beginning of the split-belt condition in healthy young adults, intralimb parameters (gait parameters coordinated within one leg; e.g., stance length, stance time) change rapidly, while interlimb parameters (which rely on the coordination between two limbs; e.g., step length, double support time) are slowly adapted (Figure 1.2). During post-adaptation tied-belt condition, intralimb parameters quickly return to baseline values, resembling the characteristics of movements adjusted via reactive feedback mechanisms. In contrast, aftereffects are observed in interlimb parameters during post-adaptation, which is in agreement with the characteristics of movements adjusted via predictive feedforward mechanisms where the stored adaptive changes must be actively de-adapted.
1.3.1 Age-related changes in feedback adaptation during split-belt walking

Older adults lack robust, quick changes in temporal intralimb kinematics during split-belt adaptation (Bruijn, Van Impe, Duysens and Swinnen 2012; Roemmich and others 2014). During split-belt adaptation, older adults adapt relative swing time slower and compensate this by changing swing speed faster than younger adults (Bruijn, Van Impe, Duysens and Swinnen 2012). However, adaptation in stance length asymmetry with split-belt walking is not affected with increased age (Roemmich and others 2014), suggesting a minimal effect of age on spatial reactive adaptation. Older adults alter relative stance times less, especially in the fast leg (Bruijn, Van Impe, Duysens and Swinnen 2012; Roemmich and others 2014), suggesting that an increase in age alters temporal reactive adaptation. Age-related changes in reactive temporal adaptation is also likely to be associated with the effects of aging on dynamic walking stability (Vervoort and others 2020), where the body center of mass is outside the base of support for approximately 80% of the walking cycle. The decreased ability for reactive temporal adaptations during split-belt walking may suggest changes in the spinal cord mechanisms with aging. Table 1.1 summarizes the studies that examined age-effects on reactive intralimb kinematic adaptation.
<table>
<thead>
<tr>
<th>Study</th>
<th>Participants</th>
<th>Outcome</th>
<th>Predictive (Interlimb parameters)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bruijn, Van Impe, and Swinnen (2012)</td>
<td>Y: n = 8, 22.1 ± 3.6 yrs O: n = 12, 73.1 ± 4.7 yrs</td>
<td>No age effect in stance length adaptation. O adapted %swing time slower compared to Y. O changed swing speed faster compared to Y.</td>
<td>O adapted SLsym less and showed less aftereffects. O adapted SLsym slower.</td>
</tr>
<tr>
<td>Ducharme, Kent and van Emmerik (2019)</td>
<td>Y: n = 15, 28.9 ± 5.6 yrs O: n = 15, 64.7 ± 2.7 yrs</td>
<td>NA</td>
<td>No age effect in overall change in limb phase deviation. No age effect in rate of limb phase adaptation.</td>
</tr>
<tr>
<td>Iturralde and Torres-Oviedo (2019)</td>
<td>n = 16, 61 ± 9.9 yrs (range: 46-78 yrs)</td>
<td>NA</td>
<td>SLsym aftereffects were not correlated with age.</td>
</tr>
<tr>
<td>Malone and Bastian (2016)</td>
<td>Y: n = 10, 22.5 ± 2.6 yrs O: m = 10, 54.9 ± 2.8 yrs</td>
<td>NA</td>
<td>No age effect in overall change or rate of SLsym adaptation or de-adaptation.</td>
</tr>
<tr>
<td>Roemmich and others (2014)</td>
<td>Y: n = 15, 22.3 ± 3.3 yrs O: n = 15, 65.2 ± 8.1 yrs</td>
<td>Y adapted stance length symmetry more from mid to late split-belt adaptation compared to O. O demonstrated smaller aftereffects in stance time symmetry compared to Y.</td>
<td>No age effect in overall change or rate of SLsym adaptation or de-adaptation.</td>
</tr>
<tr>
<td>Sombric, Harker, Sparto and Torres-Oviedo (2017)</td>
<td>Y: n = 11, 25.4 ± 5.5 yrs O : n = 11, 77.2 ± 2.8 yrs</td>
<td>NA</td>
<td>O adapted SLsym and step position (but not step time) slower compared to Y. O show similar overall change during adaptation and aftereffects in SLsym, step position, and step time compared to Y.</td>
</tr>
<tr>
<td>Vervoort and others (2019a)</td>
<td>Y: n = 11, 23.3 ± 3.13 yrs O: n = 10, 55.3 ± 2.91 yrs</td>
<td>NA</td>
<td>No effect of age in overall change during adaptation in SLsym, DSSym, or muscle activation patterns.</td>
</tr>
<tr>
<td>Vervoort and others (2019b)</td>
<td>Y: n = 10, 21.5 ± 1.0 yrs O: n = 12, 67.8 ± 5.8 yrs</td>
<td>O increased swing speed of the fast leg during adaptation (more compared to Y). Y increased swing time in the fast leg during adaptation (more compared to O).</td>
<td>No effect of age in overall change and rate adaptation in SLsym, DSSym, or limb excursion symmetry.</td>
</tr>
<tr>
<td>Vervoort and others (2020)</td>
<td>Lifespan study; 12-13 adults per decade. N = 75, 48 ± 17.95 yrs (range: 18-79 yrs)</td>
<td>NA</td>
<td>Initial changes in SL was not correlated to age. Smaller initial change in DS and single support of the slow leg only was significantly associated with increased age. Smaller early change (step 6-30, similar to rate of adaptation as most change occurs during these steps) in SL, DS, and single support significantly associated with increased age.</td>
</tr>
</tbody>
</table>

Table 1.1. Studies that have examined aging effects on locomotor adaptation with a split-belt paradigm.  
Y = Younger adults; O = Older adults; SLsym = Step length symmetry; DSSym = Double support symmetry.
1.3.2 Aging does not reduce overall change in feedforward adaptation during split-belt walking

Age has been shown to have different effects on the rate vs. the overall change in interlimb adaptation via predictive mechanisms during split-belt treadmill walking. Sombric and colleagues (2017) examined effects of age in split-belt adaptation and found no age-related difference in the overall change during adaptation in spatial and temporal interlimb parameters (Figure 1.3), which is in line with a number of other recent studies that examined age-related differences in overall change during adaptation (Ducharme, Kent and van Emmerik 2019; Iturralde and Torres-Oviedo 2019; Malone and Bastian 2016; Roemmich and others 2014; Vervoort and others 2019a). While Bruijn and colleagues (2012) reported less aftereffects in step length symmetry in older adults compared to younger adults, a more recent correlation analysis showed that the aftereffects in step length symmetry were not correlated with age (Iturralde and Torres-Oviedo 2019). Overall, with regard to overall change in kinematic adaptation during split-belt treadmill walking, the majority of studies report that older adults are able to adapt the same amount of interlimb parameters compared to young adults (Table 1.1) (Ducharme, Kent and van Emmerik 2019; Iturralde and Torres-Oviedo 2019; Malone and Bastian 2016; Vervoort and others 2019a). Together, this suggests that aging does not influence the capacity to adapt via feedforward mechanisms during split-belt walking, which is also in line with the observations that older adults are able to adapt to trip- and slip perturbations (Karamanidis, Epro, McCrum and Konig 2020).
Figure 1.3. Age-related changes in split-belt locomotor adaptation. A, (Y)oung (25.4 ± 5.5 yrs) and (O)lder participants (77.2 ± 2.8 yrs) walked with the split-belt treadmill with 0.5 m/s on the non-dominant leg and 1.0 m/s on the dominant leg side. B, Different locomotor studies examine the overall change/magnitude of adaptation (i.e., the amount participants adapt in the new environment) with different calculation techniques. In this study, the difference between the steady state (mean of last 50 strides during adaptation) of step length asymmetry and step velocity was calculated for the extent of adaptation (what we refer in our review as the overall change in adaptation). Both younger and older groups adapted similar amounts with the split-belt treadmill. C, To calculate the rate of adaptation, the step length symmetry was fitted to an exponential function to determine the time constant (# of strides) that participants took to reach 63.2% of the steady state for step length symmetry. Older adults took more time to adapt to the split-belt environment. Error bars are standard error. Modified from Sombric et al., 2017.

1.3.3 Aging reduces rate of feedforward adaptation during split-belt walking

In contrast to the overall change in interlimb adaptation, there is conflicting evidence on the age-related changes on the rate of interlimb adaptation during split-belt treadmill. During split-belt adaptation, Bruijn and colleagues (2012) and Sombric and colleagues (2017) found that older adults adapt interlimb parameters slower. However, other studies have reported that healthy aging did not affect the rate of step length adaptation during split-belt walking (Ducharme, Kent and van Emmerik 2019; Malone and Bastian 2016; Vervoort and others 2019a; Vervoort and others 2019b). The differences in outcome may be due to the differences in the age range of the older cohorts; in the studies that found differences in the rate of kinematic
adaptation, the age ranges were older compared to the studies that did not find differences in the rate of kinematic adaptation (Table 1.1). This is supported by a recent lifespan study by Vervoort and colleagues (2020) who examined split-belt adaptation in people spanning from age 18-79 years old and found associations between increased age and smaller early changes in double support and step lengths. This supports that perhaps there is a gradual decrease of adaptation in predictive kinematic parameters with an increase in age.

It is important to note that aging is complex and other covariates may play a significant role in the aging effects on the rate of kinematic adaptation during split-belt treadmill. For example, physical activity level influences gait parameters during locomotion (Wang and others 2015), and an aging study by Ducharme and colleagues (2019) showed that there was no difference in the rate of limb phase adaptation in young and older adults matched for physical activity levels. This highlights the importance of considering other covariates that may play a role in the variability in the aging process that may influence proprioception-driven locomotor adaptation.

Although the effect of aging on the rate of adaptation is inconclusive, the age-related effect is more variable compared to the overall change in kinematics during adaptation. This suggests that the neural mechanism underlying rate and overall change during adaptation is differentially altered with age. Alternatively, this may suggest that older adults have different prioritization compared to younger adults; for example, older adults may prioritize stability (Darter, Labrecque and Perera 2018; Park and Finley 2017) over energy optimization processes (Finley, Bastian and Gottschall 2013; Stenum and Choi 2020).
1.4 Visuomotor locomotor adaptation: Young vs. Older adults

Vision provides important sensory information about the demands of the walking environment to appropriately adapt locomotion. To study lower limb reactive mechanisms during visuomotor perturbations, stepping targets can be shifted at random, diminishing the possible predictive adaptation that occurs with repetition. Previous studies have shown that healthy young adults are able to alter their leg trajectories in response to random, sudden shifts in stepping targets from static standing positions and during treadmill walking (Reynolds and Day 2005). This demonstrates the existence of a short-latency reactive visuomotor pathway that humans use to respond to sudden changes in visual information (e.g., obstacles, pet running around leg). Visual control of leg movements must also be constantly adapted to maintain accuracy; internal models of visuomotor calibrations are updated through trial-and-error processes in predictive control of locomotion (e.g., accurately predict stair height). When healthy young adults wear prism goggles that shift visual information laterally, participants initially deviate their foot placement, but with repeated trials, are able to reduce this lateral deviation (Alexander, Flodin and Marigold 2011). After removal of the prism goggles, there is a large negative aftereffect (i.e., deviated walking trajectory in the opposite direction), suggesting the presence of predictive adaptation mechanisms to form a new internal model to accommodate the visually-distorted environment (Alexander, Flodin and Marigold 2011).

Locomotor adaptation can also be induced by altering real-time visual biofeedback of specific gait parameters, such as joint angles (Cherry-Allen, Statton, Celnik and Bastian 2018; Statton, Toliver and Bastian 2016). For example, real-time visual feedback on hip and knee flexion angles can be distorted during the
adaptation phase so that participants would need to flex the knee or hip angles more to achieve the same level of the visual feedback target (Statton, Toliver and Bastian 2016). With this intervention, it has been shown that healthy young participants are able to adapt their hip and knee kinematics and show aftereffects (Statton, Toliver and Bastian 2016). When the visuomotor adaptation paradigm is presented simultaneously with a split-belt adaptation paradigm, healthy young participants are able to adapt both their lower extremity flexion angle (from the visuomotor task) and step length symmetry (from the split-belt task) simultaneously (Statton, Toliver and Bastian 2016). Cherry-Allen and colleagues (2018) used simultaneous real-time visual feedback and split-belt adaptation paradigm in post-stroke patients to study cortical control with dual interventions: simultaneous split-belt treadmill adaptation and knee angle learning task with distorted visual feedback. Post-stroke patients can simultaneously adapt knee flexion angles and step length symmetry (Cherry-Allen, Statton, Celnik and Bastian 2018). However, unlike in healthy adults who show strong aftereffects in kinematics adapted with visual-feedback and split-belt (Statton, Toliver and Bastian 2016), post-stroke patients only showed strong aftereffects in step length symmetry adapted via split-belt (Cherry-Allen, Statton, Celnik and Bastian 2018). This suggests that the cortex plays a larger role in visuomotor adaptation compared to split-belt adaptation.

1.4.1 Age-related changes in feedback adaptation during visuomotor locomotor adaptation

Aging studies on feedback adaptation during perturbed visually-guided stepping have shown that older adults may have impaired reactive feedback
processes (Table 1.2). When visual cues on the floor were laterally perturbed while participants were standing, older adults demonstrated delayed reactive adaptation compared to young adults, but the size of stepping error (i.e., spatial accuracy) was not impaired with increased age (Tseng, Stanhope and Morton 2009; Tseng, Stanhope and Morton 2010). With perturbed visual stepping targets in the anterior-posterior direction during treadmill walking, older adults demonstrated larger stepping error compared to younger adults (Mazaheri and others 2015). In line with this, Spedden and colleagues (2019) examined visually-guided walking and found that older adults demonstrate greater error and lower accuracy rates compared to younger adults (Spedden, Choi, Nielsen and Geertsen 2019). This suggests that accuracy in visuomotor tasks during walking may be more compromised in older adults, because unlike stationary stepping tasks, reaction times are not able to be prolonged during locomotion. The age-related reduction in both reactive adaptation during split-belt walking and visuomotor locomotor adaptation may be explained by shared neural pathways as the motor neurons in the spinal cord serves as the final common pathway - together this suggests a possibility of an age-related change in the spinal cord mechanism that controls reactive adaptations during gait. Delayed feedback responses to adjust stepping pattern may be one potential reason for the environment-related increased risk of falls (e.g., stairs, pets) in older adults (Pereira, Santos, Doring and Portella 2017).
<table>
<thead>
<tr>
<th>Study</th>
<th>Participants</th>
<th>Visuomotor paradigm</th>
<th>Measure</th>
<th>Outcome</th>
</tr>
</thead>
</table>
| Mazaheri and others (2015)                | Y: n = 15, 25.4 ± 3.0 yrs  
O: n = 15, 69.4 ± 5.0 yrs | Treadmill speed: 0.83 m/s  
Projected stepping targets on treadmill (Anterior-posterior shifts in targets at 40% of preferred step length; lateral shifts in targets at 20% of preferred step length)  
1 shift with 5-7 non-shifted target in-between  
| Normalized stepping error (% step length) | O had greater stepping error compared to Y in the anterior-posterior direction and lateral step adjustments.                                                                 |                                                                                                                                                                                                                                                                                    |                                                                                                                                                                                                         |
| Tseng, Stanhope, and Morton (2009)        | Y: n = 13, 28.4 ± 4.0 yrs  
O: n = 13, 73.9 ± 4.6 yrs | * Stationary  
Baseline trials: Stepping target placed in front, 40% of height  
Shift trials: Target first appeared in baseline position but shifted 20 cm to the right  
9 shift trials (1 shift trial randomly inserted per 6-13 baseline trials) = total of 90 stepping trials  
| Error (mm)  
Response time (RT) (ms)  
Stepping execution (ms)  
Foot trajectory modification RT (ms)  
Lateral propulsive force modification RT (ms)  
Rate of lateral force production (N/kg/ms)  
Peak lateral force (N/kg) | No age-effect in stepping error and weight transfer duration.  
O had longer RT, stepping execution phase, foot trajectory modification response time, and lateral propulsive force modification RT compared to Y.  
O had decreased rate of lateral force production and peak lateral force compared to Y. |                                                                                                                                                                                                                                                                                    |                                                                                                                                                                                                         |
| Tseng, Stenhope and Morton (2010)        | Y: n = 18, 26 ± 3.7 yrs  
O: n = 18, 72 ± 4.2 yrs | * Stationary  
20 baseline trials, 30 adaptation  
20 Baseline trials: Stepping target placed in front, 40% of height  
30 Adaptation trials: Target first appeared in baseline position but shifted 10% of height either to the left or right after 550 ms  
| Error (%)  
Total movement duration (ms)  
RT (ms)  
Weight transfer (ms)  
Stepping execution (ms) | No age-effect in stepping error and weight transfer duration.  
O had longer total movement duration, RT, and stepping execution time. |                                                                                                                                                                                                                                                                                    |                                                                                                                                                                                                         |
| Spedden, Choi, Nielsen and Geertsen (2019)| Y: n = 15, 22.1 ± 1.7 yrs  
O: n = 15, 68.3 ± 2.7 yrs | Treadmill speed: Normalize to leg length  
3 min baseline walking for familiarization, 5 min baseline walking, 5 min walking with visually-guided feedback  
Visually guided feedback: Real-time position of swing leg position and stepping targets were projected on a screen in front of participant.  
Participants were asked to adjust step length to step on targets as accurately as possible.  
| Score (%) = Accurate hits on targets / Total steps x 100  
Error (%) | O had lower scores and greater error compared to Y. |                                                                                                                                                                                                                                                                                    |                                                                                                                                                                                                         |

Table 1.2. Studies that have examined aging effects on reactive locomotor adaptation with a visuomotor stepping paradigm.  
Y = Younger adults; O = Older adults.
1.4.2 Age-related changes in feedforward adaptation during visuomotor locomotor adaptation

In addition to reactive adaptation, predictive feedforward visuomotor adaptation may also be impaired in older adults. Huitema and colleagues (2005) examined age-related effects in visuomotor locomotor adaptation with prism goggles in young, middle-aged, and older adults. Older adults adapted their walking trajectory less compared to younger adults and reported that they felt they were walking in a straight line, whereas most participants in the young and middle-aged group reported walking in a curved trajectory (Huitema and others 2005). In line with this, older adults demonstrate smaller overall change during adaptation and slower rate of adaptation and de-adaptation in angular error compared to young adults during locomotor adaptation with 30-diopter prism goggles (Figure 1.4) (Nemanich and Earhart 2015). Age-related difference in locomotor adaptation seems to be minimized with a smaller visuomotor distortion, with 20-diopter prism goggles (Bakkum, Gunn and Marigold 2021). However, even with smaller distortion, older adults demonstrate greater error during early adaptation compared to young adults (Bakkum, Gunn and Marigold 2021), together suggesting that older adults have impaired sensory realignment that is required to adapt to inaccurate visual feedback (Block and Bastian 2011).
Figure 1.4. Age-related changes in visuomotor locomotor adaptation. A-B, (Y)oung (25.0 ± 5.83 yrs) and (O)lder participants (70.1 ± 7.27 yrs) walked with the 30-diopter rightward-shifting prism glasses toward a visual target. At the beginning of adaptation participants ended towards the right of the target (A), but with several trials, participants reduced their angular error (B). C, During post-adaptation, participants took off the prism glasses (but vision of the feet and target was obscured) and presented a negative aftereffect. D, In this study, the angular error difference between the first adaptation trial and average of the last adaptation trial was calculated for the overall change during adaptation. Younger adults adapted more compared to the older adults. E, To calculate the rate of adaptation, the angular error was fitted to an exponential function to determine the time constant (# of trials) that participants took to reach 63.2% of the steady state for angular error. Older adults took more trials to adapt with the prism glasses. Error bars represent standard error. Modified from Nemanich and Earhart, 2015.

Across different paradigms, there seems to be some consistent age-related effects on predictive visuomotor adaptation during walking (Table 1.3). Prism adaptation and obstacle avoidance tasks have demonstrated that the overall change and rate of predictive locomotor adaptation are both impaired with age (Huitema and
Thus, evidence suggests that there are age-related changes in neural mechanisms that govern visuomotor locomotor adaptation. Although there are clear age-related visuomotor locomotor adaptation impairments, it is important to note adaptation is not completely annulled with increased age; older adults still demonstrate improvement with visuomotor locomotor tasks, but not as well as younger adults (Bakkum, Gunn and Marigold 2021; Huitema and others 2005; Nemanich and Earhart 2015; van Hedel and Dietz 2004).
<table>
<thead>
<tr>
<th>Study</th>
<th>Participants</th>
<th>Visuomotor paradigm</th>
<th>Measure</th>
<th>Outcome</th>
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<tbody>
<tr>
<td>Huitema and others</td>
<td>Y: n = 12, 24 ± 2.8 yrs M: n = 12, 59.7 ± 7.3 yrs O: n = 12, 76.7 ± 4.4 yrs</td>
<td>2 baseline trials, 16 adaptation trials, 2 post-adaptation trials Each trial: Walked 6.8 m toward a target at head-level Adaptation trials: Walked with prism glasses which shifted visual field 10° to the right</td>
<td>Standard deviation of lateral position (SDLP) Mean heading error Walking speed (m/s) Adaptation effect (Gradient of line fitting of SDLPs of consecutive exposure)</td>
<td>O had greater post-pre difference in SDLP compared to Y. O adapted less compared to Y Y and M demonstrated adaptation effects, whereas O didn't.</td>
</tr>
<tr>
<td>Nemanich and Earhart</td>
<td>Y: n = 15, 25.0 ± 5.8 yrs O: n = 18, 70.1 ± 7.3 yrs</td>
<td>10 baseline trials, 40 adaptation trials, 20 post-adaptation trials Each trial: Walked toward a visual target on floor Adaptation trial: Walked with 30-diopter rightward-shifting prism glasses</td>
<td>Angular error Variability (SD)</td>
<td>O had decreased magnitude of adaptation compared to Y (but no significant difference in magnitude of aftereffect) O adapted and readapted slower compared to Y O had greater variability compared to Y</td>
</tr>
<tr>
<td>van Hedel and Dietz</td>
<td>Y: n = 9, 22.7 ± 2.54 yrs O: n = 9, 63.3 ± 6.93 yrs</td>
<td>Treadmill speed: 0.69 m/s 3 blocks x 50 steps Each block: Participants stepped over obstacle over treadmill that was attached to treadmill. An acoustic warning signal indicated the obstacle was approaching. Time between obstacle was between 6-11 normal step cycles. First two blocks with normal visual input, third block without lower visual field input.</td>
<td>Number of obstacle hits Muscle activation Joint range of motion (ROM) Foot clearance Swing phase duration (%)</td>
<td>O had greater obstacle hits than Y With vision: Both O and Y improved in foot clearance and number of obstacle hits, and there were not differences in muscle activation, joint kinematics, or swing phase duration Without vision: Both O and Y improved muscle activation and swing phase duration (not change in joint kinematics), but only Y improved in foot clearance.</td>
</tr>
<tr>
<td>Bakkum, Gunn, and</td>
<td>Y: n = 12, 28.3 ± 6.9 yrs M: n = 12, 50.3 ± 6.1 yrs O: n = 12, 69.0 ± 5.4 yrs</td>
<td>25 baseline trials, 60 adaptation trials, 1 post-adaptation trials Each trial: Walked 6 m with stepping targets projected on ground Adaptation trials: Walked with 20-diopter prism glasses that shifted visual field 11.4° to the right</td>
<td>Foot placement error in the medial-lateral direction (mm)</td>
<td>All groups adapted to the visuomotor task. M had significantly less initial error during adaptation compared to Y (O also had lower initial error compared to Y, but not statistically significant) O had greater error during early adaptation compared to Y. Age was associated to reduced recall.</td>
</tr>
</tbody>
</table>

Table 1.3. Studies that have examined aging effects on predictive locomotor adaptation with a visuomotor stepping paradigm. Y = Young adults; M = Middle aged adults; O = Older adults.
1.5 Age-related changes in the neural control of locomotion

As outlined above, there are age-related changes in locomotor adaptation, but the neural mechanisms underlining these changes are unclear. The current literature suggests that there may be changes at the different levels of the nervous system that may influence locomotor adaptation.

1.5.1 Spinal cord mechanisms

The spinal mechanisms for locomotor adaptation in humans have been studied by examining split-belt treadmill adaptation in young children who are presumed to have less cortical influence compared to adults (Yang and others 2004). During split-belt treadmill walking, infants are able to modify reactive intralimb parameters such as step cycle duration, swing duration, and stance duration; infants are also able to adapt to an asymmetrical stepping pattern by taking more steps on the fast leg compared to the slow leg (Yang, Lamont and Pang 2005). This suggests that fully-developed supraspinal structures are not required to make reactive feedback locomotor adjustments during split-belt treadmill walking and that the reactive adaptations are largely due to spinal cord circuitry that are independent between limbs.

In older adults, spinal H-reflex amplitude is lower during standing and walking compared to younger adults (Chalmers and Knutzen 2000; Raffalt, Alkjaer and Simonsen 2015). This may be due to the structural changes in the spinal cord circuitry that occur with aging; these include a decrease in the number of motor units (due to a decrease in the number of motor neurons), and a decrease in the innervation ratio of muscle fibers to motor neurons (Deschenes 2011).
Changes in the ability to modulate H-reflexes with increased age may indicate changes in the spinal cord mechanisms during locomotor adaptation. Young adults increase H-reflex amplitude with muscle fatigue (Lavender and others 2020). In a recent study by Lavender and colleagues (2020) examining H-reflexes during locomotion, the modulation in H-reflex decreased with an increase in age. Interestingly, H-reflex amplitude in older adults decreases with fatigue instead of increasing (Lavender and others 2020). As spinal mechanisms likely play an important role in modifying reactive changes in muscle activity in response to sensory input (Choi, Jensen, Nielsen and Bouyer 2016), age-related changes in the excitability of these pathways could explain the reduced reactive locomotor adjustments during proprioceptive and visuomotor locomotor paradigms (Bruijn, Van Impe, Duysens and Swinnen 2012; Mazaheri and others 2015).

1.5.2 Cerebellar mechanisms

Intact cerebellar function is important for predictive, but is not as critical for reactive, locomotor adaptation driven by proprioceptive (Morton and Bastian 2006) and visual feedback (Morton and Bastian 2004; Morton, Dordevic and Bastian 2004). The cerebellum is thought to be important for processing the error between expected and actual sensory input that drives feedforward predictive locomotor adaptation (Bastian 2006). In healthy young individuals, modulation of cerebellar output has been shown to facilitate predictive adaptation during split-belt locomotor adaptation (Jayaram, Galea, Bastian and Celnik 2011). Healthy young adults are able to adapt to visuomotor locomotor paradigms with prism glasses (Alexander, Flodin and Marigold 2011), but patients with cerebellar injury adapt less to walking trajectory and demonstrate fewer aftereffects (associated with feedforward adaptation) compared to healthy adults (Morton and Bastian 2004).
Neurophysiological studies in cats suggest that the rhythmicity of cerebellar neurons act as a source of excitatory locomotor drive to the motor cortex, and the cells that exhibit both step-related rhythmicity and visual responsiveness may play an important role in visually-guided stepping adjustments (Marple-Horvat and Criado 1999).

With an increase in age, there is a reduction of gray matter in the cerebellum (Sullivan, Deshmukh, Desmond, Lim and Pfefferbaum 2000), while functional neuroimaging has shown that blood-oxygen level dependent signals in the cerebellum during imaginary walking (because participants are not able to physically walk in the scanner) are not different between younger and older adults (Zwergal and others 2012). Note that neural measurements via mental imagery of gait may not accurately represent actual neural control during locomotion as it is missing the sensory inputs (la Fougere and others 2010). However, the results from Zwergal and colleagues (2012) are in line with a study by Mitchell and colleagues (2019) who examined the age-related effects in synaptic brain activity during different types of locomotion using positron emission tomography. Walking performance was similar in both normal straight walking and complex (visually-guided, that required steering) walking between young and older adults, and both young and older adults demonstrated higher activation in the cerebellum compared to normal walking (Mitchell, Starrs, Soucy, Thiel and Paquette 2019), suggesting that cerebellar mechanisms during locomotor adaptation are likely to remain intact with increased age.

