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Motor control during a weight-bearing visuomotor task: single- and dual-task motor performance of young and older healthy humans

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MOTOR CONTROL DURING A WEIGHT-BEARING VISUOMOTOR TASK: SINGLE- AND DUAL-TASK MOTOR PERFORMANCE OF YOUNG AND OLDER HEALTHY HUMANS

by

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of the requirements for the Doctor of Philosophy
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CERTIFICATE OF APPROVAL

PH.D. THESIS

This is to certify that the Ph.D. thesis of

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ABSTRACT

A broad understanding of motor control has been achieved through research performed on upper extremity reaching, walking on level ground, and static balance. Though invaluable insights have been achieved under these testing paradigms, inherent limitations result in less being known regarding functional movement in weight-bearing. Gait studies require large numbers of consecutive steps to achieve high reliability, static balance is limited to the goal of no movement, and upper extremity reaching lacks insights into feedback from the vestibular system. Here we describe (and provide a supplemental video of) a system for testing and training the performance of a weight-bearing, visuomotor task in the form of a mini-squat according to a sinusoidal trace on a screen.

In this work, we determined that by altering both task movement rate and resistance at the knee, a hierarchy of difficulty was achieved at all ages. As age increases, there is a velocity-error tradeoff; speed of movement is attempted to be maintained while error is sacrificed. When introducing an unexpected force perturbation (rapid release of the resistance of the squat for less than a second), older adults who are least able to match the frequency of the task experience the greatest error and velocity rates during the perturbation. This exposes a possible deficit in the feedback control system of even healthy older adults, where future studies may determine if early intervention to prevent such changes may prevent future injury and disability.

When older and younger adults learned to perform the visuomotor task while performing a simultaneous cognitive task, learning was slowed as

complexity of the cognitive task increased. In older adults, a difficult cognitive task inhibited acquisition of the squatting task with no apparent improvement in trial error nor coherence. Upon retesting of the motor task, there was no difference between dual-task and single-task trained ability to consolidate the motor task in both age groups. Comparing each person's dual-task performance to their single-task performance (dual-task cost) revealed that those who trained under a dual-task condition had a smaller dual-task cost, indicating decreased cognitive attention to perform the motor task. This may indicate that dual-task training leads to freeing cognitive resources from attending to a functional movement so that they may attend to other tasks such as what may be happening in the environment. Finally, executive function as measured by the Flanker Test, explained 80% of the variability of final day visuomotor error, being a possible prognostic factor for dual-task interventions. Future directions will determine if increased automaticity of a mini-squat will lead to overall improved functional mobility and reduced lower extremity injuries when functioning in a busy community.

PUBLIC ABSTRACT

Most of our knowledge regarding controlling movement is based on upper extremity reaching, walking on level ground, and static balance tasks. Though invaluable insights were gained, inherent limitations result in less knowledge regarding movement in weight-bearing. Here, we describe a novel system for assessing the performance of a mini-squat according to a line on a screen (supplemental video provided). We determined that altering both resistance and rate of movement of the mini-squat results in a hierarchy of difficulty for young, middle, and older adults. As age increases, there is a velocity-error tradeoff. Older adults attempt to maintain the correct movement speed while sacrificing error. When there is an unexpected event during a movement (rapid release of the resistance of the squat for less than a second), older, poor performers experience the greatest error, exposing a potential for injury to older adults. When learning the mini-squat while simultaneously performing a cognitive task, learning slowed with increasing cognitive task difficulty. A difficult cognitive task even inhibited acquisition of the squatting task in older adults. Upon retesting of the motor task days later, those that learned while dual-tasking experienced greater ability to make the motor task automatic, measured by a smaller difference between their single- and dual-task motor performances. This may indicate that dual-task training leads to freeing cognitive resources attributed to movement to allow focus on the environment. Future directions will determine if improved dual-task performance of a mini-squat will lead to reduced lower extremity injuries when functioning in a busy community.

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CHAPTER 1: INTRODUCTION

Lower extremity Injuries in older adults generate greater than $18 billion in annual United States healthcare costs. (Burns, Stevens, & Lee, 2016; Stevens, Corso, Finkelstein, & Miller, 2006). Injuries in the elderly are associated with altered control of movement, decreased postural stability, and impaired automaticity of gait especially when there is a distraction drawing attention away from the motor task. Being able to consistently and accurately control movement while performing a simultaneous cognitive task (e.g. walking and talking) is essential for performing everyday tasks. Factors contributing to impairment in functional community mobility (i.e. navigating through the community without injury) are not completely understood.

The human body relies on many sensory inputs (feedback) to determine accuracy of movement including vision, vestibular, proprioception, and somatosensory information. When an error in movement is detected, or when an unexpected change in the environment occurs (e.g. crack in the sidewalk, uneven ground), the brain must process sensory information coming in to appropriately alter the information going out (control of joint motion). Injury occurs when the system controlling movement is “fooled”, or unable to maintain proper control of the trajectory of movement when something unexpected happens during a planned movement such as incorrectly predicting the height of a curb when stepping down to street level. Previous research studies provide rich resources regarding movement control of the upper extremity. Less, however, is certain regarding functional weight-bearing movements of the lower extremity where all senses are intact (vestibular, visual, and somatosensation).