1.5.3 Cortical mechanisms

The cerebral cortex is critical for the execution, but not feedforward adaptation, of motor commands during split-belt walking (de Kam, Iturralde and Torres-Oviedo 2020). However, corticospinal activity is changed with specific walking parameters during
proprioceptive-driven adaptations (Barthelemy, Alain, Grey, Nielsen and Bouyer 2012; Sato and Choi 2019), and conscious control may be involved in the rate of walking adaptation (Malone and Bastian 2010; Roemmich, Long and Bastian 2016). In visuomotor locomotor adaptation, cortical involvement is crucial to integrate visual information and translate it to appropriate motor execution (Drew and Marigold 2015). To process visual information for motor execution, multiple cortical structures are involved such as the posterior-parietal, premotor, and motor cortices (Drew and Marigold 2015). The timing of motor cortex activity in relation to the step cycle suggests that the motor cortex is important for the execution of gait modifications, and groups of pyramidal tract neurons may control synergistic muscles that are simultaneously active at different phases of the gait cycle (Drew and Marigold 2015). Modulation of the supplementary motor area, premotor cortex and posterior parietal cortex electroencephalography occurs well in advance of visually-guided modifications during treadmill walking (Nordin, Hairston and Ferris 2019), consistent with their role in the planning of visually-guided locomotion (Drew and Marigold 2015).

Aging is known to increase the demand of the prefrontal cortex during motor control (see review: Seidler and others 2010). In locomotion, older adults demonstrate higher prefrontal cortex activation compared to younger adults during normal walking, and this age-related increase in activation is also observed in dual-task walking and obstacle avoidance gait (Mirelman and others 2017), suggesting the increase in cognitive demand during locomotor tasks in older adults. Harada and colleagues (2009) found that older adults with a lower gait capacity modulated prefrontal cortex activation more between fast and slow gait speeds compared to the higher gait capacity group, suggesting a possible compensatory mechanism using cognitive mechanisms in older individuals who walk.
slower. These results provide strong evidence that older adults require more prefrontal activation during walking, and especially during dual-task walking that is cognitively demanding, which may be a compensatory mechanism to recruit and utilize additional brain regions that are not as relied upon in younger adults to increase the motor task performance level (Cabeza, Anderson, Locantore and McIntosh 2002). This is in agreement with cognitive resource theories that hypothesize that the demand in prefrontal cortex activation during motor control is increased in older adults compared to younger adults despite prefrontal cortex functional declines with age (Seidler and others 2010).

In addition, functional neuroimaging has shown that with increasing age, there is increased activation in several cortical areas specific to sensory processing during imaginary locomotion (Wai and others 2012; Zwergal and others 2012). During normal imaginary walking, there is an increase in activation in vestibular cortices, motion-sensitive visual cortices, and somatosensory cortices compared to younger adults (Zwergal and others 2012). Interestingly, while younger adults deactivate multisensory vestibular cortices, these deactivations are less in older adults, suggesting that the increased sensory cortical activations during imaginary walking is due to reduced sensory inhibition (Zwergal and others 2012). This is supported by a positron emission spectroscopy study that reported that older adults demonstrate increased cerebral activity in the precentral and fusiform gyri, decreased activity in the middle frontal gyrus, and reduced deactivation of multisensory cortices during complex walking compared to simple walking (Mitchell, Starrs, Soucy, Thiel and Paquette 2019), suggesting age-related impairment in sensorimotor processing during visually-guided walking. During walking over obstacles that requires more integration of visual input, older adults increase activation in the bilateral supplementary motor area, dorsal premotor area, posterior parietal lobe, precuneus, and visual association area compared to younger adults (Wai and others 2012). Taken together, it can be hypothesized
that the increased multisensory cortical activations reflect impaired somatosensory processing during walking in older adults.

1.5.4 Corticospinal drive

One method to quantify corticospinal involvement is by quantifying the synchrony (i.e., coherence) of motor unit activities measured by electromyography in the time and frequency domains (Farmer, Halliday, Conway, Stephens and Rosenberg 1997; Halliday and others 2003). Synchrony between different motor units in the beta-gamma frequency band (15-45 Hz) is demonstrated to be corticospinal in origin through corticomuscular coherence studies (Grosse, Cassidy and Brown 2002). Therefore, this is one way to quantify the common corticospinal drive, or the activation of motor units as the result of the common input specifically from the corticospinal neurons (Farina, Merletti and Enoka 2014). This is important because as outlined in the previous section on cortical mechanisms, the effect of increased age in cortical involvement is not uniform; some areas increase activation while some decrease. By examining corticospinal drive during locomotion that reaches the peripheral muscle, we may be able to infer the effect of aging on the output that ultimately drives the changes in locomotor kinematic adaptations.

In older adults, corticomuscular control during double support phase of gait is lower compared to young adults (Roeder, Boonstra and Kerr 2020). In line with this, Spedden and colleagues (2019) observed lower corticospinal drive measured by lower corticomuscular and intramuscular coherence in older adults compared to young adults during normal and visually-guided walking (Figure 1.5). Performance on the visually-guided locomotor task was significantly better in younger adults compared to older adults, and performance of the visually-guided walking in older adults was correlated to corticomuscular coherence.
difference between visually-guided and normal walking (Spedden, Choi, Nielsen and Geertsen 2019). Interestingly, the direction of relationship was different for corticomuscular coherence during early and late swing; larger modulation in corticomuscular coherence during early swing was associated with better performance in the visually-guided walking task, but smaller modulation in corticomuscular coherence during late swing was associated with better performance in the visually-guided walking task in older adults (Spedden, Choi, Nielsen and Geertsen 2019). The positive correlation between early swing corticomuscular coherence and visually-guided walking performance agrees with previous studies that suggests that corticospinal drive plays a role in precision-stepping tasks (Drew, Jiang, Kably and Lavoie 1996). The negative correlation between late swing corticomuscular coherence and visually-guided walking performance suggests that the corticospinal activation is specific to gait phase.

Figure 1.5. Age-related changes in corticospinal drive during locomotion. A, Pooled intramuscular coherence in the tibialis anterior in (Y)oung (22.1 ± 1.70 yrs; light blue, pink) and (O)lder participants (68.3 ± 2.7 yrs; dark blue, red) during late swing phase of gait in the beta- (13-35 Hz; light/dark blue) and gamma- (pink/red) frequency bands. The older group generally demonstrated lower beta and gamma intramuscular coherence compared to younger adults. B-C, The area under the coherence curves were calculated, which showed consistent results with the pooled coherence; older adults demonstrated less coherence in the beta- (B) and gamma-band (C) intramuscular tibialis anterior coherence compared to younger adults. Error bars are standard error. Modified from Spedden et al., 2019.
1.6 Limitations

This review focuses on the age-related changes of neural control of human locomotor adaptation, but other physiological changes that occur with increased age should not be disregarded. The reported differences in locomotor adaptation in this review are likely not exclusively due to the changes in the nervous system, but as a result of a combination of age-related changes in the muscle-tendon unit and the neuromuscular system (Wu, De Vito, Delahunt and Ditroilo 2020; Wu, Ditroilo, Delahunt and De Vito 2021). Furthermore, it is important to note that while all of the studies mentioned examined “healthy aging” there is variability in how people age; for example, people may be at very different physical activity levels, which influences spatiotemporal gait parameters (Wang and others 2015). This review highlights that even in “healthy aging” there are changes in the nervous system that may be associated with the changes in locomotor adaptation.

Studies included in this study may be considered small (n = 8-18 per age group, Tables 1.1-1.3); therefore, one of the reasons why there are conflicting findings in age-related changes in locomotor adaptation may be due to a lack of statistical power. It is important to note that this review speculates a role for the aging nervous system on locomotor adaptation; the evidence is far from conclusive at this point. However, the sample sizes in the studies mentioned are common in healthy young adult studies examining human locomotor adaptation. In addition to the lack of statistical power from sample sizes, the quantification methods for kinematic and neurophysiological changes vary between paradigms making comparisons between locomotor adaptation with different sensory demands challenging. For the future, a larger-scale aging study on locomotor adaptation will be beneficial for the field, especially if the kinematic and neurophysiological variables are examined for different paradigms are consistent.
1.7 Summary

Human locomotor adaptation involves multiple neural structures, and their functional roles in different types of walking adaptation are differentially impacted by aging. Studies on proprioceptive-driven locomotor adaptation have shown that reactive feedback adaptation and the overall change in predictive feedforward adaptation during split-belt locomotor adaptation are not affected with age (Bohm, Mademli, Mersmann and Arampatzis 2015; Ducharme, Kent and van Emmerik 2019; Malone and Bastian 2016; Vervoort and others 2019a), while rate of predictive feedforward adaptation is slower in some (but not all) older adults (Bruijn, Van Impe, Duysens and Swinnen 2012; Sombric, Harker, Sparto and Torres-Oviedo 2017). Age-related decline in corticospinal drive may play a role in reduced feedforward adaptation rate (via voluntary gait modification) during split-belt walking adaptation. In contrast to proprioceptive locomotor adaptation, visuomotor locomotor adaptation is impaired in both overall change and rate (Huitema and others 2005; Nemanich and Earhart 2015; van Hedel and Dietz 2004), and there are known reduction in corticospinal drive with aging that influence visuomotor locomotor control.

The differences observed in the age-related changes in kinematic across different locomotor adaptation paradigms are in line with the differential age-related changes in the neural mechanisms underlying locomotion (Figure 1.6). Literature on age-related changes in neural control of locomotion suggests that the input from spinal cord circuitries is reduced (Chalmers and Knutzen 2000; Raffalt, Alkjaer and Simonsen 2015), which may be responsible for decreased reactive feedback adaptations. Cerebellar mechanisms are intact with increased age (Harada, Miyai, Suzuki and Kubota 2009; Mitchell, Starrs, Soucy, Thiel and Paquette 2019; Zwergal and others 2012), and likely play a critical role in the capacity
for feedforward adaptations. With regard to cortical structures, prefrontal and sensorimotor
cortex demand measured from the cortex by neuroimaging is increased (Harada, Miyai,
Suzuki and Kubota 2009; Mirelman and others 2017; Wai and others 2012; Zwergal and
others 2012), but the corticospinal drive (i.e., the signal from the motor cortex that actually
reaches the peripheral muscle) during locomotion is reduced in older adults compared to
younger adults (Roeder, Boonstra and Kerr 2020; Spedden, Choi, Nielsen and Geertsen
2019). Taken together, this suggests that the observed similarities in feedforward
proprioceptive locomotor adaptation between younger and older adults may be due to
preserved cerebellar mechanisms. On the other hand, there is consensus that visually-
guided locomotor adaptation is impaired in older adults, and this may be due to the
increased reliance on corticospinal drive, which is important for voluntarily adjusting gait
with visual feedback. By further examining the effects of age on the neural control during
proprioceptive and visuomotor locomotor adaptation, we may be able to pinpoint neural
mechanism(s) is playing a compensatory or limiting role in age-related alterations in
locomotor adaptation.
See page 30 for details.
CHAPTER 2

OVERVIEW OF DISSERTATION RESEARCH

2.1 Overarching goals of dissertation research

My long-term goal is to understand the mechanisms of age-related changes in locomotor adaptation, and to develop novel gait interventions that target neuroplasticity in older adults. While there have been a number of studies investigating locomotor adaptation in older adults, there is currently no consensus regarding the effects of aging on the neural control underlying locomotor adaptability across different experimental paradigms. The cause of age-related changes in different types of locomotor adaptation also remains an important gap in knowledge.

This dissertation project focuses on two adaptation paradigms that are relevant for gait rehabilitation, namely split-belt treadmill locomotor adaptation and visuomotor locomotor adaptation. Split-belt treadmill was used to study interlimb adaptation when the left and right treadmill belts were moving at different speeds. This causes a mismatch between the expected and actual proprioceptive feedback causing “error” signals, and gradual adjustments in gait parameters to minimize the error (Reisman, Block and Bastian 2005). Visual feedback was used to study visuomotor adaptation of foot placement during walking. Distorting visual feedback causes a mismatch in the visual and proprioceptive information. With this paradigm, gait parameters are gradually adjusted based on given visual feedback (Statton, Toliver and Bastian 2016). Specifically, in this dissertation project I used a distorted visual feedback with an unequal screen:treadmill space ratio (i.e., visuomotor gain) for each side. With this split-visuomotor paradigm, healthy young adults
learn an asymmetrical gait pattern (Sato, Cui and Choi 2020). These experiments allow us to understand how aging impacts the ability to adjust certain movement characteristics (e.g., gait asymmetry) and to maintain movement accuracy (e.g., foot placement) in the presence of external perturbations. Understanding the neural mechanisms for locomotor adaptation, and how it changes with aging, are critical to ensure that gait interventions are appropriately targeted.

The objective of this dissertation is to examine the effects of aging on the corticospinal control mechanisms during locomotor adaptation driven by proprioception and vision. Motor adaptation studies have traditionally focused on cerebellar mechanisms; however, recent studies have shown that cortical contributions are important as well (For review: Taylor and Ivry 2014). The motor cortex likely plays different roles between proprioceptive and visuomotor locomotor adaptation. In proprioception-driven locomotor adaptation, the cortex is involved in task-specific roles (Barthelemy, Alain, Grey, Nielsen and Bouyer 2012; Sato and Choi 2019) and may be involved in the rate of adaptation (Malone and Bastian 2010; Roemmich, Long and Bastian 2016). In visuomotor locomotor adaptation, cortical involvement is crucial to integrate visual information and to translate it into appropriate motor execution (Drew, Jiang, Kably and Lavoie 1996; Drew and Marigold 2015). However, the age-related changes in corticospinal control during proprioception-driven locomotor adaptation (i.e., split-belt adaptation) and visuomotor locomotor adaptation are unknown. As there are known age-related changes in cortical structures (For review: Morrison and Baxter 2012) and the cortical contribution during locomotion (Mitchell, Starrs, Soucy, Thiel and Paquette 2019; Zwergal and others 2012), there may be age-related changes in corticospinal mechanisms during locomotor adaptation.

This dissertation project will examine whether there are age-related changes in corticospinal drive and gait adaptation. My central hypothesis is that corticospinal drive
plays a functional role in locomotor adaptation. This is based on our recent work that demonstrated that lower corticospinal drive during split-belt walking is associated with temporal adaptation in healthy young adults (Sato and Choi 2019), and prior work that demonstrated that corticospinal drive is reduced during walking in older adults (Roeder, Boonstra and Kerr 2020; Spedden, Choi, Nielsen and Geertsen 2019). To test my central hypothesis, I assessed age-related changes in corticospinal control in different locomotor adaptation paradigms that rely on different sensory feedback processes. Specifically, study 1 will examined whether age impacts corticospinal control of proprioception-driven split-belt treadmill adaptation, and study 2 examined whether age impacts corticospinal control of split-visuomotor locomotor adaptation.

2.2 Quantification of corticospinal control

A motor neuron pool has three sources of input: (1) An independent input specific to each neuron, (2) an afferent input common to all motor neurons in the motor neuron pool, and (3) a cortical input common to all motor neurons in the different motor neuron pools (Figure 2.1) (Farina, Merletti and Enoka 2014). By quantifying the coherence between two motor unit activities measured by electromyography (EMG), the strength of the common synaptic input from the cortex to the muscle, or corticospinal drive can be quantified, and was used in this dissertation project. Specifically, coherence analysis between EMG signals in the beta-gamma range (15-45 Hz) was used to quantify corticospinal drive to the specific peripheral leg muscles.
Coherence between motor unit activity is present in different frequency bands, and it is important to note that EMG oscillations in the different frequency bands are speculated to originate in different parts of the central nervous system (For review: Grosse, Cassidy and Brown 2002). EMG-EMG coherence in the delta-band (2-3 Hz) has been shown to be present during isometric contraction and slow movements (Kamen and De Luca 1992). Although the specific origin of the coherence in the delta-band is unclear, it is likely not cortical in origin as it is present in patients with internal capsule injury (Farmer, Swash, Ingram and Stephens 1993).
EMG oscillations in the theta (4-7 Hz) and alpha-band (8-12 Hz) are characteristics of physiological tremor (Bhatia and others 2018; Flood, Jensen, Malling and Lowery 2019; Kane, Hutchison, Hodaie, Lozano and Dostrovsky 2009). During slow movements, EMG theta-alpha-band oscillations are associated with the pulsatile motor output (Flood, Jensen, Malling and Lowery 2019; Vallbo and Wessberg 1993). For example, during a finger movement task, EMG alpha-band oscillations in the agonist precedes angular acceleration, and oscillations in the antagonists precedes angular deceleration. This suggests that the alpha-band oscillations are important in slow, periodic movements (Vallbo and Wessberg 1993). In cats, after the injection of harmaline that produces tremor, synchronous bursts at 8-15 Hz frequency were observed from the intracellular Purkinje cell recordings in the cerebellum and in the reticular formation neurons in the inferior olives (Llinas and Volkind 1973; Llinas 2013), suggesting the alpha-band oscillations to be olivo-cerebellar in origin. In humans, corticomuscular coherence in the theta-alpha range has been observed (Brantley and others 2016; Roeder, Boonstra, Smith and Kerr 2018), contradicting the olivocerebellar origin. However, corticomuscular theta-band coherence is pronounced in patients with Parkinson’s disease (McKeown and others 2006; Salenius, Avikainen, Kaakkola, Hari and Brown 2002), which is in agreement with the previous studies mentioned that it is related to tremors. Intermuscular theta-band coherence is correlated to Parkinson’s disease severity (Flood, Jensen, Malling and Lowery 2019), and significant theta-band intermuscular coherence has been observed in patients with writer’s cramp (that includes tremor as one of the main symptoms; Sheehy and Marsden 1982) but not in healthy controls (Choudhury and others 2018). Together, these studies demonstrate that although the pin-point origin of the EMG-EMG coherence in the theta-alpha-band is unclear, there is consensus that the origin is central and related to tremors (Choudhury and others 2018; McKeown and others 2006; Salenius, Avikainen, Kaakkola, Hari and Brown 2002)
In contrast to the slower oscillations, there are many studies that unanimously point to the origin of the beta-band (15-30 Hz) EMG oscillations as the motor cortex (Farmer, Bremner, Halliday, Rosenberg and Stephens 1993; Farmer, Halliday, Conway, Stephens and Rosenberg 1997; Halliday and others 2003; Halliday, Conway, Farmer and Rosenberg 1998). In an influential study, Farmer and colleagues (1993) measured motor unit activity from two different motor units in the intrinsic hand muscles and observed coherent discharges in the 1-12 and 16-32 Hz frequency bands. Upon further analysis, compared to the EMG-EMG coherence in the 1-12 Hz range, coherence in the 16-32 Hz range was more strongly correlated to central peaks in the cross-correlation between the two motor units (which is speculated to be a result of excitatory postsynaptic potential from monosynaptic inputs to the motor neuron; Kirkwood and Sears 1978), suggesting beta-band EMG-EMG coherence to be cortical in origin (Farmer, Bremner, Halliday, Rosenberg and Stephens 1993). In support of this, coupling between the motor cortex and EMG in the beta-band has been observed during submaximal, static contraction with both electroencephalography (Gwin and Ferris 2012; Mima and Hallett 1999a; Mima, Steger, Schulman, Gerloff and Hallett 2000) and magnetoencephalography studies (Brown, Salenius, Rothwell and Hari 1998; Conway and others 1995; Gross and others 2000). Furthermore, EMG-EMG coherence in the 15-50 Hz range has been shown to be reduced and/or absent in patients who have impaired supraspinal control such as spinal cord injury (Barthelemy and others 2010; Hansen and others 2005), cerebral palsy (Petersen, Farmer, Kliim-Due and Nielsen 2013), and cortical lesions (Datta, Farmer and Stephens 1991; Farmer, Bremner, Halliday, Rosenberg and Stephens 1993), further suggesting the corticospinal origin of EMG-EMG coherence in the beta-frequency band.

Similar to beta band EMG-EMG coherence, gamma band EMG-EMG coherence is speculated to originate from the motor cortex (Brown, Salenius, Rothwell and Hari 1998;
Gwin and Ferris 2012). Gamma-band corticomuscular coherence was first reported during maximal contractions (Brown, Salenius, Rothwell and Hari 1998); however, studies have also demonstrated corticomuscular gamma-band coupling during dynamic movements (Gwin and Ferris 2012; Marsden and others 2000; Omlor, Patino, Hepp-Reymond and Kristeva 2007). Omlor and colleagues (2007) examined corticomuscular coherence between EEG and EMG and observed beta-band coherence during an upper-extremity visuomotor task that required constant force production and observed a shift of coherence toward the gamma-band coherence during periodically modulated force condition. Marsden and colleagues (2000) demonstrated that the beta-band coherence between during an isometric muscle contraction and a shift to gamma-band coherence during self-timed phasic contraction. In line with this, Gwin and Ferris (2012) examined EEG-EMG coherence isotonic and isometric lower limb exercises and observed significant coherence in both the beta- and gamma-band, but higher gamma-band corticomuscular coherence for isotonic exercises compared to isometric exercises, suggesting that the type of muscle contraction plays a role in the frequency of observed corticomuscular coherence (Gwin and Ferris 2012). This suggests that there may be a shift between beta- and gamma-band coherence depending on task demands and type of muscle contraction. In studies that have examined both beta- and gamma-range EMG-EMG coherence during walking, between-conditions comparisons were consistent (Sato and Choi 2019; Spedden, Choi, Nielsen and Geertsen 2019; Willerslev-Olsen, Petersen, Farmer and Nielsen 2015), supporting that the origin of the beta- and gamma-band EMG-EMG coherence are consistent, and likely originates from the motor cortex.

EMG-EMG coherence can be analyzed within a single muscle (intramuscular) or between different synergistic muscles (intermuscular). In this dissertation project, I analyzed intramuscular coherence in the tibialis anterior, and intra and intermuscular coherence in
the plantarflexors. Intramuscular coherence in the tibialis anterior during the swing phase of gait has been analyzed previously with different clinical populations (Barthelemy and others 2010; Spedden, Choi, Nielsen and Geertsen 2019; Willerslev-Olsen, Petersen, Farmer and Nielsen 2015), as foot-drop during swing is a popular target to improve gait rehabilitation. To quantify corticospinal drive to the plantarflexors, intermuscular coherence between the soleus and medial gastrocnemius has been used for dynamic studies (Jensen and others 2019; Spedden, Nielsen and Geertsen 2018; Watanabe, Saito, Ishida, Tanabe and Nojima 2018b). However, intermuscular coherence analysis may yield different results compared to intramuscular coherence. Beta-gamma band intramuscular coherence is indicative of corticospinal drive, whereas intermuscular coherence has been shown to be indicative of functional coordination (Laine and Valero-Cuevas 2017). A decrease in beta-gamma intermuscular coherence may be accompanied by greater individual muscle control. Therefore, if a difference is observed in the modulation of tibialis anterior intramuscular coherence, but not in soleus and medial gastrocnemius intermuscular coherence, it will not be possible to differentiate if the difference in modulation is muscle-specific or specific to inter or intramuscular analysis. For this reason, I will analyze both inter (soleus and medial gastrocnemius) and intramuscular (medial and lateral gastrocnemius) coherence in the plantarflexors during stance phase.

In dynamic movements such as walking, EMG is filtered to remove low-frequency movement artifacts (Clancy, Bouchard and Rancourt 2001; De Luca, Gilmore, Kuznetsov and Roy 2010; Hogan 1976; Raez, Hussain and Mohd-Yasin 2006). Therefore, for coherence analysis in this dissertation project, delta- and theta-band EMG-EMG coherence will not be analyzed. To quantify corticospinal drive, I will look at EMG-EMG coherence in the beta-gamma range (15-45 Hz) as previous studies that showed that they both originate in the motor cortex (For review: Grosse, Cassidy and Brown 2002). For the alpha-band
EMG-EMG coherence, given that the origin of the coherence in alpha-band is speculated to be different from the beta-gamma range coherence, I expect the changes to be different from that of beta- and gamma-band coherence. However, I do not expect the alpha-band coherence to stay stable through all the conditions, because the central neural input to the motor unit that also governs tremors such as the olivo-cerebellar system (Llinas and Volkind 1973; Llinas 2013) likely changes during locomotor adaptation.

EMG-EMG coherence analysis provides a noninvasive method to measure cortical drive to specific muscle contractions during static posture and during dynamic movements such as walking. Advantages of EMG-EMG coherence analysis over neurostimulation techniques (e.g., transcranial magnetic stimulation) is that it can quantify corticospinal involvement without modulating corticospinal excitability, and that it provides higher temporal resolution compared to neuroimaging techniques (e.g., functional magnetic resonance imaging). However, it is important to not overinterpret the analysis because EMG-EMG coherence analysis does have its disadvantages. EMG-EMG coherence analysis has the potential of overestimation of coherence due to cross-talk of motor units (Hansen and others 2005). My steps to avoid this are outlined in the limitation sections (in 5.3); in brief, I will use the techniques used in previous studies (Hansen and others 2005) to visually inspect the data and exclude the data from participants with signs of cross-talk in the EMG signals.

2.3 Specific Aims

**Specific aim 1:** Determine the impact of age on the contribution of corticospinal drive during proprioceptive (split-belt) locomotor adaptation.
To test this specific aim, I asked participants to walk on the split-belt treadmill to adapt their gait pattern by proprioceptive feedback. The kinematic variables to quantify locomotor adaptation were step length symmetry, double support asymmetry, and step time asymmetry. For each kinematic variable, the overall and early changes during adaptation and post-adaptation were calculated.

I quantified the corticospinal drive by coherence analysis of EMG from lower leg muscles and assess group differences between young and older adults. To examine corticospinal drive, I assessed the amount of beta-gamma band (15-45 Hz) intramuscular EMG-EMG coherence in the tibialis anterior muscle, intermuscular EMG-EMG coherence in the medial gastrocnemius muscle and soleus muscle, and intramuscular EMG-EMG coherence in the gastrocnemius muscle. Intramuscular EMG-EMG coherence in the tibialis anterior was calculated for EMG activity during the swing phase of the gait cycle, and intermuscular and intramuscular EMG-EMG coherences for the plantarflexors were calculated for EMG activity during the stance phase (i.e., when the muscles are active).

**Hypothesis 1.1:** Older adults will adapt interlimb parameters the same amount as young adults, but early change in interlimb parameters during adaptation will be reduced in older adults.

My hypothesis is based on previous studies that have reported that older adults are able to adapt the same amount of interlimb parameters compared to young adults (Ducharme, Kent and van Emmerik 2019; Iturralde and Torres-Oviedo 2019; Malone and Bastian 2016; Vervoort and others 2019a), but the rate of adaptation is reduced in older adults greater than 70 years old (Bruijn, Van Impe, Duysens and Swinnen 2012; Sombric, Harker, Sparto and Torres-Oviedo 2017). Overall change was quantified by the difference in
kinematic asymmetry during plateau phase (average of last 30 strides) and initial perturbation (average of first 5 strides). Change during early adaptation was quantified by the difference in kinematic asymmetry during early adaptation (average of stride 6-30) and initial perturbation. For a metric that can infer on the rate of adaptation, change during early adaptation (when most of the adaptation occurs) was quantified by the difference in kinematic asymmetry during early adaptation and initial perturbation.

**Hypothesis 1.2:** Corticospinal drive will be less in older adults compared to young adults during split-belt walking.

My hypothesis is based on a previous study that observed lower corticospinal drive in older adults compared to young adults during normal (i.e., tied-belt treadmill) walking (Spedden, Choi, Nielsen and Geertsen 2019). In support of my hypothesis, my preliminary data has demonstrated that older adults are likely to have reduced corticospinal drive to the tibialis anterior during split-belt treadmill walking. For exploratory purposes, I will also compare differences between normal walking and visuomotor walking conditions, and explore condition and group interaction effect to examine whether aging affects modulation of corticospinal drive between conditions.