In this body of research, we aim to determine the effects of age on the control of a weight-bearing lower extremity functional task in the form of a partial mini-squat according to a line on a screen. We aim to determine differences in movement control between healthy young and older individuals when all sensory information is intact. We then aim to determine movement control differences in young and older individuals when a cognitive task (dual-task) is simultaneously performed to simulate real-world functional movement of "walking and talking". It is our goal to first identify differences in movement control during the aging process, whereby deficits can be targeted in order to develop effective intervention strategies to prevent injury in the future.

BACKGROUND

Feedforward and Feedback Control

Motor control is the precise execution of movement and consists of both feedforward and feedback portions. Feedforward is the pre-planned execution of a movement without considering results (error), while feedback is the utilization of sensory information (vision, vestibular, somatosensation, and proprioception) to determine errors in pre-planned movement in order to make corrections to ensure accuracy. Feedback is necessary to correct for possible incorrect predictions in required movement (trajectory, speed, etc), or unexpected changes in the environment in which the person is moving. Feedforward control is not based on error but instead on pre-planned knowledge of parameters needed to create movement (load, distance, speed, etc). Theories of feedforward control suggest that there is an internal model that predicts the state of and the intent of movement, passing information to an inverse dynamics model of the musculoskeletal system, thereby ensuring accuracy of the predicted movement (Kawato, 1999; Kawato, Furukawa, & Suzuki, 1987). Feedforward movement can be performed very rapidly as it is not necessary to wait for long delays required of sensory feedback information. This strategy of movement instead uses a motor set, or plan, in order to produce motion.

Feedback control was originally modeled as a servo-control system. A servo-control system relies on error-detection to guide movement. Long conduction delays of sensory feedback, however, deemed this method incapable of the precise control of motion that the human body achieves (Schmidt 2000). Currently, it is believed that human motion involves a combination of both feedforward and feedback mechanisms. The Optimal Feedback Control theory proposed by Todorov and Jordan (2002) proposed that instead of servo-control, there is use of an optimal state estimation. This theory integrates asserts that there is an efference copy of the intended movement that is compared to delayed sensory feedback. Within this theory, it is believed that the state estimator is also able to make use of altered gains of movement based on information relative to movement goals and context (Kirsch, Kearney, & MacNeil, 1993). Plainly stated, the brain compares the actual sensory information coming in, to the predicted sensory state of the body as expected by the planned movement. Using this method, the brain is then able to more rapidly estimate the state of the system, and therefore more rapidly send a message to adjust movement (Todorov & Jordan, 2002).

Perturbations used to assess feedback control

A particularly useful method to assess feedback control is the introduction of an unexpected event (perturbation) during a planned movement. Unexpected events usually involve a short period of altering the sensory system including: eliminating vision during part or all of movement, altering a reaching task goal mid-movement, movement through a force-field, or delivery of a force perturbation. Feedback responses during an unexpected perturbation were first identified by noting the effects of a sudden stretch in a muscle (Sherrington, 1910). Sherrington described the first of two epochs of responses that occur even before volitional reaction time. The first epoch is the short latency response, occurring less than 50 ms after the perturbing event. The short latency response is a relatively well described monosynaptic circuit directly to and from the spinal cord (Burke, Gillies, & Lance, 1970). The second epoch, the long latency response, was first discovered by Hammond (Hammond, 1955) and in the lower extremity occurs approximately 50-150 ms following a muscle stretch. The long-latency response is now understood to be transcortical, being influenced by not only the spinal cord, but also circuitry in the brain (Matthews, 1991).

Due to transcortical involvement of the long latency response, it appears to be highly modifiable. It can be modified by context (Hammond, 1956), either increasing or decreasing excitation of a muscle based on intent. It can even activate a number of muscles other than the muscle that detected the stretch of the perturbation (Bonnard, de Graaf, & Pailhous, 2004; Colebatch, Gandevia, McCloskey, & Potter, 1979; Dimitriou, Franklin, & Wolpert, 2012; Nakazawa, Yamamoto, & Yano, 1997; Nashed, Kurtzer, & Scott, 2015; Safavynia & Ting, 2013; Weiler, Gribble, & Pruszynski, 2015). A balance reaction task that involves a repeated perturbation leads to a more accurate and less energy expending response during the long latency period (Welch & Ting, 2014), demonstrating learning effects. The feedback response can even be altered by novel arm force field resistances (Lackner & Dizio, 1994), and adapt to novel visually shifted workspace (Cluff & Scott, 2013). Given its adaptability, many pathways and substrate have been investigated to determine contributing factors to the long-latency response. For example, it is suggested that transmission of peripheral sensory information is essential, where both group II (Matthews, 1984) and Ia afferents (Schuurmans et al., 2009) are identified as important contributors. Neural substrate that most likely contributes to the long latency response includes the somatosensory cortex, the primary motor cortex, the premotor cortex, the supplementary motor area, and the cerebellum (Boudreau, Brochier, Pare, & Smith, 2001; Jacobs & Horak, 2007; Matthews, 1991; J. Andrew Pruszynski & Scott, 2012). To many researchers' dismay, no one pathway nor brain region can yet be identified as having the ability to house the response. The long-latency response is most probably a complex combination of different contributing circuits formulating goal intent as well as pre-muscle activation (J. A. Pruszynski, Kurtzer, & Scott, 2011), and depends on the internal representation of a limb movement (I. L. Kurtzer, Pruszynski, & Scott, 2008). It appears clear that although no one pathway is the full determinate of a perturbation response, it serves to aid in optimizing movement toward an individual's goal in a changing world.

Aging and motor control

Normal aging involves many changes that affect motor and sensory systems. To just name a few, as we age there is a loss of fast motor units decreasing muscle force output potential (Lexell, 1995; Lexell, Henriksson-Larsen, Winblad, & Sjostrom, 1983; Luff, 1998), decreased proprioception from the limbs (Madhavan & Shields, 2005; Verschueren, Brumagne, Swinnen, & Cordo, 2002), altered vestibular information changing sensitivity to head movements (Anson & Jeka, 2015), and even decreases in volume and white matter morphology of brain regions associated with movement control and higher-order processing (Gunning-Dixon, Head, McQuain, Acker, & Raz, 1998; Hedden & Gabrieli, 2004; Raz, Gunning-Dixon, Head, Dupuis, & Acker, 1998). Behavioral evidence reveals that these changes lead to altered movement control. During visuomotor tasks older individuals lose the ability to predict faster movements (Newell, Mayer-Kress, & Liu, 2009), and actually decrease peak velocity when reaching to an object in order to maintain accuracy (Cooke, Brown, & Cunningham, 1989; Darling, Cooke, & Brown, 1989; Goggin & Meeuwsen, 1992). Interestingly, older people can actually generate similar movement velocity compared to younger individuals, though in order to maintain reaching accuracy, movement speed must be adjusted (N. Walker, Philbin, & Fisk, 1997). Aging also causes decreased control of single and multi-joint force production

(Christou, Zelent, & Carlton, 2003), making both fine movement control and altering loads of movement difficult for older individuals. Therefore, adjusting both velocity and resistance during a movement adds incrementing difficulty of movement for the aging individual for upper extremity reaching. Although we hypothesize that weight-bearing movement response to changes in resistance and velocity will create a similar hierarchy of difficulty, we must first validate this hypothesis in order to develop an assessment tool of lower-extremity movement control.

Examining the feedback response to unexpected perturbations during movement in older individuals may also be helpful. Here we can determine the effects of aging on the ability to correct initial movement conditions due to changes in the environment. The long-latency response (LLR) can be an interesting determinate of the non-volitional portion of the feedback response as previously discussed. It has already been demonstrated that the long-latency response of the soleus muscle in both elderly and younger people is largely enhanced when changing position from sitting to standing. The tibialis anterior, however, has an already heightened activity compared to younger adults in sitting, but is unchanged by moving from sitting to standing (Obata, Kawashima, Ohtsuki, & Nakazawa, 2012). Additionally, with altering visual or proprioceptive input, latencies of the LLR following a standing perturbation increase with advancing age in both the tibialis anterior and the soleus (Nardone, Siliotto, Grasso, & Schieppati, 1995). Even though stretch responses and balance reactions in standing are becoming better described, reactions to unexpected muscle stretch events are poorly understood during a function, weight-bearing movement.

Differences in function of brain structures are also being discovered in older compared to younger adults. When asked to perform an increasingly difficult manual task, elderly do show brain activation in similar regions of younger, though elderly have increased activation of the sensorimotor and frontal regions (Heuninckx, Wenderoth, & Swinnen, 2008). The increase in brain activity in these regions is proposed to be a compensation, relying more strongly on somatosensation and higher order processing to attempt to perform with the same accuracy as younger adults. This is supported by an experiment that discovered a decrease in cortical excitability when elderly subjects stand on foam compared to level ground (Papegaaij, Taube, Hogenhout, Baudry, & Hortobagyi, 2014). Decreased cortical excitability on foam is most probably due to decreased proprioceptive information available on the compliant surface. Interestingly, the simple intervention of wearing textured orthotics to enhance somatosensation in the feet decreased blood oxygenation in the dorsolateral prefrontal cortex during treadmill ambulation (Clark, Christou, Ring, Williamson, & Doty, 2014). This was believed to be due to the decreased need for higher order processing centers of the brain to compensate, as the extra proprioception provided by textured orthotics allowed for an appropriate level of information for the aged brain.

Accordingly, the purpose of the first portion of this body of work is to determine the effects of varying velocity and resistance of a lower-extremity weight-bearing task to achieve a hierarchy of difficulty. A hierarchy of difficulty is important to prevent possible ceiling effects in young subjects, and floor effects in the older subjects. As reviewed in this section, aging has widespread effects on all levels of the motor, afferent, and processing systems; affecting upright reaching, and balance. We aim to determine the effects of age on feedforward and feedback portions of a functional weight-bearing task. Insights into changes in motor control with normal aging will help to identify potential interventions to prevent further decrements in movement accuracy with the purpose of preventing further deterioration to prevent lower extremity injury.

Motor Learning

The process of learning a new motor skill or sequence is termed motor learning. Motor learning can be broken down into three phases: skill acquisition, consolidation, and transfer. Skill acquisition occurs during initial learning of a movement until an asymptote of accuracy is achieved. Consolidation refers to “a process whereby a memory becomes increasingly resistant to interference from competing or disrupting factors with the continued passage of time” (McGaugh, 2000). While transfer is the ability to apply the newly learned movement to a novel scenario such as an altered speed, resistance, or during a simultaneous different task.