**Hypothesis 1.3:** Reduced corticospinal drive will be associated with reduced early changes in interlimb adaptation during split-belt walking.

My hypothesis is based on previous studies that have shown that cortical input may be involved in the rate of adaptation (Malone and Bastian 2010; Roemmich, Long and Bastian 2016), which has been demonstrated to be impaired in older adults (Bruijn, Van
As previous studies have shown that corticospinal drive is reduced in individuals with older age (Roeder, Boonstra and Kerr 2020; Spedden, Choi, Nielsen and Geertsen 2019), and cortical activity is involved in the rate of adaptation on the split-belt treadmill (Malone and Bastian 2010; Roemmich, Long and Bastian 2016), age-related differences in corticospinal control during split-belt adaptation may be related to reduced early changes in kinematic adaptation in older adults.

**Specific aim 2:** Determine the impact of age on the contribution of corticospinal drive during split-visuomotor locomotor adaptation

To assess this aim, I asked participants to walk on a tied-belt treadmill (treadmill speed kept constant between legs, speed adjusted to each participant’s leg length) with split-visuomotor feedback to adapt an asymmetrical gait pattern. The kinematic variables to quantify locomotor adaptation were step error symmetry, step length symmetry, step time symmetry, and double support symmetry. For each kinematic variable, the overall and early changes during adaptation and post-adaptation were calculated.

I quantified corticospinal drive by coherence analysis of EMG from lower leg muscles and assess group differences between young and older adults. Corticospinal control was quantified in the same way as specific aim 1; the amount of beta-gamma (15-45 Hz) and gamma (30-45 Hz) intramuscular EMG-EMG coherence in the tibialis anterior muscle, intermuscular EMG-EMG coherence in the medial gastrocnemius muscle and soleus muscle, and intramuscular EMG-EMG coherence in the gastrocnemius muscle were calculated for when the muscles are active in the gait cycle (swing and stance times, respectively).
**Hypothesis 2.1:** Older adults will show reduced overall change, and reduced early change in kinematic asymmetry during adaptation compared to younger adults.

My hypothesis is based on previous studies that showed that with visuomotor tasks during walking, accuracy, overall amount, and rate of adaptation is decreased in older adults compared to younger adults (Mazaheri and others 2015; Nemanich and Earhart 2015; Spedden, Choi, Nielsen and Geertsen 2019; van Hedel and Dietz 2004). Overall change was quantified by the difference in kinematic asymmetry during plateau phase (average of last 30 strides) and initial perturbation (average of first 5 strides). Change during early adaptation was quantified by the difference in kinematic asymmetry during early adaptation (average of stride 6-30) and initial perturbation. For a metric that can infer on the rate of adaptation, change during early adaptation (when most of the adaptation occurs) was quantified by the difference in kinematic asymmetry during early adaptation and initial perturbation.

**Hypothesis 2.2:** Corticospinal drive will be less in older adults compared to young adults during visuomotor walking.

My hypothesis is based on a previous study that observed lower corticospinal drive in older adults compared to young adults during walking (Spedden, Choi, Nielsen and Geertsen 2019). In support of my hypothesis, my preliminary data has demonstrated that older adults are likely to have reduced corticospinal drive to the tibialis anterior during split-visuomotor locomotor adaptation. For exploratory purposes, I will also compare differences between normal walking and visuomotor walking conditions, and explore condition and
group interaction effect to examine whether aging affects modulation of corticospinal drive between conditions.

**Hypothesis 2.3:** Reduced corticospinal drive will be associated with overall change and early change in kinematic adaptation.

Previous studies have shown that cortical involvement is likely to be crucial to integrate visual information and translate it to appropriate motor execution during visuomotor walking (Drew, Jiang, Kably and Lavoie 1996; Drew and Marigold 2015). Therefore, I hypothesize that the corticospinal drive will play functional roles during visuomotor locomotor adaptation.

2.4 Significance and Innovation

This project is significant because it will result in a critical set of new data on age-related changes in corticospinal drive during locomotor adaptation with different sensory feedback. No study to-date has examined the age-related differences in intramuscular coherence during split-belt treadmill walking, where a clear kinematic gait pattern is stored in the nervous system, shown by aftereffects (Reisman, Block and Bastian 2005). In addition, there is evidence that visuomotor locomotor adaptation is impaired in older adults (Huitema and others 2005; Nemanich and Earhart 2015; van Hedel and Dietz 2004), but the neural mechanisms underlying this reduced ability to adapt is unclear. The proposed studies will provide insight into the age-related changes of the specific roles of corticospinal drive during locomotor adaptation, which is an important theoretical contribution in the field of motor control.
This project is innovative because it integrates concepts from aging, biomechanical adaptation, and the neural control of locomotion. Locomotor adaptation is necessary for flexible locomotion to prevent falls. Despite the number of studies that have shown that older adults have difficulty adapting to novel environments (Bierbaum, Peper, Karamanidis and Arampatzis 2010; McCrum and others 2016; Weerdesteyn, Nienhuis and Duysens 2005), there is no clear-evidence on the type of exercise intervention that is most effective for fall prevention. By integrating concepts from aging, biomechanical adaptation, and neural control, I will be able to provide new evidence towards the development of a targeted, adaptation-focused gait intervention to better prevent falls in the elderly.

2.5 Overview of Methods

2.5.1 Study design

The dissertation project was conducted with a repeated-measures crossover design with (sub-) studies to address specific aim 1 (study 1; detailed in chapter 3) and specific aim 2 (study 2; detailed in chapter 4). All participants who were recruited were asked to participate in two sessions; study 1 and study 2. The two sessions were randomized and at least one week apart from each other (Figure 2.2).
2.5.2 Participants

Young adults 18-33 years old, and older adults 65-80 years old were recruited through convenience sampling though fliers and word of mouth. For my older cohort, I chose 65-80 years old because it has been reported that age of 60 years is critical for neuromuscular changes that occur with age (Fjell and others 2013; Stalberg and Fawcett 1982). Furthermore, my literature review (Chapter 1) has shown that locomotor adaptation deficits are more likely to be present in individuals over the age of 70 years (Table 1.1). Therefore, my goal was to recruit older individuals with a group average of over 70 years.

21 young adults (18-33 years old) and 20 older adults (68-80 years old) participated in the studies included in this dissertation project (Table 2.1). One young adult was lost to follow-up and did not participate in the second session, which was for study 1. There was equipment failure for one older adult for study 1, and the participant was not able to make up the experiment at a future date. Therefore, for study 1, 20 young adults and 19 older adults participated, and for study 2, 21 young adults and 20 older adults participated.
Table 2.1. Participant characteristics for dissertation project. Characteristics of participants who were included in this dissertation project. Participant characteristics and functional assessment scores for studies 1 and 2 are reported in chapters 3 and 4, respectively.

Participants were enrolled only if they had no previous history of neurological disorder, no current major medical conditions (including cognitive), no current orthopedic injuries, and if they were able to walk without any walking aids (including ankle-foot orthoses) for at least 10 minutes. An approximately equal number of biological males and females were recruited in each group to control for possible sex differences in corticospinal drive, as there has been reported sex differences in the motor nervous system (Pitcher, Ogston and Miles 2003; Zhou, Goto, Goto, Moriyama and He 2000) and age-related brain volume loss (Murphy and others 1996).

To justify my group sizes, power calculations were performed for the main primary outcome variables for both studies 1 and 2 with preliminary data. Sample sizes and powers were explored for assessing age-related effects in kinematic adaptation (hypothesis 1.1 and 2.1) and coherence (hypothesis 2.1 and 2.2), through independent t-tests and identifying significant differences with an alpha level of 0.05 (Figures 2.3 and 2.4, and Table 2.2). My desired power was 0.8. To achieve this, 15 participants for each group seems to be adequate to identify age-related differences if differences are present (Table 2.2). Therefore, the target for recruitment was at least 20 participants in each group in anticipation of participants who decide to participate in one session but drop-out for the

<table>
<thead>
<tr>
<th></th>
<th>Young (n = 21)</th>
<th>Old (n = 20)</th>
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<tbody>
<tr>
<td>Age (yrs)</td>
<td>23 ± 4.5</td>
<td>74.9 ± 4.4</td>
</tr>
<tr>
<td>Sex (M:F)</td>
<td>9:12</td>
<td>12:9</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>169.4 ± 9.5</td>
<td>171.7 ± 8.8</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>67.8 ± 14.2</td>
<td>77.0 ± 15.7</td>
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<tr>
<td>BMI</td>
<td>23.5 ± 3.8</td>
<td>26.1 ± 4.8</td>
</tr>
</tbody>
</table>
second session. For the main variables that seem to have smaller age-related differences, the power does not increase despite increasing the sample size to 30 (Figures 2.3 and 2.4). For aim 2.1 of study 2, based on calculations from my preliminary data, the sample size may be underpowered. However, even after doubling the minimum sample size to 30, the power will not reach the desired power of 0.8, indicating that there may not be large differences in the rate of kinematic visuomotor locomotor adaptation (Figure 2.4A, and 2.4a). Furthermore, since the older adult cohort in my preliminary data was small (n = 3), I conducted a secondary analysis with published data by Nemanich and Earhart (2015) with the same assumptions (Figure 2.4A). This showed that a sample size of 15 will be sufficient to examine if there are clear visuomotor adaptation rate differences. Together, these calculations demonstrate that recruiting 20 participants per age-group, aiming for a minimum of 15 per age group will be sufficient to address aims 1 and 2.
Figure 2.3. Power calculation for study 1. Main outcome variables of interest for hypothesis 1.1 (A) and hypothesis 1.2 (B) are plotted. Dotted horizontal line indicate the optimal power desired (0.8). Solid vertical black line indicates the target sample size (n= 20). Dashed vertical black line indicates target minimum sample size (n = 15). Sub-figures (a, b) are the same as the larger plots, but with a larger x-axis.

SLsym = Step length asymmetry; DSsym = Double support asymmetry; ST sym = Step time asymmetry; TA = Tibialis anterior; PF = Plantarflexors.
Figure 2.4. Power calculation for study 2. Main outcome variables of interest for hypothesis 2.1 (A) and hypothesis 2.2 (B) are plotted. Dotted horizontal line indicate the optimal power desired (0.8). Solid vertical black line indicates the target n (n= 20). Dashed vertical black line indicates target minimum sample size (n = 15). Sub-figures (a, b) are the same as the larger plots, but with a larger x-axis.
Errorsym = Error symmetry; SLsym = Step length symmetry; DSsym = Double support symmetry; ST sym = Step time symmetry; TA = Tibialis anterior; PF = Plantarflexors.
Table 2.2. Power calculations for main effect of age for outcome variables. For each variable, the largest standard deviation (SD) was used for the calculations. Shaded variables represent primary interest variables that I expect to see between-group differences between young and old cohorts. Non-shaded variables represent exploratory variables, and therefore, power and/or effect sizes may be lower. Y = Young; O = Old; $\beta$ = Beta; $\gamma$ = Gamma; $d$ = Cohen’s d (effect size); SL = Step length; ST = Step time; DS = Double support; VM = visuomotor locomotor adaptation in Nemanich and Earhart (2015).

<table>
<thead>
<tr>
<th>Hypothesis</th>
<th>Variable</th>
<th>Y mean</th>
<th>O Mean</th>
<th>SD</th>
<th>Power</th>
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<td>8.72</td>
<td>10.67</td>
<td>0.99</td>
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<td>ST asymmetry adaptation rate</td>
<td>9.97</td>
<td>1.01</td>
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<td>1.00</td>
<td>1.29</td>
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<td>0.30</td>
<td>1.00</td>
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<td>0.72</td>
<td>0.59</td>
</tr>
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<td></td>
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<td>-1.87</td>
<td>0.52</td>
<td>0.97</td>
<td>1.35</td>
</tr>
</tbody>
</table>

2.5.3 Functional assessments

Functional assessments were performed prior to data collection to determine participant eligibility and/or to control for potentially confounding variables. A pre-screening
questionnaire was used in the initial phases of recruitment to screen out major medical conditions before recruitment. All participants who were recruited passed eligibility criteria with the functional assessments below.

1. Physical Activity Readiness Questionnaire (PAR-Q and You): PAR-Q is a questionnaire used to assess the safety of physical activity in individuals between the age of 15-69 (Thomas, Reading and Shephard 1992). Participants were screened out if they answered “yes” to any of the questions (Appendix 1). For the older adult group, if a participant was above the age of 69, I asked them to obtain an additional physician clearance form for physical activity.

2. Snellen acuity test: Snellen acuity test is the clinical test for visual acuity (Kniestedt and Stamper 2003). An alphabetic Snellen eye chart was placed on a wall and participants were asked to read the alphabet on the 20/40 line from 10 ft away from the chart. Participants were screened out if they could not correctly read every letter on the 20/40 line.

3. Advanced Short Physical Performance Battery (SPPB-A): Short Physical Performance Battery (SPPB) is a physical assessment developed by the National Institute on Aging to evaluate lower extremity function in older adults (Guralnik and others 1994). The SPPB assesses coordination abilities such as tandem stance and physical abilities such as gait speed and chair stands. However, this test has ceiling limitations for individuals who have higher physical function. For this reason, I used the SPPB-A which supplements the SPPB with more challenging tasks (Simonsick and others 2001). SPPB-A scores were
used to assess the physical activity level among the participants (Appendix 2). Participants with a SPPB-A score < 8 were excluded from the study.

4. Telephone Interview for Cognitive Status (TICS): This is a screening assessment used to detect cognitive dysfunction (Brandt, Spencer and Folstein 1988). TICS is a brief cognitive test administered over the phone that correlates highly with the Mini-Mental State Examination (Fong and others 2009) and is reliable and valid (Knopman and others 2010). Participants were excluded if they scored below a 25.

5. Fatigue Severity Scale (FSS): FSS is a questionnaire used to quantify subjective experience of fatigue through a series of 9 questions. Although initially developed for patient with rheumatologic disorders, this scale has been validated to use in all populations (Schnelle and others 2012). FSS scores were used to control for general fatigue level among the participants (Appendix 4).

6. Godin Leisure Time Questionnaire (GLTQ): GLTQ is a short questionnaire used to quantify physical activity levels (Godin and Shephard 1985), and has been validated (Amireault and Godin 2015; Gionet and Godin 1989). Participants were not excluded based on physical activity level, but the results of this questionnaire were used to approximately match physical activity levels between age groups (Appendix 5).

7. Waterloo Footedness Questionnaire – Revised (WTQ-R). WTQ-R is a short questionnaire that can determine the leg dominancy (Elias, Bryden and Bulman-Fleming 1998), and has been validated (van Melick, Meddeler, Hoogeboom, Nijhuis-van der Sanden and van Cingel 2017). Average of items 1-10 on the questionnaire was used to
determine leg dominancy (Appendix 6); 2 = strong right dominance, -2 = strong left dominance. Leg dominance was used to randomize sides during asymmetrical locomotor adaptation condition.

8. Visual Analog Fatigue Scale (VAFS): VAFS is a quick method to assess subjective experience of fatigue which asks respondents to place an “X” on a visual analog line that extends between two extremes from “no fatigue” and “worst possible fatigue” (Lee, Hicks and Nino-Murcia 1991). This scale has been reported to have high validity (Lee, Hicks and Nino-Murcia 1991), reliability, and responsiveness (Tseng, Gajewski and Kluding 2010), and was used to track fatigue during the time course of the experiment.
CHAPTER 3

IMPACT OF AGING ON CORTICOSPINAL CONTROL OF SPLIT-BELT LOCOMOTOR ADAPTATION

3.1 Introduction

Gait adaptation in response to environmental demands (i.e., uneven terrain) is essential for safe community ambulation. To study gait adaptation in a controlled environment, the split-belt treadmill allows us to study proprioception-driven locomotor adaptation. When exposed on the split-belt treadmill with one leg on a faster treadmill belt compared to the other leg, there is a mismatch between the expected and actual proprioceptive feedback (i.e., sensorimotor error); while it is expected that the treadmill to be moving at the same speed on both sides, the treadmill speeds on each side differ. To minimize this error, healthy adults immediately make reactive changes in intralimb parameters and make slower adjustments in interlimb parameters that get stored and show a negative aftereffect when both right and left treadmill belts return to the same speed (Dietz, Zijlstra and Duysens 1994; Reisman, Block and Bastian 2005).

Older adults have impaired gait adaptation (Bruijn, Van Impe, Duysens and Swinnen 2012; Nemanich and Earhart 2015), which may lead to an increased risk of falling compared to younger adults, especially during walking (Berg, Alessio, Mills and Tong 1997; Tinetti, Speechley and Ginter 1988). Prior studies on the differences in kinematic adaptation during split-belt walking in older adults suggest that older adults are able to adapt interlimb parameters to the same level as young adults (Ducharme, Kent and van Emmerik 2019; Iturralde and Torres-Oviedo 2019; Malone and Bastian 2016; Vervoort and others 2019a), but the rate of adaptation may be reduced in older adults greater than 70 years old (Bruijn,
Van Impe, Duysens and Swinnen 2012; Sombric, Harker, Sparto and Torres-Oviedo 2017). However, the age-related changes in neural control during split-belt adaptation has not yet been reported in the literature.

Studies have demonstrated that proprioception-driven locomotor adaptation such as split-belt adaptation is critically dependent on cerebellar control (Morton and Bastian 2006; Reisman, Wityk, Silver and Bastian 2007), but recent work suggests that corticospinal control is also important (Barthelemy, Alain, Grey, Nielsen and Bouyer 2012; Sato and Choi 2019). Our recent study on healthy adults has shown that beta-band intramuscular coherence (a marker of corticospinal involvement) to the tibialis anterior is increased early during split-belt treadmill adaptation compared to baseline symmetrical walking during the swing phase of gait (Sato and Choi 2019). Furthermore, the beta-band intramuscular coherence was associated with double support time asymmetry but not with step length asymmetry, suggesting that corticospinal control may play a functional role in temporal control during split-belt treadmill adaptation (Sato and Choi 2019). In older adults, corticospinal drive is reduced during walking (Roeder, Boonstra and Kerr 2020; Spedden, Choi, Nielsen and Geertsen 2019), but the relationship between age-related changes in gait adaptability and corticospinal control is not yet established.

The **objective of this study** is to determine the impact of age on the contribution of corticospinal drive during proprioceptive split-belt locomotor adaptation. This study was a cross-sectional observational study between two cohorts: young and older adults.

Corticospinal drive was quantified by the amount of beta-gamma frequency range (15-45 EMG-EMG coherence in the tibialis anterior (intramuscular) and plantarflexors (intermuscular between the medial gastrocnemius and soleus and intramuscular between the medial and lateral gastrocnemius). To quantify kinematic locomotor adaptation, changes in step length symmetry, step time symmetry, and double support symmetry was measured.
The hypotheses were: (1) Older adults will adapt interlimb parameters the same amount as young adults, but early change in interlimb parameters during adaptation will be reduced in older adults; (2) corticospinal drive will be less in older adults compared to young adults during split-belt walking; and (3) reduced corticospinal drive will be associated with reduced rate of interlimb adaptation during split-belt walking.

3.2 Methods

3.2.1 Participants

Twenty healthy young adults (18-33 years old) and 19 healthy older adults (68-80 years old) participated in this study (Table 3.1). Inclusion criteria were no previous history of neurological disorder, no current major medical conditions (including cognitive; Telephone Interview for Cognitive Status < 25), no current orthopedic injuries, ability to walk without any walking aids (including ankle-foot orthoses) for at least 10 minutes, and visual acuity over 20/40. All participants gave informed written consent before the study in accordance with the protocol approved by the Institutional Review Board of University of Florida, Gainesville, FL (Protocol # 202000764).
Table 3.1. Participant characteristics for study 1.
Mean and standard deviation are reported. Independent t-tests were used to determine group differences. To assess sex distribution difference, a two-tailed Fischer’s exact-test was used. SPPB = Short Physical Performance Battery; SPPB-A = Advanced Short Physical Performance Battery (Simonsick and others 2001). FSS = Fatigue Severity Scale. Godin = Godin Physical Activity Questionnaire; Waterloo = Waterloo Footedness Questionnaire; TICS = Telephone Interview Cognitive Status.

3.2.2 Data collection and equipment

Participants walked on an instrumented treadmill (Bertec, Columbus, OH) for 5 conditions (Figure 3.1): (1) 5 minutes with the tied-belt condition (left and right treadmill belts at the same speed) at 0.5 m/s for familiarization on the treadmill; (2) 5 minutes at 1.0 m/s with tied-belt (“pre-fast”); (3) 5 minutes at 0.5 m/s with tied-belt (“pre-slow”); (4) 10 minutes with the split-belt condition, with one treadmill belt going at 0.5 m/s and the other at 1.0 m/s for the proprioceptive locomotor adaptation; and (5) 10 minutes at 0.5 m/s with tied-belt (“post-slow”). The leg on the fast belt during split-belt adaptation (from here on referred to as the “fast leg”), and the leg on the slow belt (from here on referred to as the “slow leg”) was randomized between participants with the same leg dominancy (i.e., equal number of right leg dominant participants with the fast leg on the left and right sides), as leg dominancy
may alter the rate of adaptation (Bulea, Stanley and Damiano 2017; Kong, Candelaria and Smith 2011).

![Figure 3.1. Experimental paradigm for study 1.](image)

Double lines indicate when treadmill was set as tied-belt (both left and right treadmill belts moving at the same speed). Single lines indicate the speeds at which the treadmill belts were moving during the split-belt adaptation condition. Downward arrows indicate when participants were asked to indicate their fatigue level using the Visual Analog Fatigue Scale (VAFS). Fam. = Familiarization.

Reflective markers were placed bilaterally on the anterior superior iliac spine (pelvis), greater trochanter (hip), joint line of the knee (knee), lateral malleolus (ankle), and 5th metatarsal (toe; Figure 3.2). Two pairs of electrodes (MA411 Surface preamplifier with stainless-steel electrodes, Motion Lab System, Baton Rouge, LA, USA) were placed on the tibialis anterior, one pair of electrodes was placed on the medial gastrocnemius, and one pair of electrodes was placed on the soleus (Figure 3.3). The muscle belly of the tibialis anterior, medial gastrocnemius, and soleus were identified by palpation by the experimenter. Lower limb kinematics were recorded at 100 Hz using an 8-camera Miqua system (Qualisys, Gothenburg, Sweden). Force data from the treadmill (Bertec, Columbus,
OH) and EMG signals from a wired amplifier (MA300, Motion Lab Systems, Baton Rouge, LA, USA) were collected at 1000 Hz. EMG, force plate and kinematic data was synchronized using Qualisys Track Manager (Qualisys, Gothenburg, Sweden).

Figure 3.2. Experimental setup for study 1. Participants wore 5 reflective markers (black) on each leg. Reflective markers were placed on: (1) Anterior superior iliac spine (pelvis), (2) greater trochanter (hip), (3) joint line of the knee (knee), (4) lateral malleolus (ankle), and (5) 5th metatarsal (toe).
Figure 3.3. Electrode placement for EMG measurements. Participants wore two pairs of electrodes (red) on the anterior side (A) and three pairs of electrodes on the posterior side (B) of the lower leg. On the anterior side, the ground electrode was placed on the patella (blue), and two pairs of electrodes were placed on the tibialis anterior to calculate intramuscular coherence. On the posterior side, one pair of electrodes each was placed on the medial and lateral gastrocnemius (dark gray), and the other pair was on the lateral side of the soleus (light gray). All electrodes were placed on the muscle belly. The muscle bellies were identified by palpation by the experimenter.

3.2.3 Kinematic analysis

Locomotor adaptation was determined by calculating stride-by-stride changes in step length asymmetry, step time asymmetry, and double support asymmetry (Choi, Vining, Reisman and Bastian 2009; Finley, Long, Bastian and Torres-Oviedo 2015; Reisman, Block and Bastian 2005). Step length was calculated as the anterior-posterior distance between the ankle markers at time of heel strike (cm). Step time was calculated as the time from heel-strike of the non-reference limb to the heel-strike of the reference limb (ms; i.e., right step = right heel strike – left heel strike). Fast leg and slow leg step length and step times correspond to the leading leg being on the fast or slow belt, respectively, at heel strike (i.e.,
fast step = fast leg heel strike – slow limb heel-strike). Double support time was calculated as the duration when both legs were on the treadmill (ms). Fast leg and slow leg double support time correspond to the double support occurring at the beginning of the fast leg’s stance (i.e., fast leg double support = the time from fast leg heel-strike to slow leg toe-off) and the slow leg’s stance (i.e., fast leg toe-off – slow leg heel-strike), respectively. Step length asymmetry, step time asymmetry, and double support asymmetry will be defined as the normalized difference between legs for each stride (Equation 3.1).

\[ \text{Asymmetry} = \frac{\text{Fast leg} - \text{Slow leg}}{\text{Fast leg} + \text{Slow leg}} \]  

Eq. 3.1

Changes in locomotor asymmetry were assessed using averaged values over three different time epochs (phases) during each adaptation and post-adaptation: (1) Initial (mean of first 5 strides), (2) Early adaptation/post-adaptation (mean of strides #6-30), and (3) plateau (mean of last 30 strides) (Leech and Roemmich 2018; Leech, Roemmich and Bastian 2018). In order to assess baseline behavior, the average of first 5 strides were averaged for pre-slow and pre-fast. Overall change in adaptation and post-adaptation was identified as the asymmetry difference between plateau and initial phases during split-belt adaptation and post-adaptation, respectively. Early change was identified as the asymmetry difference between early and initial phases during split-belt adaptation and post-adaptation.

To further explore the age group differences in kinematic changes during adaptation and post-adaptation, group average of the first 250 strides of asymmetry values was fit to an exponential model (Equation 3.2) (Lang and Bastian 1999; Malone, Vasudevan and Bastian 2011). Where \( a \) is the value that the exponential fit function approaches (i.e., plateau, asymptote), \( b \) is the overall change in asymmetry required from the first stride to
the plateau value $a$, and $c$ is the number of strides it would take to achieve the ~63% of the final plateau asymmetry level (likely to be close to 0). In the model, $x$ is the stride number and $y$ is the kinematic asymmetry.

$$ y = a - b \cdot e^{-x/c} \quad \text{Eq. 3.2} $$

Although the focus of this study is on interlimb parameter changes that occur gradually, intralimb gait parameters were also assessed to comprehensively assess locomotor changes in healthy aging (Choi, Vining, Reisman and Bastian 2009; Reisman, Block and Bastian 2005). Stance length was calculated as the anterior-posterior distance of the ankle marker traveled during stance phase, from heel-strike to subsequent toe-off of the ipsilateral limb (Bruijn, Van Impe, Duysens and Swinnen 2012; Reisman, Block and Bastian 2005). Stance time was calculated as the time from heel-strike to toe-off on the same limb (s). Stance length and stance time symmetry was calculated in the same way as interlimb parameters, using equation 3.1.

3.2.4 Coherence analysis

EMG signals were high-pass filtered at 8 Hz, rectified, and normalized to have unit variance (to normalize EMG amplitude) and to have realizations of stationary zero mean time series denoted by $x$ and $y$ (Halliday and others 1995). Discrete Fourier transformation analysis was applied to short sections of the data taken at a fixed offset time to estimate the average autospectras for processes $x$ ($f_{xx}(\lambda)$) and $y$ ($f_{yy}(\lambda)$). The cross-spectrum between $x$ and $y$ ($f_{xy}(\lambda)$) was estimated in a similar manner. The short sections of data were determined after examining the processed EMG for each muscle and determining where the muscle was active during the gait cycle. Based on preliminary data, I used 0-400 ms after toe-off to calculate intramuscular coherence in the tibialis anterior (Figure 3.4A), and 500-
100 ms before toe-off to calculate intermuscular and intramuscular coherence in the plantarflexors (Figure 3.4B).

![Graph](image)

Figure 3.4. Example of processed tibialis anterior (A) and plantarflexor (B) EMG signals from a single representative participant. A. To calculate coherence during swing phase, I will use EMG signals from the proximal (black) and distal (gray) muscle belly of the tibialis anterior 0-400 ms (red-dotted lines) after toe-off (blue dotted line). B. To calculate coherence during stance phase, I will use EMG signals from the medial gastrocnemius (black) and soleus (gray) muscle 500-100 ms (red-dotted lines) before toe-off (blue dotted lines).

To distinguish if the modulation in coherence is specific to muscle-group or analysis (intra vs intermuscular), both intermuscular coherence between the medial gastrocnemius and intramuscular coherence between the medial and lateral gastrocnemius muscle during the stance phase (500-100 ms before toe-off) was calculated for the plantarflexors.

For each Fourier frequency, correlation between the EMG signals was calculated (Halliday and others 1995). The resulting coherence value provides a measure of association of the $x$ and $y$ processes on a scale from 0 to 1 (Equation 3.3). A coherence
value of 0 signifies no synchrony between the two EMG signals and a coherence value of 1 signifies perfect synchrony between the two EMG signals.

\[ |R_{xy}(\lambda)|^2 = \frac{|f_{xy}(\lambda)|^2}{f_{xx}(\lambda)f_{yy}(\lambda)} \]  

Eq. 3.3

The calculated coherence can quantify the strength and frequency of the common neural drive from the corticospinal tract in the motoneuronal pool within the muscle (Farmer, Bremner, Halliday, Rosenberg and Stephens 1993; Halliday and others 1995). To characterize coherence modulation over the course of locomotor adaptation, the coherence was calculated for each leg over the first 100 strides during each baseline condition (pre-slow, pre-fast), and over the first and last 100 strides during split-belt adaptation and post-slow de-adaptation period.

For each condition, the natural logarithm of the cumulative sum of coherence was calculated for the beta-gamma band (15-45 Hz) to quantify corticospinal drive to the lower limb muscles. EMG-EMG coherence in the alpha-band is thought to originate from a different central nervous system source compared to the beta-gamma band (although there are some studies that challenge this view; Graziadio and others 2010; Mima and Hallett 1999b; Salenius, Portin, Kajola, Salmelin and Hari 1997) EMG-EMG coherence in the alpha band (8-15 Hz) was calculated for additional analysis to examine if alpha band modulation is different from beta-gamma band modulation.

3.2.5 Statistical analysis

Age group differences in overall and early changes in kinematic adaptation (hypothesis 1.1) were assessed though independent t-tests (Table 3.2). Effect sizes for paired comparisons were calculated with Cohen’s d. Effect sizes were defined as small < 0.499, moderate = 0.500-0.799 and large > 0.800.
Since group characteristics demonstrated that physical function was different between groups (Table 3.1, for SPPB-A and SPPB), I used an analysis of covariate to examine group differences in kinematic changes controlling for physical function. Physical function was controlled between groups as the objective of this study was to examine healthy aging (i.e., no functional decline).

To determine whether there were age-related differences in coherence (hypothesis 1.2), group differences in beta-gamma band intramuscular tibialis anterior coherence, intermuscular plantarflexor coherence, and intramuscular gastrocnemius coherence were assessed through a 2-way mixed measures ANOVA with post-hoc pairwise comparisons with Bonferroni corrections. Specifically, I assessed if coherence changed between conditions by examining the main effect of conditions, and I assessed if coherence was different between groups by examining the main effect of age. Effect sizes for ANOVAs were determined by partial eta-squared ($\eta^2_p$). Effect sizes were defined as small $<$ 0.059, moderate $= 0.060$-$0.139$ and large $> 0.140$. 

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Table 3.2. Summary of statistical tests for each hypothesis in Aim 1.

<table>
<thead>
<tr>
<th>Goal</th>
<th>Question</th>
<th>Factor levels</th>
<th>Test</th>
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</thead>
<tbody>
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<td>Is there a difference between the age cohorts?</td>
<td>2</td>
<td>Age cohorts (2): Young and older</td>
</tr>
<tr>
<td></td>
<td>Variables: Overall change and early change in kinematic adaptation</td>
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<td></td>
</tr>
<tr>
<td>Hypothesis 1.2</td>
<td>Is there a difference between the age cohorts?</td>
<td>6 x 2</td>
<td>Conditions (6): Pre-fast, Pre-slow, Early adaptation, Late adaptation, Early post-adaptation, Late post-adaptation</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Age cohorts (2): Young and older</td>
</tr>
<tr>
<td></td>
<td>Variables: TA-TA intramuscular coherence, MG-Sol intermuscular coherence, MG-LG intramuscular coherence</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypothesis 1.3</td>
<td>Is CSD associated with adaptation?</td>
<td>2</td>
<td>Dependent: Kinematic adaptation parameters Independent: Beta-gamma coherence</td>
</tr>
<tr>
<td></td>
<td>Variables: Kinematics vs coherence</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CSD = Corticospinal drive; TA = Tibialis anterior; MG = Medial gastrocnemius; Sol = Soleus; LG = Lateral gastrocnemius.

To determine the contribution of corticospinal drive on proprioception-driven locomotor adaptation (hypothesis 1.3), relationship between kinematic adaptation (overall and early change) and coherence will be assessed through a stepwise multiple linear regression. The covariates considered are listed in Table 3.3. The strength of the relationships was assessed through root mean square error (RMSE) and coefficient of determination \( (r^2) \).
All statistical significance was established with an alpha level = 0.05. Statistical analyses were performed using JASP v0.14.1 (University of Amsterdam, Amsterdam, Netherlands).

<table>
<thead>
<tr>
<th>Dependent Variables (Kinematics)</th>
<th>Overall change in adaptation (Δ Plateau - Initial)</th>
<th>Step length asymmetry</th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Double support asymmetry</td>
</tr>
<tr>
<td>Early changes in adaptation</td>
<td></td>
<td>Step length asymmetry</td>
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<tr>
<td>(Δ Early - Initial)</td>
<td></td>
<td>Double support asymmetry</td>
</tr>
<tr>
<td>Covariates considered in multiple regression model</td>
<td>Group (1 = Young; 2 = Old)</td>
<td>Fast leg TA beta-gamma band</td>
</tr>
<tr>
<td></td>
<td>Early adaptation coherence</td>
<td>Slow leg TA beta-gamma band</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fast leg PF beta-gamma band</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Slow leg PF beta-gamma band</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fast leg GST beta-gamma band</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Slow leg GST beta-gamma band</td>
</tr>
</tbody>
</table>

Table 3.3. Variables in multiple linear regression models. TA = Tibialis anterior; MG = Medial gastrocnemius; Sol = Soleus; LG = Lateral gastrocnemius.
3.3 Results

3.3.1 Aging influences kinematic changes during split-belt locomotor adaptation

Participants walked with symmetrical spatial and temporal kinematics during pre-slow and pre-fast; there was no evidence of age group differences during baseline conditions for all of the kinematic asymmetry variables (Table 3.4). During initial split-belt treadmill adaptation, participants had longer step lengths on the slow leg compared to the fast leg, leading to negative asymmetry. Participants gradually adapted and reached a plateau. During post-adaptation, there was an after-effect in which participants took longer steps on the fast leg and gradually de-adapted to reach a plateau (Figure 3.5A). Overall change in step length asymmetry adaptation (Δ plateau phase – initial phase) was not different between age groups (p = 0.079, 95% confidence interval for difference in group means (95% CI) = [-0.01, 0.14], d = 0.578; Figure 3.5C, Table 3.5), but early change in step length asymmetry adaptation was greater in younger adults compared to older adults (p = 0.009, 95% CI = [0.02, 0.15], d = 0.887; Figure 3.5D). Overall and early change in step length asymmetry during post-adaptation was not significantly different between age groups (Overall Δ: p = 0.111, 95% CI = [-0.10, 0.01], d = -0.523; Early Δ: p = 0.464, 95% CI = [-0.07, 0.03], d = -0.237; Figure 3.5E-F).
Table 3.4. Age group differences in baseline kinematic asymmetry during study 1. Group differences are analyzed with a student t-test, and effect size is given by Cohen’s d. * = Levene’s test was violated and p-value reported is from a Welch test.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Asymmetry variables</th>
<th>p-value</th>
<th>95% Confidence interval for difference in group means</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Lower</td>
<td>Upper</td>
</tr>
<tr>
<td>Pre-fast</td>
<td>Step length</td>
<td>0.078</td>
<td>-0.003</td>
<td>0.05</td>
</tr>
<tr>
<td></td>
<td>Double support</td>
<td>0.121</td>
<td>-0.04</td>
<td>0.01</td>
</tr>
<tr>
<td></td>
<td>Step time*</td>
<td>0.171</td>
<td>-0.004</td>
<td>0.02</td>
</tr>
<tr>
<td>Pre-slow</td>
<td>Step length</td>
<td>0.806</td>
<td>-0.03</td>
<td>0.03</td>
</tr>
<tr>
<td></td>
<td>Double support</td>
<td>0.342</td>
<td>-0.05</td>
<td>0.02</td>
</tr>
<tr>
<td></td>
<td>Step time</td>
<td>0.710</td>
<td>-0.02</td>
<td>0.03</td>
</tr>
</tbody>
</table>
Figure 3.5. Step length asymmetry changes during study 1.
A. Stride-by-stride changes in step length asymmetry plotted for young (in black) and older adults (in red). Shaded areas are standard errors. For baseline (“pre-”) conditions the first 30 strides are plotted. For adaptation and post-adaptation conditions, the first 100 and last 30 strides are plotted. Thick dotted lines are for stride numbers 5, 30, and 100/30 strides before the last stride to indicate the different phases (Phases indicated at top of A: Initial (I) = Strides #1-5, early phase (E) = Strides #6-30, plateau (P) = Last 30 strides). B-F. Age group means and standard error bars for (B) baseline-fast and pre-slow conditions, (C) Overall change during adaptation (Δ plateau phase – initial phase), (D) early change during adaptation (Δ early phase – initial phase), (E) Overall change during post-adaptation (Δ plateau phase – initial phase), (F) early change during post-adaptation (Δ early phase – initial phase).

During initial split-belt treadmill adaptation, participants had longer double support time on the fast leg compared to the slow leg, leading to positive asymmetry. Participants gradually adapted and reached a plateau close to symmetry. During post-adaptation, there was an after-effect in which participants took longer double support time on the slow leg and gradually de-adapted to reach a plateau (Figure 3.6A). Overall and early change in double
support time asymmetry during adaptation were different between age groups (Overall Δ: p = 0.021, 95% CI = [0.01, 0.12], d = 0.770; Early Δ: p = 0.026, 95% CI = [0.01, 0.09], d = 0.742). Older adults adapted more overall, and demonstrated greater early change (i.e., more negative) in double support asymmetry during split-belt treadmill adaptation compared to younger adults (Figure 3.6C-D). During post-adaptation, overall and early change in double support asymmetry were not significantly different between age groups (Overall Δ: p = 0.657, 95% CI = [-0.06, 0.09], d = 0.143; Early Δ: p = 0.382, 95% CI = [-0.09, 0.04], d = 0.283; Figure 3.6E-F).
Figure 3.6. Double support asymmetry changes during study 1.
A. Stride-by-stride changes in double support asymmetry plotted for young (in black) and older adults (in red). Shaded areas are standard errors. For baseline (“pre-”) conditions the first 30 strides are plotted. For adaptation and post-adaptation conditions, the first 100 and last 30 strides are plotted. Thick dotted lines are for stride numbers 5, 30, and 100/30 strides before the last stride to indicate the different phases (Phases indicated at top of A: Initial (I) = Strides #1-5, early phase (E) = Strides #6-30, plateau (P) = Last 30 strides). B-F. Age group means and standard error bars for (B) baseline-fast and pre-slow conditions, (C) Overall change during adaptation (Δ plateau phase – initial phase), (D) early change during adaptation (Δ early phase – initial phase), (E) Overall change during post-adaptation (Δ plateau phase – initial phase), (F) early change during post-adaptation (Δ early phase – initial phase).

During initial split-belt treadmill adaptation, participants had longer step time on the fast leg compared to the slow leg, leading to positive asymmetry. Unlike step length asymmetry and double support asymmetry, participants adjusted their step time asymmetry relatively fast during adaptation and post-adaptation (Figure 3.7A). Overall and early change in step time asymmetry during adaptation were not different between age groups.
Overall Δ: p = 0.262, 95% CI = [-0.06, 0.02], d = -0.365; Early Δ: p = 0.673, 95% CI = [-0.2, 0.03], d = 0.136; Figure 3.7C-D). Similarly, during post-adaptation, overall and early change in step time asymmetry were not significantly different between age groups (Overall Δ: p = 0.985, 95% CI = [-0.04, 0.04], d = -0.006; Early Δ: p = 0.829, 95% CI = [-0.03, 0.04], d = 0.070; Figure 3.7E-F).

Figure 3.7. Step time asymmetry changes during study 1.
A. Stride-by-stride changes in step time asymmetry plotted for young (in black) and older adults (in red). Shaded areas are standard errors. For baseline (“pre-”) conditions the first 30 strides are plotted. For “adaptation” and “post” adaptation conditions, the first 100 and last 30 strides are plotted. Thick dotted lines are for stride numbers 5, 30, and 100/30 strides before the last stride to indicate the different phases (Phases indicated at top of A: Initial (I) = Strides #1-5, early phase (E) = Strides #6-30, plateau (P) = Last 30 strides). B-F. Age group means and standard error bars for (B) baseline-fast and pre-slow conditions, (C) Overall change during adaptation (Δ plateau phase – initial phase), (D) early change during adaptation (Δ early phase – initial phase), (E) Overall change during post-adaptation (Δ plateau phase – initial phase), (F) early change during post-adaptation (Δ early phase – initial phase).
Table 3.5. Age group differences in kinematic asymmetry during adaptation and post-adaptation for study 1.
Group differences were analyzed with a student t-test, and effect size is given by Cohen’s d.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Asymmetry variables</th>
<th>Difference</th>
<th>p-value</th>
<th>95% Confidence interval for difference in group means</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Lower</td>
<td>Upper</td>
</tr>
<tr>
<td>Adaptation</td>
<td>Overall change</td>
<td>0.079</td>
<td>-0.01</td>
<td>0.14</td>
<td>0.578</td>
</tr>
<tr>
<td></td>
<td>Early change</td>
<td>0.009</td>
<td>0.02</td>
<td>0.15</td>
<td>0.887</td>
</tr>
<tr>
<td></td>
<td>Overall change</td>
<td>0.021</td>
<td>0.01</td>
<td>0.12</td>
<td>0.770</td>
</tr>
<tr>
<td></td>
<td>Early change</td>
<td>0.026</td>
<td>0.01</td>
<td>0.09</td>
<td>0.742</td>
</tr>
<tr>
<td></td>
<td>Overall change</td>
<td>0.262</td>
<td>-0.06</td>
<td>0.02</td>
<td>-0.365</td>
</tr>
<tr>
<td></td>
<td>Early change</td>
<td>0.673</td>
<td>-0.02</td>
<td>0.03</td>
<td>0.136</td>
</tr>
<tr>
<td>Post-adaptation</td>
<td>Overall change</td>
<td>0.111</td>
<td>-0.09</td>
<td>0.01</td>
<td>-0.523</td>
</tr>
<tr>
<td></td>
<td>Early change</td>
<td>0.464</td>
<td>-0.07</td>
<td>0.03</td>
<td>-0.237</td>
</tr>
<tr>
<td></td>
<td>Overall change</td>
<td>0.657</td>
<td>-0.06</td>
<td>0.09</td>
<td>0.143</td>
</tr>
<tr>
<td></td>
<td>Early change</td>
<td>0.382</td>
<td>-0.09</td>
<td>0.04</td>
<td>-0.283</td>
</tr>
<tr>
<td></td>
<td>Overall change</td>
<td>0.985</td>
<td>-0.04</td>
<td>0.04</td>
<td>-0.006</td>
</tr>
<tr>
<td></td>
<td>Early change</td>
<td>0.829</td>
<td>-0.03</td>
<td>0.04</td>
<td>0.070</td>
</tr>
</tbody>
</table>

To examine group differences in the rate and overall change in kinematics during adaptation, an exponential model was fit to each of the kinematic asymmetry variables (Figures 3.8-3.9). For step length asymmetry, exponential coefficients $a$ (equivalent to plateau) were similar in the young and old groups, but $b$ (equivalent to overall changes) was less, and $c$ (equivalent to rate) was two-times smaller (i.e., faster) in the younger group compared to the older group.
Figure 3.8. Exponential model for step length asymmetry adaptation.
A. Exponential model for group average in stride-by-stride changes in step length asymmetry during adaptation. Shaded areas include 95% prediction intervals. Black = Young; Red = Old. B-C. Stride-by-stride plots for the young group (B) and old group (C). Open circles indicate stride-by-stride group average. \( c \) is the number of strides it would take to achieve the ~63% of the final plateau asymmetry level and is equivalent to rate.

For double support asymmetry changes during adaptation, \( a \) (equivalent to plateau) was less asymmetrical, and \( b \) (equivalent to overall changes) was greater in magnitude, while \( c \) (equivalent to rate) were similar in older adults compared to younger adults. For double support time asymmetry, as demonstrated in the overlap of prediction intervals of the models (Figure 3.9), exponential coefficients were similar between age groups.
Figure 3.9. Exponential model for double support asymmetry adaptation. 
A. Exponential model for group average in stride-by-stride changes in double support asymmetry during adaptation. Shaded areas include 95% prediction intervals. Black = Young; Red = Old. B-C. Stride-by-stride plots for the young group (B) and old group (C). Open circles indicate stride-by-stride group average. $c$ is the number of strides it would take to achieve the ~63% of the final plateau asymmetry level and equivalent to rate.

The focus of this study was interlimb variables, but I also examined intralimb variables for exploratory purposes. There was no evidence of age group differences during baseline conditions for the intralimb asymmetry variables (Table 3.6). During initial split-belt treadmill adaptation, participants had longer stance length on the fast leg compared to the slow leg, leading to positive asymmetry (Figure 3.10A). Overall and early change in stance length asymmetry during adaptation were not different between age groups (Overall $\Delta$: $p = 0.573$, 95% CI = [-0.02, 0.04], $d = 0.182$; Early $\Delta$: $p = 0.394$, 95% CI = [-0.03, 0.01], $d = -0.278$; Figure 3.10C-D). During post-adaptation, overall change in stance length asymmetry was greater (i.e., more negative) in younger adults compared to older adults ($p = 0.042$, 95% CI = [-0.05, -8.36e-4], $d = -0.674$; Figure 3.10E-F). Early change in stance length
asymmetry during post-adaptation was not significantly different between age groups ($p = 0.146$, 95% CI = [-0.03, 0.01], $d = -0.476$).

Figure 3.10. Stance length asymmetry changes during study 1.
A. Stride-by-stride changes in stance length asymmetry plotted for young (in black) and older adults (in red). Shaded areas are standard errors. For baseline (“pre-”) conditions the first 30 strides are plotted. For “adaptation” and “post” adaptation conditions, the first 100 and last 30 strides are plotted. Thick dotted lines are for stride numbers 5, 30, and 100/30 strides before the last stride to indicate the different phases (Phases indicated at top of A: Initial (I) = Strides #1-5, early phase (E) = Strides #6-30, plateau (P) = Last 30 strides). B-F. Age group means and standard error bars for (B) baseline-fast and pre-slow conditions, (C) Overall change during adaptation ($\Delta$ plateau phase – initial phase), (D) early change during adaptation ($\Delta$ early phase – initial phase), (E) Overall change during post-adaptation ($\Delta$ plateau phase – initial phase), (F) early change during post-adaptation ($\Delta$ early phase – initial phase).

During initial split-belt treadmill adaptation, participants had shorter stance time on the fast leg compared to the slow leg, leading to negative asymmetry (Figure 3.11A).
Overall and early change in stance time asymmetry during adaptation were not different between age groups (Figure 3.11C-D; Table 3.7; Overall Δ: p = 0.803, 95% CI = [-0.03, 0.03], d = -0.081; Early Δ: p = 0.051, 95% CI = [-0.04, 1.17e-4], d = -0.645). Similarly, during post-adaptation, overall and early change in stance time asymmetry were not significantly different between age groups (Overall Δ: p = 0.508, 95% CI = [-0.02, 0.01], d = -0.214; Early Δ: p = 0.503, 95% CI = [-0.01, 0.02], d = 0.217; Figure 3.11E-F).
Figure 3.11. Stance time asymmetry changes during study 1.
A. Stride-by-stride changes in stance length asymmetry plotted for young (in black) and older adults (in red). Shaded areas are standard errors. For baseline ("pre-") conditions the first 30 strides are plotted. For “adaptation” and “post” adaptation conditions, the first 100 and last 30 strides are plotted. Thick dotted lines are for stride numbers 5, 30, and 100/30 strides before the last stride to indicate the different phases (Phases indicated at top of A: Initial (I) = Strides #1-5, early phase (E) = Strides #6-30, plateau (P) = Last 30 strides). B-F. Age group means and standard error bars for (B) baseline-fast and pre-slow conditions, (C) Overall change during adaptation (Δ plateau phase – initial phase), (D) early change during adaptation (Δ early phase – initial phase), (E) Overall change during post-adaptation (Δ plateau phase – initial phase), (F) early change during post-adaptation (Δ early phase – initial phase).
Table 3.6. Age group differences in baseline kinematic asymmetry for the exploratory kinematic variables for study 1.
Group differences are analyzed with a student t-test, and effect size is given by Cohen’s d. * = Levene’s test was violated and p-value reported is from a Welch test.

Table 3.7. Age group differences in kinematic asymmetry during adaptation and post-adaptation for the exploratory kinematic variables for study 1.
Group differences are analyzed with a student t-test, and effect size is given by Cohen’s d. * = Levene’s test was violated and p-value reported is from a Welch test.

3.3.2. Potential covariate contribution to kinematic adaptation

In general, there was an increase in fatigue (Figure 3.12), but there were no group differences (F(1,36) = 0.44, p = 0.511, η² = 0.012). After controlling for physical function, overall change in step length asymmetry during adaptation was not different between groups, and there was a significant effect of age groups in early change in step length asymmetry even when adjusting for SPPB-A scores (Overall Δ: F(1, 36) = 2.20, p = 0.146,
\( n^2_p = 0.058; \) Early \( \Delta \): F(1, 36) = 9.30, \( p = 0.004, n^2_p = 0.205 \), which was consistent with previously reported results above. In contrast, overall and early change in double support asymmetry during adaptation was not different between groups when adjusting for SPPB-A scores (Overall \( \Delta \): F(1, 36) = 1.68, \( p = 0.203, n^2_p = 0.045 \); Early \( \Delta \): F(1, 36) = 3.00, \( p = 0.092, n^2_p = 0.077 \)).

Figure 3.12. Visual analog fatigue scale during Study 1. All participants were asked to rate their fatigue at eight different time points during the experiment. 0 = No fatigue; 1 = Worst possible fatigue. Black = Young adults (n = 20); Red = Older adults (n = 19). Error bars are standard error bars.

Post-adaptation age group differences for step length asymmetry and double support asymmetry changes during post-adaptation was consistent with previously reported, and was not statistically significant after adjusting for SPPB-A scores (all \( p \)'s > 0.100).
For intralimb parameters, when adjusted for SPPB-A scores, there were no age-group differences in overall and early changes in stance length asymmetry, and overall change in stance time asymmetry during adaptation (Stance length overall $\Delta$: $F(1, 36) = 0.003$, $p = 0.959$, $n_{p}^2 = 7.60e^{-5}$; Stance length early $\Delta$: $F(1, 36) = 2.24$, $p = 0.143$, $n_{p}^2 = 0.059$; Stance time overall $\Delta$: $F(1, 36) = 0.152$, $p = 0.699$, $n_{p}^2 = 0.004$). However, early change in stance time asymmetry was less in younger adults compared to older adults ($F(1, 36) = 5.24$, $p = 0.028$, $n_{p}^2 = 0.127$). Age group differences in intralimb kinematic changes were all statistically not significant after adjusting for SPPB-A scores (all $p$'s > 0.100).

3.3.2 EMG-EMG coherence differences between age-groups

Overall, all coherence had significant main effect of groups. All coherence except fast leg plantarflexor beta-gamma-band coherence and gastrocnemius beta-gamma-band coherence had a significant main effect of conditions. However, it is important to note that the treadmill speed may influence intra and intermuscular coherence (i.e., speed-equivalent comparisons: Fast leg pre-fast vs. split-belt conditions, Slow leg pre-slow vs. split-belt adaptation and post-slow conditions). Statistically significant between speed-equivalent conditions are reported in the text and are highlighted in bold brackets in the figures; all statistically significant comparisons are shown in the figures.

Alpha-band tibialis anterior coherence in the fast leg during swing phase was different between conditions and between groups, but condition x group effect was not significant (Figure 3.13A; Condition: $F(5, 185) = 7.60$, $p < 0.001$, $n_{p}^2 = 0.170$; Group: $F(1,37) = 11.05$, $p = 0.002$, $n_{p}^2 = 0.230$; Condition x group: $F(5, 185) = 0.52$, $p = 0.762$, $n_{p}^2 = 0.014$). Overall, alpha-band tibialis anterior coherence in the fast leg during swing phase was lower in older adults compared to younger adults (95% CI = [-0.89, -0.22], $d = -0.532$). However,
post-hoc comparisons within condition and between groups did not show any statistically significant differences. Post-hoc tests between condition tests showed that baseline pre-fast alpha-band coherence in the tibialis anterior during swing in the fast leg was higher compared to all the other conditions.

Alpha-band tibialis anterior coherence in the slow leg during swing phase was different between conditions and between groups, but condition x group effect was not significant (Figure 3.13B; Condition: $F(4.27, 157.80) = 9.99, p < 0.001, \eta^2_p = 0.213$; Group: $F(1, 37) = 9.96, p = 0.003, \eta^2_p = 0.212$; Condition x group: $F(4.27, 157.80) = 1.37, p = 0.246, \eta^2_p = 0.036$). Alpha-band tibialis anterior coherence in the slow leg during swing phase was lower in older adults compared to younger adults (95% CI = [-0.95, -0.21], $d = -0.505$). Post-hoc comparisons within condition and between groups did not show any statistically significant differences. Post-hoc between condition tests showed that tibialis anterior alpha band coherence in the slow leg increased during early split-belt compared to baseline-pre-slow, and was higher compared to early and late post-adaptation. Late split-belt coherence was not significantly higher compared to baseline pre-slow, but was higher compared to early and late post-adaptation.

Beta-gamma-band tibialis anterior coherence in the fast leg during swing phase was different between conditions and between groups, but condition x group effect was not significant (Figure 3.13C; Condition: $F(2.49, 92.10) = 3.24, p = 0.034, \eta^2_p = 0.081$; Group: $F(1, 37) = 19.29, p < 0.001, \eta^2_p = 0.343$; Condition x group: $F(2.49, 92.10) = 1.13, p = 0.336, \eta^2_p = 0.030$). Beta-gamma-band tibialis anterior coherence in the fast leg during swing phase was lower in older adults compared to younger adults (95% CI = [-0.93, -0.34], $d = -0.703$). Post-hoc comparisons within condition and between groups showed that older adults had lower coherence during pre-fast and early split belt conditions compared to
younger adults. Speed-equivalent conditions did not show any statistically significant
differences.