Our understanding of motor learning has evolved greatly in the past several decades, though competing theories and frameworks continue to exist. The process of skill acquisition and retention is currently thought to involve two probably parallel processes: a fast-learning process with a rapid decay in its representation, and a slow-learning process that is thought to contribute to long-term consolidation (Doyon et al., 2002; Hikosaka, Nakamura, Sakai, & Nakahara, 2002; Lee & Schweighofer, 2009). The fast process is thought to be highly attention (cognitively) demanding, though providing very rapid improvements in accuracy. The slower process is thought to require less attentional demand, and generate gradual improvements in movement error. Motor learning has generally been investigated under two different modes: motor sequence learning, and motor adaptation. Both are associated with changes in cortico-striatal and cortico-cerebellar networks, though responses between the two modes of learning differ substantially.

Motor sequence learning is generally studied by sequences of complex finger tapping, as this is easily performed in imaging modalities such as positron emission tomography (PET) and magnetic resonance imaging (MRI) scanners. During sequence learning, early (fast) skill acquisition involves increased blood flow to the dorsolateral prefrontal cortex (DLPFC), dorsal premotor area, anterior cingulate cortex, inferior parietal region, rostral striatum, and cerebellar cortex. Sequence learning starts with delivery of visual information from the inferior parietal cortex to the DLPFC and dorsal premotor area in order to make a judgment for action (Yamagata, Nakayama, Tanji, & Hoshi, 2009). Information is then passed via the basal ganglia to generate movement, and finally is optimized by the cerebellum during execution (Coynel et al., 2010). After the early learning period, movement relies less on feedback and more on feedforward control, becoming faster and more reliable. Following early learning, activation is reduced in the cerebellar cortex and the associative area of the striatum, shifting activity to the parietal cortex (intraparietal sulcus and the precuneus), supplementary motor area, ventrolateral prefrontal cortex, and the sensorimotor regions of the striatum (posteroventral putamen).(Coynel et al., 2010; Doyon et al., 2002; Lehericy et al., 2005) Essentially, as a motor sequence skill becomes more automatic, the cerebellum becomes much less important; relying almost solely on the forward sequence model of the cortico-basal ganglia loop.

Motor adaptation however, is studied most classically by transformation of visual information regarding a hand movement to a target, or by application of a force field to the upper extremity via a robotic system. In motor adaptation, regions of increased activation are very similar to that of motor sequence learning and include the DLPFC, ventral putamen, primary sensory cortex, and the posterior parietal cortex (Bernier & Grafton, 2010; Krakauer et al., 2004; Seidler, Noll, & Chintalapati, 2006). Once an asymptote in error has been reached, activity then decreases in the cortico-basal ganglia loop, and increases in the cortico-cerebellar loop (Della-Maggiore, Landi, & Villalta, 2015; Della-Maggiore & McIntosh, 2005; Shadmehr & Holcomb, 1997). This indicates that automated adaptation to movement relies more heavily on cortico-cerebellar pathways than that of the striatum.

Though motor sequence learning and motor adaptations both utilize striatal and cerebellar circuits in early learning, late expression of the learning appears to be segregated. Automaticity of learned sequences occurs through the basal ganglia, while motor maps for adaptations are expressed in circuits involving the anterior cerebellum. Regardless of pathways, central to these theories is that error is processed as the difference between actual and intended movement, which is then translated into motor mapping (Anguera, Seidler, & Gehring, 2009). Motor mapping, however, may not be the whole story of motor learning. There probably exists a cross-sensory error signal that aids in adjusting to the discrepancies in limb movement, as motor adaptation does not always transfer to an altered sense of position in trained subjects (Henriques & Cressman, 2012). Cressman and Henriques (Cressman & Henriques, 2015) were able to demonstrate that motor adaptation and sensory adaptation can occur independently thus suggesting that there are two processes: the sensorimotor error signal (desired vs. actual movement), and the cross-sensory error signal (the difference between visual and proprioceptive information). The authors suggest that this model is aligned with previous theories (Shadmehr, Smith, & Krakauer, 2010) where changes in the predicted and actual sensory consequences of movement occur in the posterior parietal cortex in conjunction with the premotor cortex and the sensorimotor cortex, and the actual forward model motor commands that are compared to that of the parietal cortex is housed in the cerebellum. This information processing of different sensory modalities may be what allows an update to a new internal model to generate accurate motor programs even after injuries or aging processes that affect the sensory system.

Consolidation, the process in which a learned motion becomes a more stable memory, is usually measured by off-line gains, or the better performance in the early portion of the retesting session compared to the end of the learning phase. When learning a motor sequence task, sleep has been demonstrated to improve consolidation compared to an awake period away from the motor task (Fogel et al., 2014; M. P. Walker, Brakefield, Morgan, Hobson, & Stickgold, 2002; M. P. Walker et al., 2003). Interestingly, other types of motor remembering may not be affected by sleep, as learning of a motor sequence embedded into a task (implicit learning) has demonstrated variable results (Albouy et al., 2015; Nemeth et al., 2010; Song & Nakayama, 2007). Investigations are now focused on potential substrate and connectivity in the brain associated with types of memory consolidation and how sleep interacts with this circuitry (Albouy, King, Maquet, & Doyon, 2013). Largely, influences of aging and attention on consolidation of newly learned movements are not completely understood.