Beta-gamma-band tibialis anterior coherence in the slow leg during swing phase was
different between conditions and between groups, but condition x group effect was not
significant (Figure 3.13D; Condition: F(4.35, 160.96) = 11.86, p < 0.001, \( \eta^2_p = 0.243 \); Group:
F(1, 37) = 25.52, p < 0.001, \( \eta^2_p = 0.408 \); Condition x group: F(4.35, 160.96) = 1.42, p =
0.227, \( \eta^2_p = 0.037 \)). Beta-gamma-band tibialis anterior coherence in the slow leg during
swing phase was lower in older adults compared to younger adults (95% CI = [-1.20, -0.51],
d = -0.809). Beta-gamma band tibialis anterior coherence in the slow leg showed
statistically lower coherence in older adults compared to younger adults in every condition.
Early split-belt coherence was higher compared to baseline pre-slow, late split-belt, and
early and late post-adaptation. Coherence during late split-belt adaptation was higher
compared to early post-adaptation.
Figure 3.13. Tibialis anterior coherence during swing during study 1. Natural logarithm of cumulative alpha (A, C) and beta-gamma (B, D) intermuscular coherence between the distal and proximal tibialis anterior in the fast (A-B) and slow leg (C-D) during study 1. Black = Young; Red = Old; X = group means; Error bars = standard error. Brackets indicate between-condition comparisons where $p < 0.05$. Thick brackets indicate speed-matched between-condition comparisons where $p < 0.05$. * indicate between-groups comparisons within condition where $p < 0.05$. All comparisons were corrected for multiple comparisons using the Bonferroni method.

Alpha-band plantarflexor coherence in the fast leg during stance phase was different between conditions and between groups, and condition x group effect was significant (Figure 3.14A; Condition: $F(4.32, 159.94) = 7.91, p < 0.001, \eta^2_p = 0.176$; Group: $F(1, 37) = 9.10, p = 0.005, \eta^2_p = 0.197$; Condition x group: $F(4.32, 159.94) = 4.95, p < 0.001, \eta^2_p =$
Alpha-band plantarflexor coherence in the fast leg was lower in older adults compared to younger adults (95% CI = [-1.16, -0.23], d = -0.483). However, post-hoc comparisons within condition and between groups did not show any statistically significant differences. Post-hoc between condition tests showed that baseline pre-fast plantarflexor alpha-band coherence during pre-fast was higher compared to pre-slow, and early and late post-adaptation. Plantarflexor alpha-band coherence during pre-slow was lower compared to early and late post-adaptation.

Alpha-band plantarflexor coherence in the slow leg during stance phase was different between conditions and between groups, and condition x group effect was significant (Figure 3.14B; Condition: F(2.81, 103.94) = 9.98, p < 0.001, η²_p = 0.212; Group: F(1, 37) = 10.88, p = 0.002, η²_p = 0.227; Condition x group: F(2.81, 103.94) = 3.12, p = 0.032, η²_p = 0.078). Alpha-band plantarflexor coherence in the slow leg was lower in older adults compared to younger adults (95% CI = [-1.37, 0.33], d = -0.528). Post-hoc comparisons within condition and between groups showed that older adults had significantly lower coherence during late post-adaptation compared to young adults. Post-hoc between condition tests showed that slow leg plantarflexor alpha-band coherence increased during split-belt adaptation in which during early adaptation coherence was higher compared to late post-adaptation, and late adaptation coherence was higher compared to pre-slow and early and late post-adaptation conditions.

Beta-gamma-band plantarflexor coherence in the fast leg during stance phase was different between groups, but not between conditions, and condition x group effect was not significant (Figure 3.14C; Condition: F(3.07, 113.60) = 1.19, p = 0.317, η²_p = 0.031; Group: F(1, 37) = 22.82, p < 0.001, η²_p = 0.381; Condition x group: F(3.07, 113.60) = 2.48, p = 0.063, η²_p = 0.063). Beta-gamma-band plantarflexor coherence in the fast leg was lower in older adults compared to younger adults (95% CI = [-1.48, -0.60], d = -0.765). Post-hoc
comparisons within condition and between groups showed that older adults had lower coherence during all conditions except for baseline pre-fast.

Beta-gamma-band plantarflexor coherence in the slow leg during stance phase was different between conditions and between groups, but condition x group effect was not significant (Figure 3.14D; Condition: $F(2.47, 91.22) = 3.00, p = 0.044, \eta^2_p = 0.075$; Group: $F(1, 37) = 24.82, p < 0.001, \eta^2_p = 0.401$; Condition x group: $F(2.47, 91.22) = 2.37, p = 0.088, \eta^2_p = 0.060$). Beta-gamma-band plantarflexor coherence in the fast leg was lower in older adults compared to younger adults (95% CI = [-1.58, -0.67], $d = -0.798$). Post-hoc comparisons within condition and between groups showed that older adults had significantly lower coherence during pre-slow, late split-belt and early and late post-adaptation compared to younger adults. Post-hoc between condition tests showed that coherence during early split-belt was higher compared to baseline pre-slow.
Plantarflexor coherence during stance during study 1. Natural logarithm of cumulative alpha (A, C) and beta-gamma (B, D) intermuscular coherence between the medial gastrocnemius and soleus in the fast (A-B) and slow leg (C-D) during study 1. Black = Young; Red = Old; X = group means; Error bars = standard error. Brackets indicate between-condition comparisons where $p < 0.05$. Thick brackets indicate speed-matched between-condition comparisons where $p < 0.05$. * indicate between-groups comparisons within condition where $p < 0.05$. All comparisons were corrected for multiple comparisons using the Bonferroni method.

Alpha-band gastrocnemius coherence in the fast leg during stance phase was different between conditions and between groups, but condition x group effect was not significant (Figure 3.15A; Condition: $F(3.09, 114.31) = 4.55, p = 0.004, \eta^2_p = 0.110$; Group: $F(1, 37) = 6.55, p = 0.015, \eta^2_p = 0.150$; Condition x group: $F(3.09, 114.31) = 1.13, p = 103$
0.339, $\eta^2_p = 0.030$). Alpha-band gastrocnemius coherence in the fast leg was lower in older adults compared to younger adults (95% CI = [-1.06, -0.123], $d = 0.410$). However, post-hoc comparisons within condition and between groups did not show any statistically significant differences. Post-hoc between condition tests showed that coherence during baseline pre-slow was lower early post-adaptation.

In the slow leg, alpha-band gastrocnemius coherence was different between conditions and between groups, but condition x group effect was not significant (Figure 3.15B; Condition: $F(2.73, 101.14) = 4.47$, $p = 0.007$, $\eta^2_p = 0.108$; Group: $F(1, 37) = 7.00$, $p = 0.012$, $\eta^2_p = 0.159$; Condition x group: $F(2.73, 101.14) = 1.03$, $p = 0.377$, $\eta^2_p = 0.027$).

Alpha-band gastrocnemius coherence in the slow leg was lower in older adults compared to younger adults (95% CI = [-1.27, -0.17], $d = -0.424$). However, post-hoc comparisons within condition and between groups did not show any statistically significant differences. Post-hoc between condition tests showed that coherence during early and late adaptation was higher compared to early post-adaptation.

Beta-gamma-band gastrocnemius coherence in the fast leg during stance phase was between groups, but not between conditions, and condition x group effect was not significant (Figure 3.15C; Condition: $F(2.88, 106.70) = 1.70$, $p = 0.173$, $\eta^2_p = 0.044$; Group: $F(1, 37) = 14.29$, $p < 0.001$, $\eta^2_p = 0.279$; Condition x group: $F(2.88, 106.70) = 1.17$, $p = 0.323$, $\eta^2_p = 0.031$). Beta-gamma-band gastrocnemius coherence in the fast leg was lower in older adults compared to younger adults (95% CI = [-1.46, -0.440], $d = -0.605$). Post-hoc comparisons within condition and between groups showed that older adults had lower coherence during early post-adaptation compared to young adults.

Beta-gamma-band gastrocnemius coherence in the slow leg during stance phase was between groups, but not between conditions, and condition x group effect was not significant (Figure 3.15D; Condition: $F(2.62, 97.06) = 1.89$, $p = 0.143$, $\eta^2_p = 0.049$; Group:
F(1, 37) = 19.39, p < 0.001, η²_p = 0.344; Condition x group: F(2.62, 97.06) = 0.12, p = 0.929, η²_p = 0.003). Beta-gamma-band gastrocnemius coherence in the slow leg was lower in older adults compared to younger adults (95% CI = [-1.62, -0.60], d = -0.705). Post-hoc comparisons within condition and between groups showed that older adults had lower coherence during pre-slow, early and late split-belt adaptation, and early and late post-adaptation.
Gastrocnemius coherence during stance during study 1.

Natural logarithm of cumulative alpha (A, C) and beta-gamma (B, D) intermuscular coherence between the medial and lateral gastrocnemius in the fast (A-B) and slow leg (C-D) during study 1. Black = Young; Red = Old; X = group means; Error bars = standard error. Brackets indicate between-condition comparisons where p < 0.05. Thick brackets indicate speed-matched between-condition comparisons where p < 0.05. * indicate between-groups comparisons within condition where p < 0.05. All comparisons were corrected for multiple comparisons using the Bonferroni method.

3.3.3 Corticospinal drive to lower leg muscles is associated to kinematic changes during split-belt locomotor adaptation

Stepwise multiple linear regression was used to predict overall and early changes in step time asymmetry and double support asymmetry. Multiple linear regression model
parameters and coefficients are shown in Table 3.8. A significant regression model was found for all of the kinematic outcomes.

Overall change in step length asymmetry was predicted by slow leg tibialis anterior beta-gamma coherence during early adaptation (Figure 3.16A; $\beta = 0.048$, $p = 0.035$). Early changes in step length asymmetry was predicted by group (coded as 1 = Young and 2 = Old; $\beta = -0.084$, $p = 0.009$) alone. None of the coherence values during early adaptation contributed to the model for early changes in step length asymmetry during adaptation.

For overall change in double support asymmetry during adaptation, slow leg tibialis anterior beta-gamma coherence during early adaptation significantly contributed to the prediction (Figure 3.16B; $\beta = 0.040$, $p = 0.017$). The model to predict early changes in double support asymmetry during adaptation had the highest $r^2$ and lowest RMSE out of all the models ($r^2 = 0.303$, RMSE = 0.057). Slow leg tibialis anterior beta-gamma coherence and fast leg plantarflexor coherence during early adaptation significantly contributed to the model (Figure 3.17; Slow leg TA: $\beta = 0.046$, $p < 0.001$; Fast leg PF: $\beta = -0.028$, $p = 0.009$).
Table 3.8. Multiple linear regression models for study 1.
RMSE = Root mean square error; SL = Step length; DS = Double support; TA = Tibialis anterior; PF = plantarflexors.
Figure 3.16. Regression models for overall (A) step length asymmetry and (B) double support asymmetry changes during study 1.
Black X = Young participants; Red X = Old participants.
Figure 3.17. 3D regression models for early change in double support asymmetry during study 1.
On x and y axis are coherence values, and on z axis is early change in double support asymmetry. A and B are the same models but different views: (A) Horizontal axis in front is the slow leg tibialis anterior beta-gamma coherence, and (B) horizontal axis in front is the fast leg plantarflexor beta-gamma coherence. Black = Young participants; Red X = Old participants.
3.4 Discussion

This study examined the effects of age on the contribution of corticospinal drive to split-belt walking adaptation. The three hypotheses were supported by this study: (1) Older adapted step length asymmetry the same amount as young adults, but early change in during adaptation will be reduced in older adults; (2) corticospinal drive was less in older adults compared to young adults during split-belt walking; and (3) corticospinal drive to the tibialis anterior in the slow leg during early adaptation predicted overall changes in step length and double support asymmetry, and corticospinal drive to the tibialis anterior in the slow leg and to the plantarflexors in the fast leg predicted early change in double support asymmetry during adaptation.

3.4.1 Aging influences interlimb kinematic changes during split-belt locomotor adaptation

Older adults adapted the same amount of step length asymmetry, but early changes during adaptation were less compared to younger adults. Bruijn and colleagues (2012) reported a more symmetrical plateau of step length in younger adults compared to older adults at the end of split-belt locomotor adaptation. As demonstrated in our stride-stride plots and exponential models, older adults do seem to plateau at a level more asymmetrical and to adapt slower compared to younger adults. In addition, the effect size in overall change in step length asymmetry was moderate ($d = 0.578$), which may suggest that older adults have a slightly smaller overall change in step length asymmetry compared to younger adults. The smaller early change in step length asymmetry in older adults agrees with previous split-belt studies that evaluated similar age-groups and showed a slower rate of
adaptation (Bruijn, Van Impe, Duysens and Swinnen 2012; Sombric, Harker, Sparto and Torres-Oviedo 2017).

In contrast to step length asymmetry, both overall and early changes in double support asymmetry adaptation were different between older and younger adults. There are fewer studies that report double support asymmetry changes with aging, but our results on overall adaptation on double support asymmetry are in contrast with previous studies on aging (Vervoort and others 2019a; Vervoort and others 2019b). This difference in outcome may reflect a variety of factors that can contribute to aging that impact the study population (e.g., level of daily physical activity, cognitive function, etc.) but it is important to note that our participant group was older compared to the other studies (Vevoort et al., 2019a older adults age: 55.3 ± 2.9 yrs; Vevoort et al., 2019b older adults age: 67.8 ± 5.8 yrs). The influence of increased age on the rate or early change in double support asymmetry adaptation is unclear, but interestingly this study found a larger early change in double support asymmetry during adaptation in older adults compared to younger adults. However, when adjusted for physical function (SPPB-A scores), the age-group differences in double support asymmetry were not statistically significant. This may suggest that the strategy to alter double support asymmetry is a compensatory strategy in older adults with decreased physical function.

3.4.2 Reactive intralimb kinematic adjustments during split-belt locomotor adaptation may be reduced with increased age

In contrast to interlimb parameters, there were no group differences in stance length and stance time asymmetry during adaptation, but older adults had smaller overall change in stance length asymmetry during post-adaptation. However, after adjusting for physical
function, early change in stance time asymmetry during adaptation was larger in older adults, while there was no age-related differences in intralimb changes during post-adaptation. As intralimb parameters are expected to be immediately adjusted in response to environment changes (Bastian 2008), unlike for the interlimb parameters, a greater early change in intralimb parameters will indicate slower adjustments (i.e., smaller change in intralimb parameters will indicate immediate change during initial adaptation, while greater change will indicate that participants are still changing intralimb parameters at the 30th stride). The slower change in stance time asymmetry in older adults compared to younger adults is consistent with previous split-belt studies that have reported age-related changes in intralimb kinematic adaptation (Bruijn, Van Impe, Duysens and Swinnen 2012; Roemmich and others 2014; Vervoort and others 2019b). Bruijn and colleagues (2012) reported no significant age differences in stride length adaptation while older adults adapted swing time slower and compensated for this by changing swing speed faster than younger adults. In regard to post-adaptation, Roemmich and colleagues (2014) reported a reduced reactive temporal asymmetry during post-adaptation. In their study, stance time asymmetry in older adults did not differ significantly between baseline and post-adaptation, whereas the young participants showed a higher stance time asymmetry during post-adaptation compared to baseline (Roemmich and others 2014). This is in agreement with the observed age group difference in overall change in stance length asymmetry during post-adaptation in this study, but this difference may be due to changes in physical function in older adults. Taken together, older adults adjust intralimb kinematic parameters slower during split-belt adaptation compared to younger adults, and may have reduced aftereffects in stance length asymmetry. However, there is a lack of literature examining effects of age on reactive intralimb kinematic adaptation in general, and more studies should be done for conclusive evidence.
3.4.3 Aging influences corticospinal drive during split-belt locomotor adaptation

Corticospinal drive quantified by beta-gamma-band coherence was lower in older adults compared to younger adults. This is in agreement with previous studies that examined EMG-EMG coherence in older and younger adults during walking and visually guided walking (Gennaro and de Bruin 2020; Spedden, Choi, Nielsen and Geertsen 2019). This finding is interesting and important because multiple studies have reported increased demand in cortical brain resources, especially during walking in older adults compared to younger adults (Chen and others 2017; Hawkins and others 2018; Mirelman and others 2017). This may suggest that even though older adults may think more about walking compared to younger adults, the output from the motor cortex that reaches the muscle is reduced, which may be due to the physiological changes in the corticospinal structures (e.g., decrease in the number of motor units, decrease in the innervation ratio of muscle fiber:motor neuron (Deschenes 2011)).

Previously, an increase in slow leg beta-band coherence in tibialis anterior from baseline pre-slow to early split-belt adaptation has been reported in younger adults (Sato and Choi 2019), which was also found in this study. Consistent with previous findings (Sato and Choi 2019) this increase in beta-gamma tibialis anterior coherence in the slow leg during early adaptation was followed by a decrease during late adaptation (Figure 3.13D). This may be related to changes in corticospinal excitability that result from a change in ankle dynamics. In a previous study with force-field adaptation, there was an increase in corticospinal excitability with resisted ankle dorsiflexion and a decrease in corticospinal excitability with facilitated ankle dorsiflexion (Barthelemy, Alain, Grey, Nielsen and Bouyer 2012). The sudden difference in the treadmill speeds during early split-belt adaptation may
increase the corticospinal excitability, in turn increasing the corticospinal drive to the slow leg tibialis anterior during swing phase.

In general, older adults demonstrated decreased modulation in corticospinal drive compared to younger adults. In support of this, Watanabe and colleagues (2018) have also demonstrated a reduced modulation in plantarflexor intramuscular coherence during different standing balance tasks in older adults compared to younger adults (Watanabe, Saito, Ishida, Tanabe and Nojima 2018a). One possible hypothesis is that the reduced beta-gamma coherence during walking in older adults may be impairing the ability to modulate, due to a ceiling effect.

The focus of this study was on corticospinal drive (beta-gamma coherence), but alpha-band coherence was also examined as it may be related to the olivo-cerebellar system (Llinas and Volkind 1973; Llinas 2013). Similar to beta-gamma coherence that is related to corticospinal drive, older adults demonstrated lower alpha-band coherence compared to younger adults, but effect size was generally smaller compared to beta-gamma coherence group differences. This is in part consistent with neuroimaging studies that showed intact cerebellar function during mobility in older adults (Mitchell, Starrs, Soucy, Thiel and Paquette 2019; Zwergal and others 2012). However, as demonstrated in the alpha-band coherence in this study, there may be a variability in neural mechanism that may underlie certain age-related changes in mobility. For example, in a study by Boyne and colleagues (2018) the lower resting functional connectivity in the cerebellum was associated to walking capacity (Boyne and others 2018). Also, in contrast to beta-gamma coherence in which older adults seemed to modulate coherence less compared to younger adults, older adults modulated alpha-band coherence more compared to younger adults (as indicated by the significant interaction effect in the alpha band coherence in the plantarflexors; Figure 3.14). Corticomuscular coherence in the alpha band has been suggested to be related to
processing of sensory feedback (Hansen and Nielsen 2004), which is in line with the
cerebellum’s importance with sensorimotor processing (For review: Baumann and others
2015; Manto and others 2012; Sokolov, Miall and Ivry 2017). This may suggest that older
adults may have altered sensory processing with changes in the walking environment
compared to that of younger adults.

3.4.4 Corticospinal drive in to the lower leg musculature are associated with kinematic
changes during split-belt locomotor adaptation

Slow leg tibialis anterior beta-gamma coherence significantly contributed to predict
overall change in step length and double support asymmetry during split-belt adaptation. In
our previous study, we found that negative association between beta and gamma
coherence in the tibialis anterior in the slow leg and initial double support asymmetry
perturbation during split-belt adaptation in healthy young adults (i.e., higher beta and
gamma coherence to the tibialis anterior was associated to lower double support
asymmetry during initial split-belt adaptation) (Sato and Choi 2019). In our present analysis,
we found a positive relationship (i.e., positive unstandardized β-values) between overall
changes in step length and double support asymmetry adaptation and slow leg tibialis
anterior beta-gamma coherence. It’s important to note that the overall changes takes into
account both the initial and plateau values. Therefore, higher beta-gamma coherence in the
slow leg tibialis anterior was related to larger overall step length asymmetry change but
smaller (i.e., less negative) overall double support asymmetry change during adaptation.
This is in agreement with our previous study (Sato and Choi 2019), and supports the
specific role of corticospinal drive during split-belt locomotor adaptation.
Interestingly, only the grouping variable significantly contributed to predict early change in step length asymmetry adaptation. Statistically, this is equivalent to an independent t-test and is consistent with the group comparisons (Figure 3.5). This suggests that corticospinal drive to the major lower limb ankle muscles are not associated with the early changes in step length asymmetry. This is in contrast with my hypothesis as I predicted that the corticospinal drive will largely play a role in making appropriate adjustments to sensory demand early during adaptation. However, the results are in line with a split-belt adaptation study which demonstrated that step length adaptation was intact even post-hemispherectomy (Choi, Vining, Reisman and Bastian 2009). Together, this may suggest that other neural mechanisms may underlie the early change in step length asymmetry adaptation.

Slow leg tibialis anterior beta-gamma coherence and fast leg plantarflexor beta-gamma coherence significantly contributed to predict early change in double support asymmetry. This is the only kinematic adaptation variable that showed relationship with plantarflexor corticospinal drive. Larger beta-gamma coherence in the slow leg tibialis anterior and smaller beta-gamma coherence in the fast leg plantarflexors was related to smaller (i.e., less negative) early change in double support asymmetry during adaptation. Higher intermuscular coherence in the beta-gamma band has been shown to be indicative of functional coordination (i.e., synergy), while lower intermuscular coherence has been indicative of greater individual muscle control (Laine and Valero-Cuevas 2017). Therefore, in addition to the corticospinal drive to the tibialis anterior, synergy in the plantarflexor may be important for changes in double support asymmetry during split-belt adaptation. It is important to note that slow leg tibialis anterior intramuscular coherence positively contributed to the model, while the fast leg plantarflexor intermuscular coherence negatively contributed to the model predicting early change in double support asymmetry adaptation.
This suggests that more corticospinal drive is not necessarily always “better”; to make appropriate gait adjustments, but there should be a balance of corticospinal drive to each muscle or muscle groups which is specific to the desired outcome.

3.5 Conclusions

With a split-belt locomotor paradigm that perturbed the normal, symmetrical gait pattern, older adults demonstrated different adaptation strategies compared to younger adults. Specifically, older adults demonstrated reduced early change in step length, and greater overall and early changes in double support. Within the older population, there are more inter-subject variability in double support adaptation, and physical function is a predictor of different timing strategies on the split-belt treadmill. During this locomotor paradigm, corticospinal drive was less in older adults compared to younger adults. In both age groups, the corticospinal drive to the tibialis anterior during the swing phase on the slow treadmill belt and corticospinal drive to the plantarflexor during stance phase on the fast treadmill belt during adaptation were associated to the kinematic changes. This work contributes to the growing literature in the age-related changes in motor learning that suggests that the capacity to alter locomotor patterns in older adults are not impaired, but the strategies and underlying neural mechanisms may be altered with increased age. Future studies should examine whether there are compensatory neural mechanisms that counteract the under-activation of the corticospinal drive that was observed in this study.
CHAPTER 4

IMPACT OF AGING ON CORTICOSPINAL CONTROL OF VISUOMOTOR LOCOMOTOR ADAPTATION

4.1 Introduction

To rapidly adapt gait mechanics to the demands of the immediate environment, humans use proprioceptive, vestibular, and visual information (Peterka 2018; Takakusaki 2017). Visual information is especially important to process and predict what is expected from the environment to maximize dynamic stability via feedforward mechanisms (Patla 1998; Patla, Niechwiej, Racco and Goodale 2002). To investigate visuomotor locomotor adaptation, visual perturbations are introduced during visually guided walking tasks (Alexander, Flodin and Marigold 2011; Cherry-Allen, Statton, Celnik and Bastian 2018; Michel, Vernet, Courtine, Ballay and Pozzo 2008; Morton and Bastian 2004; Nemanich and Earhart 2015; Statton, Toliver and Bastian 2016). Distorted visual feedback causes a mismatch between the visual and proprioceptive system, and to correct for this, sensory realignment is crucial to gradually minimize movement error (For review: Redding, Rossetti and Wallace 2005). With sensory realignment, the relationship between different sensory modalities (proprioception and vision in this case) is spatially re-mapped to minimize multi-sensory misalignment (Block and Bastian 2011; Redding and Wallace 1993; Welch and Warren 1980). Negative aftereffects (errors in the opposite direction compared to early adaptation) following visuomotor adaptation are dependent on sensory realignment (Redding and Wallace 1993; Redding and Wallace 1996), suggesting that for complete adaptation to visuomotor tasks, sensory realignment is required via predictive-feedforward mechanisms.
Walking impairments in older adults are often exacerbated in complex environments that require visuomotor coordination (Black, Kimlin and Wood 2014; Mirelman and others 2017). With an increase in age, both reactive and predictive visuomotor locomotor adaptations are impaired (Huitema and others 2005; Nemanich and Earhart 2015; van Hedel and Dietz 2004). During locomotion with prism goggles, older adults demonstrate smaller overall changes in adaptation and slower rate of adaptation and de-adaptation in angular error compared to young adults (Huitema and others 2005; Nemanich and Earhart 2015). Older adults may experience difficulty with sensory realignment that is required to adapt to inaccurate visual feedback (Block and Bastian 2011; Welch and Warren 1980). However, the underlying neural mechanisms of age-related changes in visuomotor locomotor adaptation is not known.

Our previous study using real-time visual feedback of foot placement distorted the relationship between screen space and treadmill space (i.e., visuomotor gain), causing kinematic adaptation to occur (Choi, Jensen and Nielsen 2014; Sato, Cui and Choi 2020). During the early phase of adaptation when visuomotor gain was altered on one side, participants saw errors in their foot placement (distance between target and location of foot placement); this drove changes in step length so that one leg stepped longer than the other, achieving a plateau in step length asymmetry that is equivalent to the set visual distortion (Choi, Jensen and Nielsen 2014; Sato, Cui and Choi 2020). During de-adaptation when the visuomotor gain is set to equal again, participants show aftereffects in their step lengths, demonstrating storage of spatial realignment via predictive mechanisms (Choi, Jensen and Nielsen 2014; Sato, Cui and Choi 2020).

During visuomotor adaptation, cortical involvement is crucial to integrate visual information and translate it for appropriate motor execution (Drew, Jiang, Kably and Lavoie 1996; Drew and Marigold 2015). In older adults, corticospinal drive measured by
corticomuscular and intramuscular coherence is reduced compared to young adults during normal and visually-guided walking (Spedden, Choi, Nielsen and Geertsen 2019). Furthermore, age-related changes in corticospinal drive have been associated with decreased visuomotor accuracy during visually guided walking (Spedden, Choi, Nielsen and Geertsen 2019). However, the role of corticospinal drive during visuomotor locomotor adaptation is unclear. By investigating plastic neural changes that occur with visuomotor locomotor adaptation, we may be able to modify interventions so that they can target specific kinematic changes in populations with gait dysfunction.

The **objective of this study** was to determine the impact of age on the contribution of corticospinal drive during visually distorted locomotor adaptation. This study was a cross-sectional observational study between two cohorts: young and older adults. Corticospinal drive was quantified by the amount of EMG-EMG coherence in the beta-gamma band (15-45 Hz). To quantify kinematic locomotor adaptation, I measured error asymmetry, step length asymmetry, step time asymmetry, and double support asymmetry. For each kinematic variable, overall and early changes during adaptation and post-adaptation were be calculated. I hypothesized that: (1) Older adults will show reduced overall change in kinematic asymmetry adaptation and reduced early changes in kinematic asymmetry adaptation compared to younger adults; (2) corticospinal drive will be reduced in older adults compared to young adults during visuomotor walking adaptation; and (3) reduced corticospinal drive will be associated with reduced overall and early changes in kinematic adaptation.
4.2 Methods

4.2.1 Participants

Twenty-one healthy young adults (18-33 years old) and 20 healthy older adults (68-80 years old) participated in this study (Table 4.1). Inclusion criteria was no previous history of neurological disorder, no current major medical conditions (including cognitive), no current orthopedic injuries, ability to walk without any walking aids (including ankle-foot orthoses) for at least 10 minutes, and visual acuity over 20/40. All participants gave informed written consent before the study in accordance with the protocol approved by the Institutional Review Board of University of Florida, Gainesville, FL (Protocol # 202000764).