Cognition and motor learning

Motor learning and execution has long been thought to be related to cognitive capabilities, as generating new movements requires the ability to attend to and process the entire workspace or environment. Working memory is the process that allows the maintenance and manipulation of information over a short period of time (Baddeley, Logie, Bressi, Della Sala, & Spinnler, 1986), and has been shown to depend on a wide variety of neural structures. In particular, however, the cerebellum has been demonstrated to increase in activation with increasing working memory demand, and fMRI studies are able to predict those with greater working memory capacities by improved efficiency in activation of the cerebellum during graded working memory capacity increases (Bo & Seidler, 2009; Kuper et al., 2015). Further supporting the relationship between working memory and motor learning stems from clinical data indicating that working memory capacity correlates with the rate at which a motor sequence is learned (Bo, Borza, & Seidler, 2009; Bo & Seidler, 2009). It seems no surprise, however, that the cerebellum is directly connected to the dorsolateral prefrontal cortex (Ramnani, 2006), the association of the cerebellum to higher level functioning. Transcutaneous magnetic stimulation studies inhibiting activation in the dorsolateral prefrontal cortex even has been shown to decrease working memory capacity, probably affecting the closed circuit loop between the cerebellum and the pre-frontal cortex (Robertson, Tormos, Maeda, & Pascual-Leone, 2001).

The function of the dorsolateral prefrontal cortex (DLPFC) is probably most associated with executive function, or the properties of cognitive flexibility, problem-solving, and response maintenance (Alvarez & Emory, 2006). Early in motor learning, activation in the prefrontal cortex is strong due to increased attentional and processing demand. As learning is improved and automaticity ensues, activation in the prefrontal cortex decreases. It has been shown that as cognitive tasks become increasingly demanding, that activations in this region increase and is proposed to be a bottle-necking location when performance begins to degrade(Tachibana et al., 2012). Although evidence has suggested cognition and mobility have effects on each other, there is support that executive function declines precede limitations in mobility (Elovainio et al., 2009). One clinical study of 179 community-dwelling adults was even able to predict improvement in mobility due to training, based on executive function measures of the Wisconsin Card Sorting test and the Flanker Inhibition test (N. P. Gothe et al., 2014). In an attempt to increase overall executive function experimentally, it has even been shown that stimulation of the DLPFC and the cingulate gyrus through transcutaneous direct current leads to decreased dual-task cost, or the difference in performance of a single versus a dual-task(Zhou et al., 2014).

Motor learning and aging

Aging, as previously described, involves a plethora of changes in many systems involved in motor control and motor learning. Interestingly, older individuals have been shown to be able to continue to learn relatively simple movements similarly to younger adults (King, Fogel, Albouy, & Doyon, 2013; Seidler, 2006). This is demonstrated by achieving a similar performance (reduced errors) after a period of practice. When task complexity increases, however, the rate of initial learning is slowed and performance potential is decreased (Anguera, Reuter-Lorenz, Willingham, & Seidler, 2011; Bennett, Howard, & Howard, 2007; Bennett, Madden, Vaidya, Howard, & Howard, 2011; Bo et al., 2009; Spencer, Gouw, & Ivry, 2007). There is strong support that the reduction in rate of learning and actual performance is linked to altered activation of both processing and motor execution regions of the brain (King et al., 2013). Reduction in motor learning may actually be linked to cognitive function of working memory capacity due to inability to activate cognitive resources to chunk information into appropriate sizes (Bo et al., 2009). Most studies involving motor learning uses an upper extremity task due to the increased ease of using imaging modalities. Much less, however, is known regarding learning a weight-bearing lower-extremity task as necessary for everyday mobility.

Once a motor sequence skill has been acquired, older adults show decreased off-line gains that are seen in younger adults regardless of similar error after skill acquisition (Fogel et al., 2014; Spencer et al., 2007; Wilson, Baran, Pace-Schott, Ivry, & Spencer, 2012). This suggests that the process of consolidation is impaired, and has been hypothesized to be due to many factors. Fogel (2012) determined that reduced sleep spindle oscillation was related to decreased cortico-striatal network activity, thus causing decreased consolidation. Whereas King (2016) presents that activity in the motor execution of the brain is related to consolidation, where older individuals have lost the appropriate excitability in the motor areas (King et al., 2016). Yet others (Roig 2014) believe that interference from other memories is following motor tasks is occurring (Roig, Ritterband-Rosenbaum, Lundbye-Jensen, & Nielsen, 2014). It appears that as the aging brain experiences structural changes, it is adapting its connectivity in order to perform at the highest level that it possibly can. Unfortunately, it appears that consolidation of memories may be adversely affected by adaptations associated with aging.

Cognitive-Motor Dual-Task Training

One strategy that has been gaining greater attention in rehabilitation paradigms is training of movements in a cognitive-motor dual-task. Here, a cognitive task is given (e.g. counting backward from 100 by 7's) while performing a specified motor task (e.g. reaching to a visually represented point). This is thought to push the performance of a movement into "automaticity", or the ability to accurately execute a motor program with limited cognitive resources; the real-life equivalent of the ability to “walk-and-talk” simultaneously. In those with lower extremity motor and sensory changes (Yogev, Plotnik, Peretz, Giladi, & Hausdorff, 2007), movement that was once automated now requires increased attentional demand to process the altered ascending and descending information. In healthy controls, performing an adaptation motor task and a cognitive choice reaction time tasks, the simultaneous cognitive task actually facilitated motor learning (Goh, Sullivan, Gordon, Wulf, & Winstein, 2012; Roche et al., 2007). Can mobility be enhanced by forcing the automaticity or motor adaptation to match the new sensory/motor environment?

A vast array of brain regions is involved in the performance of concurrent tasks. Brain regions identified include: ventrolateral and dorsolateral prefrontal cortex, dorsal anterior cingulate cortex, striatum, bilateral inferior and superior parietal cortex, premotor cortex, supplementary motor area, and cerebellum (Erickson et al., 2005; Hartley, Jonides, & Sylvester, 2011; Low, Leaver, Kramer, Fabiani, & Gratton, 2009; Lu, Liu, Yang, Wu, & Wang, 2015; Schubert & Szameitat, 2003; C. N. Wong et al., 2015). During extensive training of a dual-task, however, improvements in both the cognitive and the motor tasks occur until they reach the ability to perform each task similarly to that of the single-task. Here, activations of each brain region also decreased to the level of nearly the single-task condition with the exception of different findings between studies for the pre-frontal cortex. The prefrontal cortex during automaticity of a repeated finger pattern task (SRT) actually increased in some studies (Poldrack et al., 2005), while activation decreased in others (Erickson et al., 2007a).

Functional changes in each brain region and the vast connectivity between regions allows for extensive discussion and multiple theories as to how optimization of both the cognitive and the motor tasks occur. It does appear evident, however, that the supplementary motor area plays a key role in the circuitry involved in generation of a coordinated chunking of a complex movement (Tanji, 1994; Tanji & Shima, 1996; Wiestler & Diedrichsen, 2013). The updated movement plan is probably aided through loops involving the ventral striatum(Akkal, Dum, & Strick, 2007), the primary motor cortex (Tanji, 1994), and the cerebellum (Akkal et al., 2007). In order for those with movement impairments to regain accuracy of movement and atomization, a new internal representation of movement must also be simultaneously updated, and probably occurs through feedback loops with the posterior parietal cortex(Shadmehr & Krakauer, 2008).

Once a movement is learned, it must then be able to be generalized to different contexts such as speed, force, and location. Although results indicate that under a dual-task paradigm improvements in reaching reaction times to a specific location does not transfer to new locations(Sanli & Lee, 2014), and reaction time in reacting doesn't transfer between modes of vocalization and upper extremity reaching(Strobach, Frensch, Soutschek, & Schubert, 2012). It is unknown if transfer of a motor program will occur between prescribed speed and delivered resistance of a movement as we intend to test in this study.

There is clinical evidence that dual-task training of gait and balance can generate improvements in those with neurologic compromise. Wang and colleagues (Wang et al., 2015) recently published a meta-analysis reporting significant and clinically important improvements in gait speed, Berg Balance Scale, and center of pressure sway area after dual-task training. Older adults with history of falls have been shown to improve in Berg Balance Scale and Activities Specific Balance Confidence Scale(Buraggada, 2004), and those with dementia improve in gait speed(Schwenk, Zieschang, Oster, & Hauer, 2010). An extensive review of dual-task training in those with central neurologic impairment(Fritz, Cheek, & Nichols-Larsen, 2015) revealed improvements in spatiotemporal parameters of single-task gait. Further, gains in individuals after stroke may even be greater under a dual-task paradigm with visual restriction(D. Kim, Ko, & Woo, 2013).

Interestingly, dual-task testing may also shed light onto trans-cortical feedback responses as part of the generalizability of motor learning. Several studies have attempted to identify the effects of a dual-task on perturbation responses. These have revealed that motor responses are in competition with cognitive responses by the detection of delays in either a stepping reaction to a balance perturbation (Little & Woollacott, 2015; Sun & Shea, 2015), or delays in cognitive response (Nnodim, Kim, & Ashton-Miller, 2015; P. J. Patel & Bhatt, 2015) when prioritizing stability (motor response) over the cognitive task. Response delays and motor inaccuracies during dual-tasks also appear to be influenced by neural degradation associated with advanced age (Cheng, Pratt, & Maki, 2013; Elaine Little & Woollacott, 2014). It may be that prior experience, or increasing the central set by previous exposure, improves reactions to unexpected perturbation in static standing (Horak, Diener, & Nashner, 1989). Little research is known regarding perturbation responses during a lower extremity movement under the influence of dual-task training or motor automaticity.

Generalizability of investigations appears to be limited due to significant variations in training frequency, duration, and method as well as poor reporting and standardization of lesions of the brain associated with central neurologic impairment and older age. Here, we will discover valuable insights in the ability to access an internal model during a learned movement while attentional demands are altered in a dual-task paradigm. It may be that when a movement has reached automaticity during a dual-task, where context and goal are determined by an ongoing state rather than an attended state, perturbation responses are optimized.