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Table 4.1. Participant characteristics for study 2. Mean and standard deviation are reported. Independent t-tests were used to determine group differences. To assess sex distribution difference, a two-tailed Fischer’s exact-test was used. SPPB = Short Physical Performance Battery; SPPB-A = Advanced Short Physical Performance Battery (Simonsick and others 2001). FSS = Fatigue Severity Scale. Godin = Godin Physical Activity Questionnaire; Waterloo = Waterloo Footedness Questionnaire; TICS = Telephone Interview Cognitive Status.
4.2.2 Data collection and equipment

Participants walked on an instrumented treadmill (Bertec, Columbus, OH). The speed of the treadmill was based on each participant’s leg length (m), which was measured from the greater trochanter to the lateral malleolus for each leg and averaged between limbs. Step length (m) for the visuomotor task was determined as two-thirds of the leg length, and the speed of the treadmill and visuomotor task was determined as 1.33 x step length (speed (m/s) = step length (m) x cadence (90 steps/60 seconds)). A cadence of 90 steps/minute has been determined as a comfortable cadence for participants performing a similar visuomotor task in a different study (Choi, Jensen and Nielsen 2016).

Reflective markers were placed bilaterally on the anterior superior iliac spine (pelvis), greater trochanter (hip), joint line of the knee (knee), lateral malleolus (ankle), and 5th metatarsal (toe; Figure 4.1). Two pairs of electrodes (MA411 Surface preamplifier with stainless-steel electrodes, Motion Lab System, Baton Rouge, LA, USA) were placed on the tibialis anterior, one pair of electrodes was placed on the medial gastrocnemius, and one pair of electrodes was placed on the soleus (EMG electrode placement was the same as for study 1; for reference: Figure 3.3). The muscle belly of the tibialis anterior, medial gastrocnemius, and soleus was identified by palpation by the experimenter. Lower limb kinematics were recorded at 100 Hz using an 8-camera Miqus system (Qualisys, Gothenburg, Sweden). Force data from the treadmill (Bertec, Columbus, OH) and EMG signals from a wired amplifier (MA300, Motion Lab System, Baton Rouge, LA, USA) were collected at 1000 Hz. EMG, force plate and kinematic data were synchronized using Qualisys Track Manager 2.14 (Qualisys, Gothenburg, Sweden).

A screen in front of the treadmill was used to project the visuomotor task (Figure 4.1). Real-time position of the toe was projected on the screen as a blue dot (Figure 4.2). Based on calculated step lengths and speed of the treadmill, red square targets were
projected on the screen when the leg is in swing phase. When the visuomotor gain is set to 1.0, the speed at which the targets move down will be the same as the treadmill speed (equal on both sides). When the visuomotor gain is set to 0.9, the relationship between the screen and treadmill space was distorted in a way that screen space was reduced relative to treadmill space (screen space = treadmill space x 0.9). As a result, when the visuomotor gain is decreased, the target speed decreased on the screen, and the participants needed to alter gait kinematics to hit the target.

Figure 4.1. Experimental setup for study 2. Participants wore 5 reflective markers (black) on each leg. Reflective markers were placed on: (1) Anterior superior iliac spine (pelvis), (2) greater trochanter (hip), (3) joint line of the knee (knee), (4) lateral malleolus (ankle), and (5) 5th metatarsal (toe).
Figure 4.2. Progression of visuomotor task starting from left heel-strike. Real-time toe location during the swing phase of gait will be displayed as a solid blue dot on the screen. Red boxes represent the target that will be displayed on the screen. Empty blue circles represent the position of the toe on the opposite (stance) leg (not visible to the participant). Red and blue arrows indicate which direction the target and toe location will move (respectively) and will not be displayed on the screen. Bottom numbers (0.70) indicate the speed of the visuomotor task (equivalent to treadmill speed).

Participants walked on the treadmill for 7 conditions (Figure 4.3): (1) 5 min with no visual feedback for familiarization on the treadmill; (2) 5 min with no visual feedback for baseline; (3) 300 steps with symmetrical visuomotor gain set at 0.9:0.9 (“pre-slow”); (4) 300 steps with symmetrical visuomotor gain set at 1.0:1.0 (i.e., the same speed as the treadmill), but with longer between-target distances (1.1 x calculated step length) resulting in longer step lengths (“pre-long”); (5) 300 steps with symmetrical visuomotor gain set at 1.0:1.0 (“pre-fast”); (6) 600 steps with split-visuomotor gain for adaptation (0.9:1.0); (7) 600 steps with equal visuomotor gain (1.0:1.0) for post-adaptation. The leg on the side with 1.0 visuomotor gain during adaptation (from here on referred to as the “fast leg”), and the leg on the lower gain (0.9; from here on referred to as the “slow leg”) was randomized between
participants with the same leg dominancy, as leg dominancy may alter the rate of adaptation (Bulea, Stanley and Damiano 2017; Kong, Candelaria and Smith 2011).

Figure 4.3. Experimental paradigm for study 2. Double lines indicate when visuomotor gain will be equal for both left and right treadmill belts. Singular lines indicate the visuomotor gain for each right and left side during the split-visuomotor adaptation condition. Downward arrows indicate when participants will be asked to indicate their fatigue level using the Visual Analog Fatigue Scale (VAFS). Fam. = Familiarization; VM = Visuomotor; VF = Visual feedback.

4.2.3 Kinematic analysis

Visuomotor adaptation was determined by calculating stride-by-stride changes in error asymmetry, step length asymmetry, step time asymmetry, and double support asymmetry. Target error was defined as the difference between the location of the toe at heel stride to the center of the target (mm; Figure 4.4). Step length was calculated as the anterior-posterior distance between the toe markers at time of heel strike (cm). Step time was calculated as the time from heel-strike of the non-reference limb to the heel-strike of the reference limb (ms). Fast and slow step length and step times corresponded to the leading leg being on the high or low gain visuomotor feedback, respectively, at heel strike.
Double support time was calculated as the duration when both legs are on the ground (ms). Fast leg and slow leg double support time corresponded to the double support occurring at the end of the fast leg’s stance (i.e., the time from slow leg heel-strike to fast leg toe-off) and the slow leg’s stance (i.e., the time from fast leg heel-strike to low leg toe-off), respectively.

![Diagram of double support time](image)

**Figure 4.4.** Example of screen during visuomotor task at left heel strike. Real-time toe location during the swing phase of gait will be displayed as a solid blue dot on the screen. Red boxes represent the target that will be displayed on the screen. Bottom numbers (0.70) indicate the speed of the visuomotor task (equivalent to treadmill speed). Error is calculated as the difference between toe location and the center of target at heel strike. A negative error indicates undershooting of foot placement, and a positive error indicates overshooting of foot placement.

Step length asymmetry, step time asymmetry, and double support asymmetry were defined as the normalized difference between legs, for each stride (Equation 4.1). Error is already normalized to leg length, so the error asymmetry was defined at the difference between limbs for each stride (fast leg – slow leg).

\[
\text{Asymmetry} = \frac{\text{Fast leg} - \text{slow leg}}{\text{Fast leg} + \text{slow leg}}
\]

Eq. 4.1
Changes in locomotor asymmetry were assessed using averaged values over three different time epochs (phases) during each adaptation and post-adaptation: (1) Initial (mean of first 5 strides), (2) Early adaptation/post-adaptation (mean of strides #6-30), (3) plateau (mean of last 30 strides) (Leech and Roemmich 2018; Leech, Roemmich and Bastian 2018). In order to assess baseline behavior, the average of first 30 strides were averaged for baseline with no visual feedback, pre-slow, pre-long, and pre-fast. Overall change in adaptation and post-adaptation was identified as the asymmetry difference between plateau and initial phases during split-belt adaptation and post-adaptation, respectively. Early change was identified as the asymmetry difference between early and initial phases during split-belt adaptation and post-adaptation, respectively.

To further explore the age group differences in kinematic changes during adaptation and post-adaptation, group average of the first 250 strides of asymmetry values was fit to an exponential model (Equation 4.2) (Lang and Bastian 1999; Malone, Vasudevan and Bastian 2011). Where a is the value that the exponential fit function approaches (i.e., plateau, asymptote), b is the overall change in asymmetry required from the first stride to the plateau value a, and c is the number of strides it would take to achieve the ~63% of the final plateau asymmetry level.

\[ y = a - b \times e^{-x/c} \]  
Eq. 4.2

4.2.4 Coherence analysis

Coherence was analyzed in the same way as in study 1. EMG signals were high-pass filtered at 8 Hz, rectified, and normalized to have unit variance (to normalize EMG amplitude) and to have realizations of stationary zero mean time series denoted by x and y (Halliday and others 1995). Discrete Fourier transformation analysis was applied at short
sections of data taken at a fixed offset time to estimate the average autospectras for processes $x (f_{xx}(\lambda))$ and $y (f_{yy}(\lambda))$. The cross-spectrum between $x$ and $y (f_{xy}(\lambda))$ was also estimated in a similar manner. The short sections of data to calculate coherence was determined after examining the processed EMG for each muscle and determining where the muscle is active during the gait cycle. I used 0-400 ms after toe-off to calculate intramuscular coherence in the tibialis anterior, and 500-100 ms before toe-off to calculate intermuscular and intramuscular coherence in the plantarflexors, similar to study 1 (For reference, see Figure 3.4).

For each Fourier frequency, correlation between the EMG signals were calculated (Halliday and others 1995). The resulting coherence value provide a measure of association of the $x$ and $y$ processes on a scale from 0 to 1 (Equation 4.3). A coherence value of 0 signify no synchrony between the two EMG signals and a coherence value of 1 signify perfect synchrony between the two EMG signals.

$$|R_{xy}(\lambda)|^2 = \frac{|f_{xy}(\lambda)|^2}{f_{xx}(\lambda)f_{yy}(\lambda)}$$  

Eq. 4.3

The calculated coherence can quantify the strength and frequency of the common neural drive from the corticospinal tract in the motoneuronal pool within the muscle (Farmer, Bremner, Halliday, Rosenberg and Stephens 1993; Halliday and others 1995). To characterize coherence modulation over the course of locomotor adaptation, the coherence was calculated for each leg over the first 100 strides during each baseline conditions and over the first and last 100 strides during split-visuomotor adaptation and de-adaptation. For each condition, the natural logarithm of the cumulative sum of coherence will be calculated for the beta-gamma band (15-45 Hz).

For each condition, the natural logarithm of the cumulative sum of coherence was calculated for the beta-gamma band (15-45 Hz) to quantify corticospinal drive to the lower
limb muscles. EMG-EMG coherence in the alpha-band is speculated to originate from a different central nervous system source compared to the beta-gamma band (although there are some studies that challenge this view; Graziadio and others 2010; Mima and Hallett 1999b; Salenius, Portin, Kajola, Salmelin and Hari 1997) EMG-EMG coherence in the alpha band (8-15 Hz) was calculated for additional analysis to examine if alpha band modulation is different from beta-gamma band modulation.

4.2.5 Statistical analysis

Age group differences in overall and early changes in kinematic adaptation (hypothesis 2.1) was assessed though independent t-tests (Table 4.2). Effect sizes for paired comparisons were calculated with Cohen’s d. Effect sizes were defined as small < 0.499, moderate = 0.500-0.799 and large > 0.800.

Since group characteristics demonstrated that physical function was different between groups (Table 4.1, for SPPB-A and SPPB), I used an analysis of covariate to examine group differences in kinematic changes controlling for physical function. Physical function was controlled between groups as the objective of this study was to examine healthy aging (i.e., no functional decline).

To determine whether there were age-related differences in corticospinal drive (hypothesis 2.2), group differences in beta-gamma band intramuscular tibialis anterior coherence, intermuscular plantarflexor coherence, and intramuscular gastrocnemius coherence were assessed through a 2-way mixed measures ANOVA with post-hoc pairwise comparisons with Bonferroni corrections. Specifically, I assessed if coherence changed between conditions by examining the main effect of conditions, and I assessed whether corticospinal drive was different between groups by examining the main effect of age
groups. Effect sizes for ANOVAs were determined by partial eta-squared ($\eta^2_p$). Effect sizes were defined as small $< 0.059$, moderate $= 0.060-0.139$ and large $> 0.140$.

<table>
<thead>
<tr>
<th>Goal</th>
<th>Question</th>
<th>Factor levels</th>
<th>Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypothesis 2.1</td>
<td>Is there a difference between the age cohorts?</td>
<td>2</td>
<td>Age cohorts (2): Young and older</td>
</tr>
<tr>
<td></td>
<td>Variables: Overall change and early change in kinematic adaptation</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypothesis 2.2</td>
<td>Is there a difference between the age cohorts?</td>
<td>8 x 2</td>
<td>Conditions (6): No visual feedback baseline, Pre-slow, Pre-long, Pre-fast, Early adaptation, Late adaptation, Early post-adaptation, Late post-adaptation</td>
</tr>
<tr>
<td></td>
<td>Variables: TA-TA intramuscular coherence, MG-Sol intermuscular coherence, MG-LG intramuscular coherence</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypothesis 2.3</td>
<td>Is CSD associated with adaptation?</td>
<td>2</td>
<td>Dependent: Kinematic adaptation parameters Independent: Beta-gamma coherence</td>
</tr>
<tr>
<td></td>
<td>Variables: Kinematics vs coherence</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 4.2. Summary of statistical tests for each hypothesis in Aim 2. CSD = Corticospinal drive (quantified by coherence); TA = Tibialis anterior; MG = Medial gastrocnemius; Sol = Soleus.

To determine the contribution of corticospinal drive on proprioception-driven locomotor adaptation (hypothesis 2.3), relationship between kinematic adaptation (overall
and early change) and coherence will be assessed through a stepwise multiple linear regression. The covariates considered are listed in Table 4.3. The strength of the relationships will be assessed through root mean square error (RMSE) and coefficient of determination ($r^2$).

Table 4.3. Variables in multiple linear regression models for study 2. TA = Tibialis anterior; PF = Plantarflexors; GST = Gastrocnemius.

<table>
<thead>
<tr>
<th>Dependent Variables (Kinematics)</th>
<th>Overall change during adaptation (Δ Plateau - Initial)</th>
<th>Early changes in adaptation (Δ Early - Initial)</th>
<th>Group (1 = Young; 2 = Old)</th>
<th>Early adaptation coherence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Error asymmetry</td>
<td>Step length asymmetry</td>
<td>Step length asymmetry</td>
<td>Fast leg TA beta-gamma band</td>
<td></td>
</tr>
<tr>
<td>Step time asymmetry</td>
<td>Step time asymmetry</td>
<td>Step time asymmetry</td>
<td>Slow leg TA beta-gamma band</td>
<td></td>
</tr>
<tr>
<td>Double support asymmetry</td>
<td></td>
<td>Double support asymmetry</td>
<td>Fast leg PF beta-gamma band</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Slow leg PF beta-gamma band</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Fast leg GST beta-gamma band</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Slow leg GST beta-gamma band</td>
<td></td>
</tr>
</tbody>
</table>

All statistical significance was established with an alpha level = 0.05. Statistical analyses were performed using JASP v0.14.1 (University of Amsterdam, Amsterdam, Netherlands).

Changes from proposed methods include the calculation of early change to replace the rate calculation, and performing a multiple linear regression analysis to assess associations, and is consistent with that of study 1 (For reference, see section 3.2.6).
4.3 Results

4.3.1 Aging influences kinematic adaptation during split-visuomotor locomotor adaptation

Participants walked with symmetrical error, spatial, and temporal kinematics during pre-slow, pre-long, and pre-fast; there were no evidence of age group differences during baseline conditions for all of the kinematic asymmetry variables (Table 4.4).

<table>
<thead>
<tr>
<th>Condition</th>
<th>Asymmetry variables</th>
<th>p-value</th>
<th>95% Confidence interval for difference in group means</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>No VF</td>
<td>Step length</td>
<td>0.445</td>
<td>-0.04 - 0.02</td>
<td>-0.241</td>
</tr>
<tr>
<td></td>
<td>Step time</td>
<td>0.925</td>
<td>-0.01 - 0.01</td>
<td>-0.030</td>
</tr>
<tr>
<td></td>
<td>Double support</td>
<td>0.627</td>
<td>-0.02 - 0.03</td>
<td>0.153</td>
</tr>
<tr>
<td>Pre-slow</td>
<td>Error*</td>
<td>0.881</td>
<td>-16.28 - 14.04</td>
<td>-0.048</td>
</tr>
<tr>
<td></td>
<td>Step length*</td>
<td>0.894</td>
<td>-0.03 - 0.03</td>
<td>-0.042</td>
</tr>
<tr>
<td></td>
<td>Step time</td>
<td>0.998</td>
<td>-0.02 - 0.02</td>
<td>-6.93e-4</td>
</tr>
<tr>
<td></td>
<td>Double support</td>
<td>0.705</td>
<td>-0.02 - 0.03</td>
<td>0.119</td>
</tr>
<tr>
<td>Pre-long</td>
<td>Error</td>
<td>0.781</td>
<td>-12.63 - 16.68</td>
<td>0.087</td>
</tr>
<tr>
<td></td>
<td>Step length</td>
<td>0.105</td>
<td>-0.03 - 3.00e-4</td>
<td>-0.518</td>
</tr>
<tr>
<td></td>
<td>Step time</td>
<td>0.954</td>
<td>-0.02 - 0.02</td>
<td>0.018</td>
</tr>
<tr>
<td></td>
<td>Double support</td>
<td>0.760</td>
<td>-0.03 - 0.04</td>
<td>0.096</td>
</tr>
<tr>
<td>Pre-fast</td>
<td>Error</td>
<td>0.831</td>
<td>-11.07 - 13.70</td>
<td>0.067</td>
</tr>
<tr>
<td></td>
<td>Step length</td>
<td>0.929</td>
<td>-0.02 - 0.02</td>
<td>0.028</td>
</tr>
<tr>
<td></td>
<td>Step time</td>
<td>0.655</td>
<td>-0.01 - 0.02</td>
<td>0.141</td>
</tr>
<tr>
<td></td>
<td>Double support</td>
<td>0.791</td>
<td>-0.03 - 0.04</td>
<td>0.083</td>
</tr>
</tbody>
</table>

Table 4.4. Age group differences in baseline kinematic asymmetry during study 2. Group differences are analyzed with a student t-test, and effect size is given by Cohen’s d.

* = Levene’s test was violated and p-value reported is from a Welch test.

During initial visuomotor adaptation, participants overshot the target with their fast leg, and undershot the targets with their slow leg. Even at plateau, participants slightly overshot and undershot with the fast and slow leg, respectively (around 5 cm for each leg), leading to an asymmetry of 10 cm. During post-adaptation, there was a negative after-effect...
in which participants undershot the target with their slow leg and overshot the target with the fast leg (Figure 4.5A). Overall change (Δ plateau phase – initial phase) and early change in error asymmetry during adaptation (Δ early phase – initial phase) was not different between age groups (Figure 4.5C-D; Table 4.5; Overall Δ: p = 0.987, 95% confidence interval for difference in group means (95% CI) = [-20.32, 20.00], d = -0.005; Early Δ: p = 0.723, 95% CI = [-22.33, 15.63], d = -0.112). In contrast, both overall and early change in error asymmetry during post-adaptation was greater in young adults compared to older adults (Overall Δ: p = 0.037, 95% CI = [1.51, 44.14], d = 0.677; Early Δ: p = 0.002, 95% CI = [13.86, 55.30], d = 1.055; Figure 4.5E-F).
Figure 4.5. Error asymmetry changes during study 2.
A. Stride-by-stride changes in error asymmetry plotted for young (in black) and older adults (in red). Shaded areas are standard errors. For baseline (“pre-”) conditions the first 30 strides are plotted. For adaptation and post-adaptation conditions, the first 100 and last 30 strides are plotted. Thick dotted lines are for stride numbers 5, 30, and 100/30 strides before the last stride to indicate the different phases (Phases indicated at top of A: Initial (I) = Strides #1-5, early phase (E) = Strides #6-30, plateau (P) = Last 30 strides). B-F. Age group means and standard error bars for (B) baseline-fast and pre-slow conditions, (C) Overall change during adaptation (Δ plateau phase – initial phase), (D) early change during adaptation (Δ early phase – initial phase), (E) Overall change during post-adaptation (Δ plateau phase – initial phase), (F) early change during post-adaptation (Δ early phase – initial phase).

Participants gradually adapted their step length during split-visuomotor adaptation so that they took longer steps on their slow leg compared to the fast leg and reached a plateau of negative step length asymmetry. During post-adaptation, participants gradually de-adapted to reach a symmetrical step lengths (Figure 4.6A). Overall and early change in step
length asymmetry during adaptation was not different between age groups (Overall Δ: p = 0.562, 95% CI = [-0.05, 0.03], d = -0.183; Early Δ: p = 0.526, 95% CI = [-0.05, 0.02], d = -0.200; Figure 4.6C-D). Overall change in step length asymmetry during post-adaptation was not significantly different between age groups, but early change was greater in young adults compared to older adults (Overall Δ: p = 0.089, 95% CI = [-0.01, 0.08], d = 0.545; Early Δ: p = 0.006, 95% CI = [0.02, 0.11], d = 0.928; Figure 4.6E-F).
Figure 4.6. Step length asymmetry changes during study 2.
A. Stride-by-stride changes in step length asymmetry plotted for young (in black) and older adults (in red). Shaded areas are standard errors. For no visuomotor feedback (VF) and baseline (“pre-”) conditions, the first 30 strides are plotted. For adaptation and post-adaptation conditions, the first 100 and last 30 strides are plotted. Thick dotted lines are for stride numbers 5, 30, and 100/30 strides before the last stride to indicate the different phases (Phases indicated at top of A: Initial (I) = Strides #1-5, early phase (E) = Strides #6-30, plateau (P) = Last 30 strides). B-F. Age group means and standard error bars for (B) baseline-fast and pre-slow conditions, (C) Overall change during adaptation (Δ plateau phase – initial phase), (D) early change during adaptation (Δ early phase – initial phase), (E) Overall change during post-adaptation (Δ plateau phase – initial phase), (F) early change during post-adaptation (Δ early phase – initial phase).

Participants gradually adapted their step time during visuomotor adaptation so that they took shorter step times on their slow leg compared to the fast leg and reached a plateau of positive step time asymmetry. During post-adaptation, participants gradually de-adapted to reach a symmetrical step time (Figure 4.7A). Overall change in step time asymmetry was greater in young adults compared to older adults (p < 0.001, 95% CI =
Early change in step time asymmetry during adaptation was not different between age groups (p = 0.337, 95% CI = [-0.01, 0.04], d = 0.304; Figure 4.7D). Overall change and early change in step time asymmetry during post-adaptation was not significantly different between age groups (Overall Δ: p = 0.093, 95% CI = [-0.05, 0.01], d = -0.537; Early change: p = 0.164, 95% CI = [-0.04, 0.01], d = -0.444; Figure 4.7E-F).
Figure 4.7. Step time asymmetry changes during study 2.
A. Stride-by-stride changes in step time asymmetry plotted for young (in black) and older adults (in red). Shaded areas are standard errors. For no visuomotor feedback (VF) and baseline ("pre-") conditions the first 30 strides are plotted. For adaptation and post-adaptation conditions, the first 100 and last 30 strides are plotted. Thick dotted lines are for stride numbers 5, 30, and 100/30 strides before the last stride to indicate the different phases (Phases indicated at top of A: Initial (I) = Strides #1-5, early phase (E) = Strides #6-30, plateau (P) = Last 30 strides). B-F. Age group means and standard error bars for (B) baseline-fast and pre-slow conditions, (C) Overall change during adaptation (Δ plateau phase – initial phase), (D) early change during adaptation (Δ early phase – initial phase), (E) Overall change during post-adaptation (Δ plateau phase – initial phase), (F) early change during post-adaptation (Δ early phase – initial phase).

Participants gradually altered their double support time during visuomotor adaptation so that they took shorter double support times on their slow leg compared to the fast leg and reached a plateau of positive double support asymmetry. During post-adaptation, participants gradually de-adapted to reach symmetrical double support times (Figure 4.8A). During adaptation, both overall and early change in double support time asymmetry was not
significantly different between age groups (Overall Δ: p = 0.366, 95% CI = [-0.03, 0.07], d = 0.286; Early Δ: p = 0.451, 95% CI = [-0.02, 0.05], d = 0.238; Figure 4.8C-D). Similarly, during post-adaptation overall change and early change in double support time asymmetry was not significantly different between age groups (Overall Δ: p = 0.594, 95% CI = [-0.05, 0.03], d = -0.167; Early Δ: p = 0.175, 95% CI = [-0.06, 0.01], d = -0.431; Figure 4.8E-F).

Figure 4.8. Double support asymmetry changes during study 2.
A. Stride-by-stride changes in double support asymmetry plotted for young (in black) and older adults (in red). Shaded areas are standard errors. For no visuomotor feedback (VF) and baseline (“pre-”) conditions the first 30 strides are plotted. For adaptation and post-adaptation conditions, the first 100 and last 30 strides are plotted. Thick dotted lines are for stride numbers 5, 30, and 100/30 strides before the last stride to indicate the different phases (Phases indicated at top of A: Initial (I) = Strides #1-5, early phase (E) = Strides #6-30, plateau (P) = Last 30 strides). B-F. Age group means and standard error bars for (B) baseline-fast and pre-slow conditions, (C) Overall change during adaptation (Δ plateau phase – initial phase), (D) early change during adaptation (Δ early phase – initial phase), (E) Overall change during post-adaptation (Δ plateau phase – initial phase), (F) early change during post-adaptation (Δ early phase – initial phase).
Table 4.5. Age group differences in kinematic asymmetry during adaptation and post-adaptation for study 2.
Group differences are analyzed with a student t-test, and effect size is given by Cohen’s d. * = Levene’s test was violated and p-value reported is from a Welch test.

To further explore the group differences in kinematic changes during adaptation, an exponential model was fit to each of the kinematic asymmetry variables (Figures 4.9-4.12).
For error and step length asymmetry, exponential coefficients were similar between the young and old groups. In both error asymmetry and step length asymmetry adaptation, young and older adults take about 10 strides to reach ~63% of overall change.
Figure 4.9. Exponential model for error asymmetry adaptation during study 2.
A. Exponential model for group average in stride-by-stride changes in error asymmetry during adaptation. Shaded areas include 95% prediction intervals. Black = Young; Red = Old. B-C. Stride-by-stride plots for the young group (B) and old group (C). Open circles indicate stride-by-stride group average. $c$ is the number of strides it would take to achieve the $\sim63\%$ of the final plateau asymmetry level and equivalent to rate.

Young: $y = 68.45 - 139.83 \cdot \exp(-x/10.28)$
Old: $y = 71.07 - 124.67 \cdot \exp(-x/12.1)$
Figure 4.10. Exponential model step length asymmetry adaptation during study 2. A. Exponential model for group average in stride-by-stride changes in step length asymmetry during adaptation. Shaded areas include 95% prediction intervals. Black = Young; Red = Old. B-C. Stride-by-stride plots for the young group (B) and old group (C). Open circles indicate stride-by-stride group average. \( c \) is the number of strides it would take to achieve the \(~63\%\) of the final plateau asymmetry level and equivalent to rate.

For step time asymmetry changes during adaptation, \( a \) (equivalent to plateau) was less asymmetrical, and \( b \) (equivalent to overall changes) was less, while \( c \) (equivalent to rate) was similar in older adults compared to younger adults. The differences in coefficients are also visible in the small overlap of prediction intervals compared to other kinematic variables.
Figure 4.11. Exponential model for step time asymmetry adaptation during study 2. A. Exponential model for group average in stride-by-stride changes in step time asymmetry during adaptation. Shaded areas include 95% prediction intervals. Black = Young; Red = Old. B-C. Stride-by-stride plots for the young group (B) and old group (C). Open circles indicate stride-by-stride group average. $c$ is the number of strides it would take to achieve the $\sim 63\%$ of the final plateau asymmetry level and equivalent to rate.