Cognition and automaticity

Dual-task paradigms are becoming more common in both clinical and mechanistic studies in order to shed light on varying requirements of executive function on motor tasks. Following stroke, concurrent gait and cognitive task demonstrate increased oxygenated hemoglobin concentration in the prefrontal cortex compared to a healthy control group(Al-Yahya et al., 2015). Interestingly, this was increased for stroke survivors for both single and dual task, though increased to a greater degree in the dual-task. This may be related to increased top-down control of movement required for ambulation now that more attentional resources are required for the movement. This concept is supported by fMRI data demonstrating increased DLPFC activation in older adults compared to young adults during dual-tasking, but interestingly those who performed better on the dual-task had decreased prefrontal cortex activation(Hartley et al., 2011). This is supported by a recent study that indicates that the prefrontal cortex doesn't necessarily increase in efficiency by regional resource allocation, but increases in speed of information transmission and processing. Although this points to the prefrontal cortex as being the major driver in dual-task processing, evidence suggests that a multitude of networks are actually at play, involving the cerebellum, the premotor cortex (Goh, Lee, & Fisher, 2013), and the supplementary motor cortex (Ikeda et al., 1999). It may be that the ability to rely less on cognitively demanding top-down information, and to automate through a bottom-up movement paradigm, that dual-tasking can improve over time.

Although evidence supports that executive function can improve through cognitive training, little is known regarding if cognitive training alters cognitive-motor dual tasks capabilities. One study in older adults was able to demonstrate equal improvements in gait parameters with just executive function training compared to cognitive-motor dual-task training (Azadian, Torbati, Kakhki, & Farahpour, 2016). Interestingly, however, in another study involving young, healthy adults, increasing working memory capacity through cognitive training did not improve visuomotor adaptation learning (Anguera et al., 2012). This may indicate that a ceiling effect exists once working memory capacity is large enough to meet demands, or even that the working memory is functioning along with another process.

Most studies involving working memory capacity and executive function in learning novel skills involve those that are either healthy, or those with central impairments affecting cognition or neural circuitry. The efficacy of dual-task training is somewhat controversial and may be due to variances in disease severity, peripheral nervous system changes, and neural substrate. Here, we propose to fill the gap in the ability to learn, recall, and transfer a single motor and a dual cognitive-motor weight-bearing, visuomotor task in the healthy aging.

WEIGHT-BEARING VISUOMOTOR TASK

The weight-bearing visuomotor task investigated in this body of work was implemented using a previously developed therapeutic exercise system (Shields, 2006). A video of this system is provided in the supplemental material. Custom designed hardware and software were used to assess the accuracy of a sagittal plane, single limb, mini-squat according to a line on a screen. This apparatus consists a stable frame instrumented with a rack and pinion gear and braking device controlled by a microcomputer. A subject stands in the frame with their knee strapped to the end of the rack in series with a force transducer, where the sagittal component of the squatting motion is digitized and displayed on a screen resting on the frame in direct sight of the individual. Knee flexion range of motion was approximately 0-25 degrees, with a linear translation at the knee of 9.7 cm.

The microcomputer is able to adjust the resistance of the break, thus allowing the ability to rapidly control the level of resistance provided to both knee flexion and extension. Resistance at the knee was standardized as a percentage of each person’s body weight entered into the computer at the start of the experiment. With precise computerized control, we are also able to rapidly eliminate the resistance of the break delivered to the knee for less than a second during the flexion phase of the task. This perturbation is delivered during a randomly selected cycle, though is never delivered in the first cycle in order to allow sufficient time for the subject to “get on target”. The random selection of cycle combined with the user’s goal of staying on the target line allows for an unexpected event without compensatory pre-perturbation stiffening of muscle about the knee (a common static balance strategy), as stiffening is not optimal in continuing to stay on task. The system can then measure the capability of the motor system to respond to an unexpected force perturbation during a prescribed weight-bearing motion. Studies investigating the timing of lower extremity injuries indicate the nervous system response to an unexpected rapid stretch of a muscle generates injuries such as anterior cruciate ligament ruptures (Koga et al., 2010; Withrow, Huston, Wojtys, & Ashton-Miller, 2006). Here, the quadriceps muscle is loaded and then experiences a rapid stretch when the break is released, allowing us to investigate the nervous system response in real-time during weight-bearing motion. When the brake is re-applied less than a second later, the resistance is restored to the previous level preventing a collapse of the individual and restoring the original motor task.

To create the visuomotor task, custom software traces a sinusoid waveform on the computer monitor, while concurrently displaying the linear displacement of the knee. This allows the user to have real-time feedback of their performance. The presented task is standardized to a sinusoidal waveform that begins starting from full knee extension into flexion. The sinusoid consists of five cycles, terminating in the starting position of full knee extension. Previously, studies using this system utilized a constant frequency of the visuomotor task, though for the purposes of these studies, the system has been programmed to display three different frequencies in order to alter motor task properties. For ease of understanding the conditions of the motor task, although a sinusoid is not composed of a constant velocity, changes in frequency (rate of movement) of the sinusoid target is generally termed “velocity”.