For double support time asymmetry changes during adaptation, $a$ (equivalent to plateau), and $b$ (equivalent to overall changes) were similar between the young and older groups and is visible by the overlap in prediction intervals. However, $c$ (equivalent to rate) was about two-times larger (i.e., slower adaptation) in older adults compared to younger adults.
Figure 4.12. Exponential model double support time asymmetry adaptation during study 2. A. Exponential model for group average in stride-by-stride changes in double support asymmetry during adaptation. Shaded areas include 95% prediction intervals. Black = Young; Red = Old. B-C. Stride-by-stride plots for the young group (B) and old group (C). Open circles indicate stride-by-stride group average. \( c \) is the number of strides it would take to achieve the \(~63\%\) of the final plateau asymmetry level and equivalent to rate.

3.3.2 Potential covariate contribution to kinematic adaptation

In general, there was an increase in fatigue (Figure 4.13; \( F(6, 234) = 32.41, p < 0.001, \eta^2_p = 0.454 \)), but there were no group differences (\( F(1, 39) = 0.32, p = 0.575, \eta^2_p = 0.008 \)).
Figure 4.13. Visual analog fatigue scale during study 2. All participants were asked to rate their fatigue at seven different time points during the experiment. 0 = No fatigue; 1 = Worst possible fatigue. Black = Young adults (n = 21); Red = Older adults (n = 20). Error bars are standard error bars.

Since group characteristics demonstrated that physical function was different between groups (Table 4.1, for SPPB-A and SPPB), I used an analysis of covariance to examine group differences in kinematic changes controlling for physical function. Consistent with previously reported, overall change in error asymmetry, step length asymmetry, and double support asymmetry during adaptation was not different between groups after adjusting for SPPB-A scores (all p’s > 0.100). For overall change in step time asymmetry adaptation, group differences were still present after adjusting for SPPB-A scores (F(1,38) = 16.10, p < 0.001, \( \eta^2_p = 0.298 \)). In contrast with previously reported, group difference in early change in step time asymmetry adaptation was significant after adjusting for SPPB-A scores (F(1,38) = 4.70, p = 0.036, \( \eta^2_p = 0.110 \)).

For post-adaptation, in contrast with previously reported, overall change in error asymmetry was not significant between age groups after adjusting for SPPB-A scores (F(1,
However, age group differences in early change in error asymmetry and step length asymmetry during post-adaptation was significant even after adjusting for SPPB-A scores (Error asymmetry: \( F(1, 38) = 5.04, p = 0.031, \eta^2_p = 0.117 \); Step length asymmetry: \( F(1, 38) = 4.92, p = 0.033, \eta^2_p = 0.115 \)). All other post-adaptation kinematic group comparisons were consistent with previously reported and was not statistically significant (all p's > 0.05).

### 4.3.2 EMG-EMG coherence differences between age-groups

Alpha-band tibialis anterior coherence in the fast leg during swing phase was different between conditions and between groups, but condition x group effect was not significant (Figure 4.14A; Condition: \( F(5.23, 203.93) = 7.25, p < 0.001, \eta^2_p = 0.157 \); Group: \( F(1,39) = 20.93, p < 0.001, \eta^2_p = 0.349 \); Condition x group: \( F(5.23, 203.93) = 0.89, p = 0.493, \eta^2_p = 0.022 \)). Overall, alpha-band tibialis anterior coherence in the fast leg during swing phase was lower in older adults compared to younger adults (95% CI = [-1.04, -0.40], \( d = -0.715 \)). Post-hoc comparisons within condition and between groups showed that older adults had lower coherence during pre-long, early and late split-visuomotor adaptation, and late post-adaptation. Post-hoc between condition tests showed that baseline no visuomotor condition and pre-slow coherence was higher compared to all later conditions.

Similar to the fast leg, alpha-band tibialis anterior coherence in the slow leg during swing phase was different between conditions and between groups, but condition x group effect was not significant (Figure 4.14B; Condition: \( F(5.18, 201.84) = 6.13, p < 0.001, \eta^2_p = 0.136 \); Group: \( F(1,39) = 18.32, p < 0.001, \eta^2_p = 0.320 \); Condition x group: \( F(5.18, 201.84) = 1.50, p = 0.188, \eta^2_p = 0.037 \)). Alpha-band tibialis anterior coherence in the slow leg during swing phase was lower in older adults compared to younger adults (95% CI = [-1.02, -0.37], \( d = -0.668 \)). Post-hoc comparisons within condition and between groups showed that older
adults had lower coherence for all conditions. Tibialis anterior alpha band coherence in the slow leg during pre-long was slightly decreased compared to no visuomotor feedback, then increased during early split visuomotor adaptation compared to pre-long, then decreased by late post-adaptation.

Beta-gamma-band tibialis anterior coherence in the fast leg during swing phase was different between conditions and between groups, but condition x group effect was not significant (Figure 4.14C; Condition: F(7, 273) = 7.65, p < 0.001, $\eta^2_p = 0.164$; Group: F(1, 39) = 31.82, p < 0.001, $\eta^2_p = 0.449$; Condition x group: F(7, 273) = 1.84, p = 0.080, $\eta^2_p = 0.045$). Beta-gamma-band tibialis anterior coherence in the fast leg during swing phase was lower in older adults compared to younger adults (95% CI = [-1.16, -0.55], $d = -0.881$). Post-hoc comparisons within condition and between groups showed that older adults had lower coherence during pre-long and early post-adaptation conditions compared to younger adults. Post-hoc between conditions comparisons showed that coherence generally decreased over time; coherence during no visual feedback was higher compared to early and late post-adaptation, and coherence during pre-slow was higher compared to late split-visuomotor adaptation and early and late post-adaptation. There was a slight increase in coherence during early split-visuomotor adaptation and it was significantly higher compared to late post-adaptation.

Beta-gamma-band tibialis anterior coherence in the slow leg during swing phase was different between conditions and between groups, and condition x group effect was significant (Figure 4.14D; Condition: F(5.04, 196.70) = 3.25, p = 0.008, $\eta^2_p = 0.077$; Group: F(1, 39) = 40.15, p < 0.001, $\eta^2_p = 0.507$; Condition x group: F(5.04, 196.70) = 2.65, p = 0.024, $\eta^2_p = 0.064$). Beta-gamma-band tibialis anterior coherence in the slow leg during swing phase was lower in older adults compared to younger adults (95% CI = [-1.26, -0.65], $d = -0.990$). Post-hoc comparisons within condition and between groups showed that older
adults had lower coherence for all conditions. Between condition post-hoc tests revealed that coherence during late post-adaptation was lower compared to pre-slow and early split-visuomotor adaptation. Post-hoc between conditions within group (to examine the interaction effect) showed that coherence during pre-slow and early split-visuomotor adaptation was higher compared to late post-adaptation in younger adults only.

Figure 4.14. Tibialis anterior coherence during swing during study 2. Natural logarithm of cumulative alpha (A, C) and beta-gamma (B, D) intermuscular coherence between the distal and proximal tibialis anterior in the fast (A-B) and slow leg (C-D) during study 2. Black = Young; Red = Old; X = group means; Error bars = standard error. Brackets indicate between-condition comparisons where p< 0.05. * indicate between-groups comparisons within condition where p < 0.05. All comparisons were corrected for multiple comparisons using the Bonferroni method.
Alpha-band plantarflexor coherence in the fast leg during stance phase was different between conditions and between groups, but condition x group effect was not significant (Figure 4.15A; Condition: F(4.74, 185.02) = 2.80, p = 0.020, \( \eta_p^2 = 0.067 \); Group: F(1, 39) = 5.46, p = 0.025, \( \eta_p^2 = 0.123 \); Condition x group: F(4.74, 185.02) = 1.07, p = 0.376, \( \eta_p^2 = 0.027 \)). Alpha-band plantarflexor coherence in the fast leg was lower in older adults compared to younger adults (95% CI = [-1.19, -0.09], d = -0.365). However, post-hoc comparisons within condition and between groups did not show any statistically significant group differences. Post-hoc between condition tests showed coherence during no visual feedback was higher compared to pre-long and early split-visuomotor adaptation.

Alpha-band plantarflexor coherence in the slow leg during stance phase was different between conditions, but not between groups, and condition x group effect was not significant (Figure 4.15B; Condition: F(4.48, 174.51) = 5.84, p < 0.001, \( \eta_p^2 = 0.130 \); Group: F(1, 39) = 1.30, p = 0.262, \( \eta_p^2 = 0.032 \); Condition x group: F(4.48, 174.51) = 0.74, p = 0.578, \( \eta_p^2 = 0.019 \)). Post-hoc between condition tests showed that coherence during pre-slow and pre-long was reduced compared to no visuomotor feedback, but there was an increase during split-visuomotor adaptation in which coherence during early and late split-visuomotor adaptation was significantly higher compared to pre-slow and pre-long. Alpha-band coherence remained higher during early post-adaptation and was significantly higher compared to pre-long.

Beta-gamma band plantarflexor coherence in the fast leg during stance phase was different between groups, but not between conditions, and condition x group effect was not significant (Figure 4.15C; Condition: F(3.93, 153.26) = 2.21, p = 0.072, \( \eta_p^2 = 0.054 \); Group: F(1, 39) = 11.69, p = 0.001, \( \eta_p^2 = 0.231 \); Condition x group: F(3.93, 153.26) = 1.43, p = 0.228, \( \eta_p^2 = 0.035 \)). Beta-gamma-band plantarflexor coherence in the fast leg was lower in
older adults compared to younger adults (95% CI = [-1.31, -0.34], d = -0.534). Post-hoc comparisons within condition and between groups showed that older adults had lower coherence during early post-adaptation. Although the main effect of condition was not statistically significant, paired comparisons showed significantly higher coherence during no visual feedback compared to early and late split-visuomotor adaptation.

Beta-gamma band plantarflexor coherence in the slow leg during stance phase was different between conditions and between groups, but condition x group effect was not significant (Figure 4.15D; Condition: F(4.47, 174.26) = 5.16, p < 0.001, η²_p = 0.117; Group: F(1, 39) = 8.96, p = 0.005, η²_p = 0.187; Condition x group: F(4.47, 174.26) = 0.91, p = 0.471, η²_p = 0.023). Beta-gamma-band plantarflexor coherence in the fast leg was lower in older adults compared to younger adults (95% CI = [-1.33 -0.26], d = -0.467). Post-hoc comparisons within condition and between groups showed significant group differences in the no visual feedback condition. Post-hoc between condition showed that coherence during split-visuomotor adaptation was elevated compared to no visual feedback, pre-long, and pre-fast conditions.
Figure 4.15. Plantarflexor coherence during stance during study 2. Natural logarithm of cumulative alpha (A, C) and beta-gamma (B, D) intermuscular coherence between the medial gastrocnemius and soleus in the fast (A-B) and slow leg (C-D) during study 2. Black = Young; Red = Old; X = group means; Error bars = standard error. Brackets indicate between-condition comparisons where p< 0.05. * indicate between-groups comparisons within condition where p < 0.05. All comparisons were corrected for multiple comparisons using the Bonferroni method.

Alpha-band gastrocnemius coherence in the fast leg during stance phase was different between groups, but not between conditions, and condition x group effect was not significant (Figure 4.16A; Condition: F(7, 273) = 1.17, p = 0.320, $\eta^2_p = 0.029$; Group: F(1, 37) = 6.99, p = 0.012, $\eta^2_p = 0.152$; Condition x group: F(7, 273) = 0.70, p = 0.675, $\eta^2_p =$
Alpha-band gastrocnemius coherence in the fast leg was lower in older adults compared to younger adults (95% CI = [-1.13, -0.15], d = -0.413). However, post-hoc comparisons within condition and between groups did not show any statistically significant differences.

In the slow leg, alpha-band gastrocnemius coherence during stance phase was different between conditions and between groups, but condition x group effect was not significant (Figure 4.16B; Condition: F(4.53, 176.65) = 3.51, p = 0.006, \(\eta^2_p = 0.082\); Group: F(1, 39) = 13.24, p < 0.001, \(\eta^2_p = 0.254\); Condition x group: F(4.53, 176.65) = 0.54, p = 0.725, \(\eta^2_p = 0.014\)). However, post-hoc comparisons within condition and between groups did not show any statistically significant differences. Post-hoc between condition comparisons showed that coherence during late split-visuomotor adaptation was elevated compared to pre-long and pre-fast.

Beta-gamma-band gastrocnemius coherence in the fast leg was lower in older adults compared to younger adults (95% CI = -1.42, -0.64], d = -0.828). Post-hoc comparisons within condition and between groups showed that younger adults had higher coherence during all conditions except for late post-adaptation.

Beta-gamma-band gastrocnemius coherence in the slow leg was different between conditions and between groups, but condition x group effect was not significant (Figure 4.16C; Condition: F(4.83, 188.40) = 1.87, p = 0.104, \(\eta^2_p = 0.046\); Group: F(1, 39) = 28.10, p < 0.001, \(\eta^2_p = 0.419\); Condition x group: F(4.83, 188.40) = 0.67, p = 0.641, \(\eta^2_p = 0.017\)). Beta-gamma-band gastrocnemius coherence in the fast leg was lower in older adults compared to younger adults (95% CI = [-1.13, -0.15], d = -0.413). However, post-hoc comparisons within condition and between groups did not show any statistically significant differences. Post-hoc between condition comparisons showed that coherence during late split-visuomotor adaptation was elevated compared to pre-long and pre-fast.
in older adults compared to younger adults (95% CI = [-1.66 -0.74], d = -0.823). Post-hoc comparisons within condition and between groups showed that younger adults have higher coherence compared to older adults during all conditions. Post-hoc between condition tests showed that coherence during late split-visuomotor adaptation was higher compared to pre-long and pre-fast.

Figure 4.16. Gastrocnemius coherence during stance during study 2. Natural logarithm of cumulative alpha (A, C) and beta-gamma (B, D) intermuscular coherence between the medial and lateral gastrocnemius in the fast (A-B) and slow leg (C-D) during study 2. Black = Young; Red = Old; X = group means; Error bars = standard error. Brackets indicate between-condition comparisons where p < 0.05. * indicate between-groups comparisons within condition where p < 0.05. All comparisons were corrected for multiple comparisons using the Bonferroni method.
Overall, all beta-gamma coherence had a significant main effect of groups. All alpha coherence values except for slow leg intermuscular plantarflexor coherence and slow leg intramuscular gastrocnemius coherence was significantly different between groups. All beta-gamma coherence except for fast leg beta-gamma intermuscular plantarflexor coherence and fast leg alpha and beta-gamma intramuscular gastrocnemius coherence showed a significant main effect of conditions.

4.3.3 Corticospinal drive to lower leg muscles is associated to kinematic adaptation during split-visuomotor adaptation

Stepwise multiple linear regression was used to predict magnitude and early changes in error and kinematic asymmetry. Multiple linear regression model parameters and coefficients are shown in Table 4.6. A significant regression model was found for overall change in step time asymmetry during adaptation only. Slow leg tibialis anterior beta-gamma coherence during early adaptation significantly predicted overall change in step time asymmetry adaptation (Figure 4.17; $\beta = 0.040$, $p < 0.001$).
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Table 4.6. Multiple linear regression models for study 2. RMSE = Root mean square error; SL = Step length; DS = Double support; TA = Tibialis anterior; PF = plantarflexors; N.S. = Not statistically significant (p > 0.05).
4.4 Discussion

This study examined the effects of age on the contribution of corticospinal drive during visuomotor walking adaptation. My three hypotheses were supported in this study: (1) Older adults adapted error asymmetry and step length asymmetry similarly compared to younger adults, but older adults altered step time asymmetry less compared to younger adults; (2) corticospinal drive was reduced in older adults compared to young adults during visuomotor walking adaptation; and (3) reduced corticospinal drive to the tibialis anterior in the slow leg during early split-visuomotor adaptation was associated to smaller overall changes in step time asymmetry.

Figure 4.17. Regression model for overall change in step time asymmetry during study 2. Black X= Young participants; Red X = Old participants.
4.4.1 Aging influences temporal but not spatial and error asymmetry adaptation during split-visuomotor adaptation

Older adults adapted error asymmetry and step length asymmetry with the split-visuomotor adaptation paradigm similarly compared to younger adults; this was also demonstrated with the exponential models. This finding was unexpected and in contrast to my hypothesis, as previous studies have shown slower adaptation in older adults compared to younger adults during a visually-guided walking (Nemanich and Earhart 2015). This contrast in outcome may be due to the difference in tasks and outcome measure. In other studies that examined age-related changes with visuomotor locomotor adaptation, participants walked with prism glasses for several trials along a walking path, and adaptation was measured based on trial-by-trial outcomes on walking trajectory errors (Huitema and others 2005). In my study, kinematic adaptation was calculated based on stride-by-stride changes, and not within trial performance and therefore requires more precision. The similar error asymmetry and step length asymmetry adaptation between age groups are in support with a recent study by Bakkum and colleagues (2021) who examined visuomotor locomotor adaptation with prism goggles as well but quantified single-stride foot-placement error to quantify adaptation between trials (Bakkum, Gunn and Marigold 2021). In this study, older adults demonstrated similar foot placement error during adaptation and post-adaptation compared to younger adults (Bakkum, Gunn and Marigold 2021). Together, this may suggest that age-related changes in kinematic adaptation during visually-guided walking is specific to task and outcome measure.

During post-adaptation, overall change and early change in error asymmetry and early change in step length asymmetry was less in older adults compared to younger adults. Although a very different task, a recent study with upper extremity visuomotor rotation task showed similar results; older adults adapted rotational degrees similarly compared to young
adults, but de-adaptation was exponential for young adults but linear for older adults (Bindra, Brower, North, Zhou and Joiner 2021). Age group differences in early changes in both error asymmetry and step length asymmetry was consistent after adjusting for physical function. The slower post-adaptation may suggest older adults have a harder time switching back and forth between learned gait patterns.

This study is the first study of my knowledge to examine temporal adaptation in addition to spatial adaptation during a walking visuomotor task (that is not a stepping reaction task). Controlling both the spacing and timing of foot placement is important to appropriately alter stability (For review: Bruijn and van Dieen 2018), which may play a role in the differences observed in this study. In this study, early change in step time asymmetry was less in older adults compared to younger adults, and the exponential group models in double support asymmetry suggest that the rate of adaptation is slower in older adults compared to younger adults. This suggests that for split-visuomotor adaptation, aging influences temporal adaptation compared to spatial adaptation. This finding is in support of my hypothesis that older adults will adapt less at a slower rate during the split-visuomotor locomotor adaptation task compared to younger adults. There was a clear age-difference in temporal adaptation but not for error asymmetry adaptation and step length asymmetry adaptation. This is consistent with previous studies with split-belt locomotor adaptation that have suggested that temporal and spatial adaptation are controlled independently (Gregory, Sup and Choi 2021; Malone, Bastian and Torres-Oviedo 2012; Stenum and Choi 2020).

Previously it has been demonstrated that people walk with a preferred step time asymmetry, but not step length asymmetry that coincide with their lowest metabolic cost (Stenum and Choi 2020). For the purposes of this study we did not examine metabolic cost, but older adults are known to have a higher metabolic cost during walking compared to younger adults during walking (Aboutorabi, Arazpour, Bahramizadeh, Hutchins and Fadayevatan
2016). Older adults may prioritize to keep symmetrical step times in an attempt to decrease metabolic cost during the split-visuomotor locomotor adaptation paradigm.

4.4.2 EMG-EMG coherence is modulated with split-visuomotor adaptation

In this study, EMG-EMG coherence was measured for four different baseline conditions, as differences in the common descending drive has not been observed between different visuomotor conditions. Alpha-band coherence in the intramuscular coherence in the tibialis anterior and intermuscular coherence in the plantarflexors was different between baseline conditions, but beta-gamma coherence was not different between baseline conditions. EMG-EMG coherence was analyzed separately for the limb to allow for appropriate comparisons during the adaptation phase, but for the baseline conditions as both legs are symmetrically moving, the comparisons between baseline conditions that are most convincing are the comparisons that were consistent between the fast and slow limbs. In the tibialis anterior and in the plantarflexors, baseline walking with no visuomotor feedback had higher alpha-band coherence compared to pre-long. Although there has been debate about the origin of the alpha-band EMG-EMG coherence, studies have suggested that it may have relations to the olivo-cerebellar system (Llinas and Volkind 1973; Llinas 2013). Corticomuscular coherence between electroencephalography and electromyography has suggested that oscillations in the alpha band may be related to processing of sensory feedback (Hansen and Nielsen 2004). Taken together, this suggests that sensory processing in the cerebellum may be altered in the pre-long condition compared to normal walking.

In the intermuscular coherence in the plantarflexors and intramuscular coherence in the gastrocnemius, beta-gamma coherence was decreased in the fast leg, while it was
increased in the slow leg during adaptation compared to baseline conditions. EMG-EMG coherence in the beta-gamma range (15-45 Hz) has been shown to be indicative of corticospinal drive (For review: Grosse, Cassidy and Brown 2002). The asymmetrical modulation is consistent with what was previously reported with changes in corticospinal drive during split-belt walking adaptation (Sato and Choi 2019). During early split-belt adaptation, beta and gamma-band EMG-EMG coherence was increased compared to baseline walking in the slow leg only (Sato and Choi 2019). The results in this study provide additional evidence that the corticospinal drive is asymmetrically modulated in locomotor interventions that asymmetrically alter gait mechanics.

In general, there were less modulation between conditions in intramuscular coherence in the gastrocnemius compared to intramuscular tibialis anterior coherence and intermuscular plantarflexor coherence. This may suggest that corticospinal drive to the tibialis anterior and synergistic control (indicated by the intermuscular coherence (Laine and Valero-Cuevas 2017)) in the plantarflexors are modulated in different visuomotor environments with the same treadmill speed, but individual gastrocnemius control stays relatively stable. However, this does not mean there were no modulation in intramuscular gastrocnemius coherence. Higher alpha and beta-gamma coherence was observed in the slow leg during late split-visuomotor adaptation compared to baseline pre-long and pre-fast. This is consistent with the intermuscular plantarflexor coherence in the slow leg that also demonstrated higher alpha and beta-gamma coherence during late split-visuomotor adaptation compared to pre-long in both alpha and beta-gamma, and compared to pre-fast in the beta-gamma band coherence. The specific modulation in the plantarflexor and gastrocnemius coherence in the stance phase suggests that by late adaptation, participants may be altering their corticospinal drive to accommodate the learned visuomotor error.
To my knowledge, this is the first study that examined changes in EMG-EMG coherence with visuomotor locomotor adaptation so the implications of the observed modulation is still unclear. However, the results may suggest an importance in muscle-specific corticospinal control during locomotor adaptation.

4.4.3 Aging influences corticospinal drive during split-visuomotor adaptation

Corticospinal drive quantified by beta-gamma-band coherence was lower in older adults compared to younger adults. This is in agreement with previous studies that examined EMG-EMG coherence in older and younger adults during walking and visually guided walking (Gennaro and de Bruin 2020; Spedden, Choi, Nielsen and Geertsen 2019). This may suggest that age-related physiological changes (e.g., fewer motor units (Deschenes 2011), lower myelinated fiber density (Sala and others 2012)), or reorganization of sensorimotor networks with increased age (Seidler and others 2010) may be altering the transmissions of neural oscillations to the lower limb muscles.

In relation to the compensation-related utilization of neural circuits (CRUNCH) hypothesis, which hypothesizes the an age related overcompensation of cortical structures to compensate for performance decline (Reuter-Lorenz and Cappell 2008), the cortical networks may be compensating for the decreased corticospinal drive. For example, it is well reported that older adults over-activate the prefrontal cortex when performing motor and cognitive tasks (Cabeza, Anderson, Locantore and McIntosh 2002); in a memory task prefrontal overactivation in older adults is inversely associated with medial temporal lobe activation (Gutchess and others 2005). During locomotion, the lower corticospinal drive in older adults may be compensated by other structures in the nervous system.
Interestingly, even though studies in the past have demonstrated increased corticospinal drive with visually-guided walking compared to normal walking (Jensen and others 2018; Spedden, Choi, Nielsen and Geertsen 2019), we did not see a significant between-conditions difference between the no visual feedback condition and the other visual feedback. However, it is important to note that in younger adults there was a slight increase in corticospinal drive during pre-slow compared to no visual feedback. In older adults this increase was close to non-existent, and in general, less modulation in corticospinal drive was observed in older adults. The decreased modulation is also supported in the interaction effect in the slow leg tibialis anterior, which demonstrated changes in corticospinal drive in younger, but not older adults. This may suggest an important difference that older adults have lower corticospinal drive in general and therefore, may have less reserve to modulate corticospinal drive during different locomotor tasks, even when needed.

4.4.4 Corticospinal drive in the tibialis anterior in the slow leg during swing is associated with step time asymmetry change during split-visuomotor walking

Slow leg tibialis anterior beta-gamma coherence significantly contributed to predict overall change in step time asymmetry during split-visuomotor locomotor adaptation. This may suggest that during this split-visuomotor task, corticospinal drive during swing phase is associated with step time adaptation. This is partially in support with our previous publication with split-belt locomotor adaptation that showed association between corticospinal drive and double support asymmetry but not step length asymmetry (Sato and Choi 2019). In this study, there were no associations between corticospinal drive and step length asymmetry changes nor error asymmetry changes during split-visuomotor
adaptation. The consistent outcomes of relationships between corticospinal drive with temporal but not spatial gait parameters during locomotor adaptation may suggest that corticospinal drive plays a specific role to control the timing of gait kinematics.

It is also important to note that neither the plantarflexors nor the gastrocnemius coherence was associated to kinematic adaptation with split-visuomotor locomotor adaptation. Previous studies in cats have demonstrated that cortical control, namely the posterior parietal cortex is important for planning the foot trajectory (Drew, Andujar, Lajoie and Yakovenko 2008; Drew and Marigold 2015). The lack of relationships between the corticospinal drive during the stance phase suggests that with this task, corticospinal drive is important for corrections during swing phase to make appropriate timing adjustments, rather than pre-planning the trajectory during stance phase.

4.5 Conclusions

With a split-visuomotor paradigm that required participants to learn a new visuomotor map, participants altered their gait pattern to minimize sensorimotor error. Older adults adapted error asymmetry and step length asymmetry similarly compared to younger adults, but adaptation of step time asymmetry was different between age groups. During this locomotor adaptation paradigm, corticospinal drive was less in older adults compared to younger adults, and the corticospinal drive to the tibialis anterior during the swing phase on the leg that took longer steps during adaptation was associated to the overall change in step time asymmetry adaptation. This work is the first to my knowledge to examine age-related changes in temporal and spatial kinematic adaptation during visuomotor locomotor adaptation, and find neural associations related to the interindividual variation in visuomotor gait adaptation. This work contributes to the growing literature in the age-related changes in
motor learning that suggests that the capacity of older adults to alter their locomotor pattern is intact, and the underlying neural strategies are likely to be different with increased age. Future studies should examine whether neural control is over-activated in other regions of the nervous system to compensate for the reduced corticospinal drive. Identifying specific age-related changes in neural control strategies during locomotor adaptation will be important to design appropriately targeted rehabilitation paradigms for older adults with gait dysfunctions.
Chapter 5

CONCLUSIONS AND FINAL REMARKS

5.1 Overview

The ability to adjust the timing and spacing of leg movement is important for functional walking. Studies in healthy adults have demonstrated that different parts of the human nervous system contribute to reactive (feedback) and predictive (feedforward) adjustments made during adaptation, and that cortical mechanisms may play a greater role during visuomotor adaptation compared to proprioceptive locomotor adaptation (Sato and Choi 2020). In this set of studies, I examined 21 younger and 20 older adults to determine the impact of aging on corticospinal contribution to split-belt treadmill and split-visuomotor locomotor adaptation. Study 1 showed that older adults adapted kinematic parameters differently, and corticospinal drive was lower in older adults compared to young individuals during split-belt walking adaptation. Corticospinal drive to the tibialis anterior in the slow leg during early adaptation was associated with overall changes in step length and double support asymmetry, and corticospinal drive to the to the tibialis anterior in the slow leg and to the plantarflexors in the fast leg were associated with early change in double support asymmetry during adaptation. Study 2 showed that the adaptation in spatial asymmetry was similar in older adults and younger adults, but adaptation of timing asymmetry was different in older adults compared to younger adults. Similar to the split-belt treadmill adaptation, corticospinal drive was less in older adults compared to younger adults. Corticospinal drive to the tibialis anterior during the swing phase on the leg with reduced visuomotor gain during split-visuomotor adaptation was associated to the overall change in step time asymmetry adaptation.

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5.2 Changes in kinematic adaptation with increased age

Across both studies, older adults were able to adapt and store new gait kinematics with both the split-belt and the split-visuomotor locomotor adaptation. Some of the kinematic adaptation was different in older adults, suggesting that aging may lead to prioritization of certain kinematics over others. With the split-belt adaptation, overall change in step length asymmetry was similar between the age groups, but early change in step length asymmetry was less in older adults compared to younger adults (i.e., younger adults adapted faster compared to older adults). In contrast, overall and early change in double support asymmetry were greater during adaptation in older adults compared to younger adults. This may be due to older adults allowing initial double support asymmetry to be perturbed, while attempting to keep initial step length asymmetry during adaptation comparable to younger adults. However, when controlled for physical activity function overall and early change in double support asymmetry during adaptation were not different between age-groups, which may suggest this difference in double support asymmetry adaptation is associated with age-related deficits in physical function.

With the split-visuomotor adaptation, overall change in step time asymmetry was less in older adults compared to younger adults. All other kinematic measures did not yield a statistically significant group difference, although the exponential models may suggest that the rate of double support asymmetry adaptation may be decreased in older adults. Slower early change in step time asymmetry during adaptation in older adults compared to younger adults was also observed after controlling for physical function. Together, the results from both studies suggest that older adults may prioritize spatial asymmetry in that it
is adapted in a similar fashion compared to younger adults. In contrast, there are temporal adaptation differences between young and older adults.

Across both studies, older adults were also able to store the newly adapted walking pattern. During post-adaptation in study 1, there were no significant age group differences in interlimb kinematic changes, and all effect sizes were small to moderate. However, in study 2, overall change and early change in error asymmetry and early change in step length asymmetry were reduced in older adults compared to younger adults. Older adults showed reduced aftereffects and de-adapted slower. Therefore, older adults may have more difficulty switching from the learned adaptation gait pattern to the post-adaptation symmetrical gait pattern with the visuomotor paradigm compared to the split-belt paradigm.

For study 1, I hypothesized that "older adults will adapt interlimb parameters the same amount as young adults, but early change in interlimb parameters during adaptation will be reduced in older adults." This hypothesis was supported by step length asymmetry adaptation. However, I hypothesized that for study 2, there will be greater influence of age on adaptation in gait kinematics ("Hypothesis 2.1 Older adults will show reduced overall change, and early change in kinematic asymmetry during adaptation compared to younger adults"), which was not supported. Contrary to my hypothesis and previous studies (Huitema and others 2005; Nemanich and Earhart 2015), there was an age group difference in adaptation of timing asymmetry, but not for step length and target error. The different kinematic asymmetry that showed age-related differences in locomotor adaptation demonstrates that the effect of aging on kinematic adaptation is not only specific to gait parameter, but also specific to the gait adaptation task.
5.3 Changes in corticospinal drive with increased age

Corticospinal drive quantified by beta-gamma coherence was lower in older adults compared to younger adults in both studies 1 and 2. In general, the effect sizes for the between group comparisons were similar between studies with moderate to large effect sizes.

In study 1, condition x group interaction effect on beta-gamma coherence was statistically insignificant for all muscle groups. However, it should be highlighted that there was an increase in beta-gamma coherence during early split-belt adaptation compared to pre-slow in the young group, which is consistent with my previous publication (Sato and Choi 2019). This increase was not observed in older adults, and older adults modulated corticospinal drive to the tibialis anterior less compared to younger adults. The lower modulation in corticospinal drive in older adults was also observed in the intramuscular beta-gamma coherence in the gastrocnemius. However, this was not the case for the intermuscular coherence in the plantarflexors, in which older adults demonstrated an increase in corticospinal drive to the plantarflexors during early split-belt compared to baseline pre-slow while the corticospinal drive to the plantarflexors in young adults was relatively stable. This modulation in beta-gamma coherence may be related to changes in corticospinal excitability that results from a change in ankle dynamics in response to propioceptive input.

In study 2, there was an increase in corticospinal drive during early split-visuomotor adaptation in all three beta-gamma coherence measures. This increase is demonstrated especially in the younger adults, although condition x group interaction effect was statistically significant for the tibialis anterior coherence in the slow leg only. Post-hoc tests on the interaction effect showed that between-condition differences were statistically
significant for the young adults, but not in older adults, suggesting that older adults
modulate intermuscular coherence less compared to younger adults.

For both studies, I hypothesized that “corticospinal drive will be less in older adults
compared to young adults during locomotor adaptation.” This hypothesis was supported by
the significant group differences in the beta-gamma coherence in the leg musculature.
However, there may be age-related differences in modulation of inter- and intramuscular
beta-gamma coherence, which may suggest that the neural strategies to accommodate
changes in the environment is altered with increased age.

5.4 Relationship between kinematic adaptation and corticospinal drive

Associations between beta-gamma coherence and changes in kinematics during
adaptation were found in both studies, suggesting that corticospinal drive plays a role during
locomotor adaptation. For study 1, I hypothesized that “reduced corticospinal drive will be
associated with reduced early changes in interlimb adaptation during split-belt walking.” I
found that higher beta-gamma coherence was related to larger overall change in step length
asymmetry adaptation and smaller (i.e., less negative) overall change in double support
asymmetry adaptation. This is consistent with my previous study which showed that smaller
initial perturbations (average of first 5 strides, which may be closely related to overall
change assuming plateau is similar) in double support asymmetry were related to higher
beta- and gamma slow leg tibialis coherence during split-belt adaptation (Sato and Choi
2019). However, I did not expect the overall change in step length asymmetry during split-
belt adaptation to be related to beta-gamma coherence. In study 1, larger (i.e., more
negative) early changes in double support asymmetry were associated with larger
intermuscular beta-gamma coherence in the fast leg plantarflexor and smaller intramuscular
beta-gamma coherence in the slow leg tibialis anterior. However, there was no relationship between beta-gamma EMG-EMG coherence and early changes in step length asymmetry. This suggests the specific role of the corticospinal drive and partially supports my hypothesis.

For study 2, I hypothesized that “reduced corticospinal drive will be associated with overall change and early change in kinematic adaptation.” This hypothesis was in part supported as I found a relationship between larger overall change in step time asymmetry adaptation and beta-gamma coherence in the slow leg tibialis anterior. However, I had expected clear relationships between corticospinal drive and visuomotor walking adaptation, as previous studies have demonstrated the importance of cortical activity on visually-guided walking (Chen and others 2017; Clark, Rose, Ring and Porges 2014; Drew, Andujar, Lajoie and Yakovenko 2008; Drew and Marigold 2015). This highlights the potential differences in neural mechanisms between visually-guided walking and visuomotor walking adaptation, and the specific role of the corticospinal drive during walking adaptation.

5.5 Limitations

As with most aging studies in humans, there is a challenge in interpretation in the aging outcomes as there are many covariates that can influence aging in movement adaptation (both kinematics and corticospinal drive). To facilitate the interpretation and for as a reference for future studies, I have included functional assessments that were collected that characterize the study sample. In addition, I have tried to recruit an older sample for my older adult group (i.e., not middle age older adults). In my literature review, it can be observed that there are fewer studies with older adults with group age average > 70 years old. This is important because age-related gait dysfunctions are more prevalent with older
age (Mahlknecht and others 2013). This prompts more future studies to include participants who are older in their aging studies.

In the two studies I performed for my dissertation project, I reported kinematic asymmetry differences between age groups with and without controlling for physical function (i.e., SPPB-A score). I controlled for physical function as my dissertation project was aimed to examine effects of “healthy” aging in which you would not expect a decline of physical function. It is important to note though, a decline in physical function with an increase in age is common and is probably more representative of the typical aging population (Milanovic and others 2013; Riebe and others 2009). However, it is known that the functional decline with aging can be mitigated by participating in moderate intensity exercises regularly (Bauman, Merom, Bull, Buchner and Fiatarone Singh 2016; Brach and others 2004; Ribeiro and Oliveira 2007). The age-group differences in kinematic asymmetry after controlling for physical function (specifically double support asymmetry adaptation in study 1) highlights the variability as a result of different covariates that can influence aging. Main conclusions of this dissertation project are based on the analysis with physical function included as a covariate, but readers are encouraged to critically examine and compare the functional assessments included with the aging population of comparison (e.g., to interpret, or with other studies).

An additional factor that makes a challenge to interpret the kinematics outcomes and relationship is the lack of a universal method to quantify rate or early changes that occur during movement adaptation. Other studies have quantified the rate by exponential models, or the number of strides to achieve a certain threshold, usually defined by a plateau ± individual variability (Cherry-Allen, Statton, Celnik and Bastian 2018; Statton, Toliver and Bastian 2016). However, in studies with different sample populations (such as aging, or other neurological diseases) participants may have different variability in baseline walking.
(Chee and others 2021; Swanson and Fling 2021), which will influence the calculated rate of adaptation.

In this study, not all kinematic parameters fit the exponential model, so I used a difference measure ($\Delta_{\text{Initial phases}}$) to quantify the early changes, where most of the adaptation and de-adaptation during post-adaptation occurs at (as observed in the stride-by-stride figures). Although this measure is not equivalent to rate, it is a similar metric that aims to quantify the gradual adjustments in movement that occur during adaptation and post-adaptation. However, the double support asymmetry adaptation during study 2 capture the limitation of the early change metric to attempt to quantify rate; with the split-visuomotor adaptation, age group difference in early change in double support asymmetry was not statistically significant, but the exponential model showed that the older adults adapted double support asymmetry two-times slower compared to younger adults. To thoroughly explore the kinematic changes that occur during adaptation, I added in the group exponential models to this dissertation.

Finally, a challenge of coherence analysis used in this project is that coherence may be caused by cross-talk between motor units. To minimize the risk of cross-talk, the proximal and distal EMG electrodes were placed at least 10 cm apart from each other. Furthermore, I visually examined coherence and cumulant density plots for each participant to verify that there are no signs of cross-talk (large and narrow central peak in cumulant density and high coherence > 0.5 for more than most frequencies; Hansen and others 2005).
5.6 Future directions

This dissertation project demonstrates the task-specific role of corticospinal drive during locomotor adaptation. In the multiple linear regression models in both Studies 1 and 2, corticospinal drive was associated to specific kinematic adaptation parameters. However, in neither studies age group was not a significant contributor to the models, which may suggest that the association between corticospinal drive and kinematic adaptation do not change with aging. It is important to note though, that this dissertation project examined a small part of the nervous system. Although there is an increase in literature on the age-related changes in locomotion and its neural control, there is still a limited number of studies that study the age-related changes in the neural control during locomotor adaptation. In this dissertation, there were clear age-related differences in corticospinal drive, but older adults are able to alter their gait kinematics during locomotor adaptation. It is likely that other neural mechanisms underlie locomotor adaptation to compensate for the lower corticospinal drive, however this is still unclear with the results of this dissertation project.

One potential hypothesis of a neural mechanism that may be compensating for the corticospinal drive is the activity from the prefrontal cortex. Several studies have reported over-activation in the prefrontal cortex using functional near-infrared spectroscopy (fNIRS) in older adults during walking (Chen and others 2017; Hawkins and others 2018; Mirelman and others 2017). This is in agreement with cognitive resource theories such as the compensation-related utilization of neural circuits (CRUNCH) hypothesis, which hypothesizes that an age-related overcompensation of cortical structures compensate for performance decline (Reuter-Lorenz and Cappell 2008). However, to my knowledge, it is unknown whether oxygenated hemoglobin levels in the prefrontal cortex are altered with increased age during walking adaptation. As blocked experimental designs are appropriate for gait studies that require continuous, short, reciprocal movements (Menant and others
2020), a possible future study is to examine prefrontal activity using fNIRS with short repeated adaptation and de-adaptation on the walking adaptation tasks.

To fully understand the clinical implications of the outcomes of this dissertation project, it is important to replicate the findings with repeated exposure to the interventions. Savings, which is the faster rate of adaptation during repeated exposure, is a hallmark of sensorimotor adaptation. In everyday walking, it is important to be able to switch back and forth between learned locomotor patterns. Sombric and colleagues (2020) have demonstrated that re-learning of gait patterns is not affected by aging, but while younger adults demonstrated faster de-adaptation with repeated exposures, this was not observed in older adults. With locomotor adaptation with prism glasses, Bakkum and colleagues (2021) demonstrated that older adults demonstrate less savings in foot placement error with repeated exposure to the task. These outcomes suggest that older adults may be more resistant to switching movement patterns back and forth based on immediate environmental feedback. However, the neural contribution of the changes with re-exposure is unclear. A potential future study is to examine the neural contribution that play a role in the flexibility of motor memory that may be altered with increased age.

5.7 Concluding remarks

In conclusion, this dissertation project provides evidence for changes in kinematic strategies and corticospinal control during locomotor adaptation that occur with increased age, and the neural underpinnings that may contribute to the inter-individual variability in kinematic adaptation. These findings provide insight into the importance of corticospinal drive during locomotor adaptation and may have important implications for future development of novel interventions that aim to alter corticospinal drive to promote effective
recovery in gait in people with neurological injuries. Further research is warranted to
determine the effects of aging on the long-term changes in corticospinal drive with repeated
exposure to the same or similar locomotor interventions.
APPENDICES

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Appendix 1. Physical Activity Readiness Questionnaire and You.

**PAR-Q & YOU**

*(A Questionnaire for People Aged 15 to 69)*

Regular physical activity is fun and healthy, and increasingly more people are starting to become more active every day. Being more active is very safe for most people. However, some people should check with their doctor before they start becoming much more physically active.

If you are planning to become much more physically active than you are now, start by answering the seven questions in the box below. If you are between the ages of 15 and 69, the PAR-Q will tell you if you should check with your doctor before you start. If you are over 69 years of age, and you are not used to being very active, check with your doctor.

Common sense is your best guide when you answer these questions. Please read the questions carefully and answer each one honestly: check YES or NO.

**YES**
- Has your doctor ever said that you have a heart condition and that you should only do physical activity recommended by a doctor?
- Do you feel pain in your chest when you do physical activity?
- In the past month, have you had chest pain when you were not doing physical activity?
- Do you lose your balance because of dizziness or do you ever lose consciousness?
- Do you have a bone or joint problem (for example, back, knee or hip) that could be made worse by a change in your physical activity?
- Is your doctor currently prescribing drugs (for example, water pills) for your blood pressure or heart condition?
- Do you know of any other reason why you should not do physical activity?

**NO**

If you answered one or more questions, talk with your doctor by phone or in person before you start becoming much more physically active or before you have a fitness appraisal. Tell your doctor about the PAR-Q and which questions you answered YES.
- You may be able to do any activity you want — as long as you start slowly and build up gradually. Or, you may need to restrict your activities to those which are safe for you. Talk with your doctor about the kinds of activities you wish to participate in and follow his/her advice.
- Find out which community programs are safe and helpful for you.

**NO to all questions**

If you answered NO honestly to all PAR-Q questions, you can be reasonably sure that you can:
- Start becoming much more physically active — begin slowly and build up gradually. This is the safest and easiest way to go.
- Take part in a fitness appraisal — this is an excellent way to determine your fitness so that you can plan the best way for you to live actively. It is also highly recommended that you have your blood pressure evaluated. If your reading is over 144/94, talk with your doctor before you start becoming much more physically active.

**DELAY BECOMING MUCH MORE ACTIVE:**
- If you are not feeling well because of a temporary illness such as a cold or a fever — wait until you feel better.
- If you are or may be pregnant — talk to your doctor before you start becoming more active.

**PLEASE NOTE:** If your health changes so that you then answer YES to any of the above questions, tell your fitness or health professional. Ask whether you should change your physical activity plan.

**INFORMED USE OF THE PAR-Q:** The Canadian Society for Exercise Physiology, Health Canada, and the agents assume no liability for persons who undertake physical activity and if in doubt after completing this questionnaire, consult your doctor prior to physical activity.

**No changes permitted. You are encouraged to photocopy the PAR-Q but only if you use the entire form.**

**NOTE:** If the PAR-Q is being given to a person before he or she participates in a physical activity program or fitness appraisal, this section may be used for legal or administrative purposes.

"I have read, understood and completed this questionnaire. Any questions I had were answered to my full satisfaction."

**SIGNATURE**

**DATE**

**SIGNATURE OF PARENT or GUARDIAN (for participants under the age of majority)**

**WITNESS**

**Note:** This physical activity clearance is valid for a maximum of 12 months from the date it is completed and becomes invalid if your condition changes so that you would answer YES to any of the seven questions.
Appendix 2. Advanced Short Physical Performance Battery Test.

(Please see page 1)

SPPB-A Scoring chart

*Now let’s begin the evaluation. I would now like you to try to move your body in different movements. I will first describe and show each movement to you. Then I’d like you to try to do it. If you cannot do a particular movement, or if you feel it would be unsafe to try to do it, tell me and we’ll move on to the next one. Let me emphasize that I do not want you to try to do any exercise that you feel might be unsafe.*

*Do you have any questions before we begin?*

6 m walk, casual speed (s)

1) 4m split ____________

2) 4m split ____________

6 m BALANCE walk, casual speed (s)

1) 4m split ____________

# times stepped outside: _____

2) 4m split ____________

# times stepped outside: _____

Timed 10 x chair rise (s)

1) 5x split ____________

Static balance 30s:

Side-by-side: _____  Semi tandem: _____  Tandem: _____  One-leg: _____

Fwd feet:  R  L  Fwd feet:  R  L  Fwd feet:  R  L

*If participant did not attempt test or failed, indicate why:*

1 = Tried but unable
2 = Participant could not walk unassisted
3 = Not attempted, you felt unsafe
4 = Not attempted, participant felt unsafe
5 = Participant unable to understand instructions
6 = Other (Specify)
7 = Participant refused
Participant ID________

Scoring:

**SPPB-A**

1. Total advanced balance test score (0-1)  
   Divisor = 90s.  
  \[ \text{(Semi-tandem + tandem + One-leg)/90} \]
   ____

2. Normalized gait speed (6 m time)  
   Divisor = 2 m/s.  
   \[ (6 / \text{time})/2 \]
   ____

3. Normalized balance gait speed (6 m time)  
   \[ (6 / \text{time})/2 \]
   ____

4. Repeated chair stand ratio score  
   Divisor = 1 stand/s  
   10 stands/ time to complete  
   ____

5. Total Advanced SPPB Score  
   ____

**SPPB**

Balance score (Held for 10 s = 1; Not held for 10s or not attempted = 0)  
1. Side by side  
   ____/1

2. Semi-tandem  
   ____/1

Balance score (Held for 10 s = 2; Held for 3-9.99 s = 1; Not held for 10s or not attempted = 0)  
3. Tandem  
   ____/2

**4m Gait speed score** (> 8.7s = 1; 6.21-8.70 = 2; 4.82-6.20 = 3; <4.82 = 4)  
4. Take shorter time  
   ____/4

Repeated chair stand (>60s = 0; 16.70-60s = 1; 13.70-16.69 = 2; 11.20 – 13.69 = 3; < 11.19 = 4)  
5. Five Chair stands (split-time)  
   ____/4

**Total score**  
   ____/12
Appendix 3. Telephone Interview for Cognitive Status.

Telephone Interview for Cognitive Status

Name:
Date:
DOB:
Age:
Education level (Number of years or degree):
Examiner:

Instructions: I am going to ask you some questions to test your memory. Some of these are likely to be easy for you, but some may be difficult. Please bear with me and try to answer all the questions as best as you can. If you can’t answer a question, don’t worry. Just try your best. Are you ready?

For each of the TICS items, except item 5 and 8, single repetitions are permitted.

1. Please tell me your full name.

Score: 1 pt for correct first name, 1 pt for correct last name. /2

2. What is today’s date?
   Probe for month, date, year, day of week, and season.

Score: 1 pt each for correct month, date, day of week, and season. /5

3. Where are you right now?
   Probe for house number, street, city, state, and zipcode.

Score: 1 pt each for correct house number, street, city, state, zipcode. /5

4. Please count backwards from 20-1.
   20 19 18 17 16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1
   Score: 2 pts if completely correct on first trial. 1 pt is completely correct on second trial. /2

5. I am going to read you a list of 10 words. Please listen carefully and try to remember them. When I am done, tell me as many of the words are you can, in any order. Ready? The words are:
   Cabin, pipe, elephant, chest, silk, theater, watch, whip, pillow, giant.
   Now tell me all words you can remember.
   Score: 1 pt for each correctly recalled word. 0 pts for incorrect responses, repetitions, or intrusions. /10

6. A. I would like you to take the number 100 and subtract 7. 93
   B. Now keep subtracting 7 from the answer until I tell you to stop.
   No further prompts except to "keep going." Stop the examiner after 5 serial subtractions.
   Do not inform examinee of incorrect responses, but allow subtractions to be made from last response.
   86 79 72 65
   Score: 1 pt each for correct subtraction. /5
7. A. What do people use to cut paper? “scissors” or “shears”

B. How many things are in a dozen? “12”

C. What do you call the prickly green plant that lives in a desert? “cactus”

D. What animal does wool come from? “sheep” or “lamb”

Score: 1 pt each for correct answer. /4

8. A. Please repeat this after me: “No ifs, ands, or buts.”
B. Now, please repeat this after me: “Methodist Episcopal”
Score: 1 pt each for correct repetition. /2

9. A. Who is the President of the United States right now?

B. Who is the Vice-President?

Score: 1 pt each for correct full name. /2

10. With your finger, tap 5 times on the part of the phone you speak into.
Score: 2 pts if taps are clearly heard. 1 pt if either more than or fewer than 5 taps are heard.
0 pts if no taps are heard. /2

11. I am going to say a word and I want you to give me its opposite. For example, if I said “hot”, you would say “cold.”
A. What is the opposite of “west”? “east”

B. What is the opposite of “generous”? “cheap” “stingy” “tight” “selfish” “greedy” “mean” “meager” or other correct antonym.

Score: 1 pt for correct response. /2

Total: /41

33-41 Nonimpaired
26-31 Ambiguous
21-25 Mildly impaired
<21 Moderately to severely impaired
Appendix 4. Fatigue Severity Scale.

FATIGUE SEVERITY SCALE (FSS)

Date ___________________________ Name ___________________________

Please circle the number between 1 and 7 which you feel best fits the following statements. This refers to your usual way of life within the last week. 1 indicates “strongly disagree” and 7 indicates “strongly agree.”

<table>
<thead>
<tr>
<th>Read and circle a number.</th>
<th>Strongly Disagree</th>
<th></th>
<th>Strongly Agree</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. My motivation is lower when I am fatigued.</td>
<td>1 2 3 4 5 6 7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Exercise brings on my fatigue.</td>
<td>1 2 3 4 5 6 7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. I am easily fatigued.</td>
<td>1 2 3 4 5 6 7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Fatigue interferes with my physical functioning.</td>
<td>1 2 3 4 5 6 7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Fatigue causes frequent problems for me.</td>
<td>1 2 3 4 5 6 7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. My fatigue prevents sustained physical functioning.</td>
<td>1 2 3 4 5 6 7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. Fatigue interferes with carrying out certain duties and responsibilities.</td>
<td>1 2 3 4 5 6 7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8. Fatigue is among my most disabling symptoms.</td>
<td>1 2 3 4 5 6 7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9. Fatigue interferes with my work, family, or social life.</td>
<td>1 2 3 4 5 6 7</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

VISUAL ANALOGUE FATIGUE SCALE (VAFS)

Please mark an “X” on the number line which describes your global fatigue with 0 being worst and 10 being normal.

<table>
<thead>
<tr>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
</tr>
</thead>
</table>
Appendix 5. Godin Leisure Time Questionnaire.

Godin Leisure-Time Exercise Questionnaire

1. During a typical 7-Day period (a week), how many times on the average do you do the following kinds of exercise for more than 15 minutes during your free time (write on each line the appropriate number).

   | Times Per |
   | Week      |

   a) STRENUOUS EXERCISE
   (HEART BEATS RAPIDLY)
   (e.g., running, jogging, hockey, football, soccer,
    squash, basketball, cross country skiing, judo,
    roller skating, vigorous swimming,
    vigorous long distance bicycling)

   MODERATE EXERCISE
   (NOT EXHAUSTING)
   (e.g., fast walking, baseball, tennis, easy bicycling,
    volleyball, badminton, easy swimming, alpine skiing,
    popular and folk dancing)

   b) MILD EXERCISE
   (MINIMAL EFFORT)
   (e.g., yoga, archery, fishing from river bank, bowling,
    horseshoes, golf, snow-mobiling, easy walking)

2. During a typical 7-Day period (a week), in your leisure time, how often do you engage in any regular activity long enough to work up a sweat (heart beats rapidly)?

   | OFTEN | SOMETIMES | NEVER/RARELY |
   |       |          |              |
   1. [] | 2. []    | 3. []

Waterloo Footedness Questionnaire - Revised

Name:

Date:

Instructions: Answer each of the following questions as best as you can. If you ALWAYS use one foot to perform the described activity, circle **Ra for right always** or **La for left always**. If you USUALLY use one foot, circle **Ru for right usually** or **Lu for left usually**. If you use both feet equally often, circle **Eq**. Please do not simply circle one answer for all questions, but imagine yourself performing each activity in turn, and then mark the appropriate answer. If necessary, stop and pantomime the activity.

1. Which foot would you use to kick a stationary ball at a target straight in front of you?
   - La
   - Lu
   - Eq
   - Ru
   - Ra

2. If you had to stand on one foot, which foot would it be?
   - La
   - Lu
   - Eq
   - Ru
   - Ra

3. Which foot would you use to smooth sand at the beach?
   - La
   - Lu
   - Eq
   - Ru
   - Ra

4. If you had to step up onto a chair, which foot would you place on the chair first?
   - La
   - Lu
   - Eq
   - Ru
   - Ra

5. Which foot would you use to stomp on a fast-moving bug?
   - La
   - Lu
   - Eq
   - Ru
   - Ra

6. If you were to balance on one foot on a railway track, which foot would you use?
   - La
   - Lu
   - Eq
   - Ru
   - Ra

7. If you wanted to pick up a marble with your toes, which foot would you use?
   - La
   - Lu
   - Eq
   - Ru
   - Ra

8. If you had to hop on one foot, which foot would you use?
   - La
   - Lu
   - Eq
   - Ru
   - Ra

9. Which foot would you use to help push a shovel into the ground?
   - La
   - Lu
   - Eq
   - Ru
   - Ra

10. During relaxed standing, people initially put most of their weight on one foot, leaving the other leg slightly bent. Which foot do you put most of your weight on first?
    - La
    - Lu
    - Eq
    - Ru
    - Ra

11. Is there any reason (i.e. injury) why you have changed your foot preference for any of the above activities?
    - YES
    - NO

12. Have you ever been given special training or encouragement to use a particular foot for certain activities?
    - YES
    - NO

13. If you have answered YES for either question 11 or 12, please explain:
REFERENCES


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