Previous publications from our lab showed that this system is safe and effective for not only young adults (Madhavan & Shields, 2005, 2007, 2009; Shields et al., 2005), but those with a history of anterior cruciate ligament (ACL) repair (Madhavan & Shields, 2011), those with quadriceps muscle fatigue (Ballantyne & Shields, 2010), older adults (Madhavan et al., 2009), and those pre and post-surgical intervention for cervical myelopathy (Abode-Iyamah et al., 2016). For increased safety and to reduce the balance aspect of single limb stance, individuals are instructed to use light finger-tip touch. We have previously shown that although light touch is aiding balance, insufficient force is exerted by the upper extremity to influence lower extremity movement, where less than 2 N force was detected at the finger during the motor task. (Madhavan et al., 2009).

We describe this task as functional motion due to being a component of movements that are commonly performed in activities of daily living. Weight bearing single limb knee flexion is necessary for activities such as stair descent and negotiating a curb. This task also allows investigation of controlling motion in weight-bearing where generalized muscle stiffening as in static balance is impractical, and all senses (vision, vestibular, somatosensation) are intact and allow feedback regarding movement control. We have previously shown that older and younger individuals can both learn to perform the visuomotor task very accurately. We have even been able to detect differences in the pre-volitional feedback response following a perturbation of those having undergone ACL repair. Better performance on this visuomotor task (lower error) also has been shown to correlate to faster walking speed capability in a patient population with cervical myelopathy (Abode-Iyamah et al., 2016). This indicates that in future studies beyond the scope of this body of research, we may be able to gain insights into other functional task such as walking, by obtaining a performance measure using this safe, fast, and reliable system. In this research, we aim to establish a hierarchy of difficulty of the weight-bearing visuomotor task as well as to determine the effects of cognitive-motor dual-tasking on the ability to acquire, retain, and transfer the learned motion in our testing apparatus.

SPECIFIC AIMS

<u>Specific Aim 1 (Chapter 2)</u>: To determine the effect of altering resistance and velocity, and unexpected accelerations on a weight-bearing visuomotor task.

Specific Aim 1a: To determine the effect of altering resistance and speed on movement accuracy of a weight-bearing visuomotor task.

Hypothesis 1a: Resistance and movement rate will have a systematic effect on movement accuracy

Specific Aim 1b: To determine the effect of unexpected accelerations on movement accuracy during a weight-bearing visuomotor task.

Hypothesis 1b: Unexpected changes in acceleration will have a velocity-dependent effect on movement accuracy

<u>Specific Aim 2 (Chapter 3):</u> To determine the effect of age on feedback and feedforward control during a weight-bearing visuomotor task.

Specific Aim 2a: To determine the effect of age on the ability to perform a weight-bearing visuomotor task.

Hypothesis 2a: As age increases absolute error and peak error will increase, and velocity matching will decrease.

Specific Aim 2b: To determine the effect of age on non-volitional feedback responses to unexpected events during a weight-bearing visuomotor task.

Hypothesis 2b: As age increases, an unexpected force perturbation will result in increased knee flexion rates, decreased knee extensor force rates, and increased error rates during the pre-volitional response.

Specific Aim 2c: To determine how overall accuracy of mixed feedforward and feedback performance (whole task) effects non-volitional feedback responses to unexpected force perturbations as age increases.

Hypothesis 2c: When normalizing non-volitional feedback responses to accuracy as measured by mean trial error and by coherence (velocity matching), older individuals will demonstrate larger knee flexion and error rates regardless of mixed feedforward and feedback performance.

Specific Aim 3 (Chapter 4): **To determine the effect of age and cognitive-motor dual-task difficulty on visuomotor learning of a weight-bearing task.**

Specific Aim 3a: To determine the effect of cognitive task difficulty on skill acquisition in younger and older adults.

Hypothesis 3a: Increased cognitive task difficulty will decrease the rate of learning of a new motor task, with a greater reduction of the rate of learning in older compared to younger adults.

Specific Aim 3b: To determine the effect of cognitive task difficulty on the consolidation of a weight-bearing visuomotor task

Hypothesis 3b: Increased cognitive task complexity will diminish consolidation of the motor task, with greater influence on older vs. younger individuals.

Specific Aim 3c: To determine the effect of cognitive task difficulty on transfer of visuomotor learning to new motor task conditions of speed and resistance.

Hypothesis 3c: Increased cognitive task difficulty will result in increased error and decreased velocity matching under new motor task conditions of resistance and speed for both younger and older adults.

Specific Aim 3d: To determine the effect of cognitive task difficulty on non-volitional feedback response to an unexpected perturbation during a weight-bearing visuomotor task.

Hypothesis 3d: Increase in cognitive difficulty will result in increased error rate and knee flexion rate during non-volitional responses to an unexpected perturbation, with a greater effect in older compared to younger individuals.

Specific Aim 3e: To determine the effect of cognitive-motor dual-task training on dual-task deficit.

Hypothesis 3e: Dual-task training will decrease dual-task deficit for both older and younger adults.

Specific Aim 3f: To determine the relationship between cognition and dual-task performance in both young and older subjects.

Hypothesis 3f: Working memory capacity will predict rate of learning during both single and dual motor tasks in young but not in older subjects, while executive function will predict performance in both young and older groups.

CHAPTER 2: SPEED, RESISTANCE, AND UNEXPECTED ACCELERATIONS MODULATE FEED-FORWARD AND FEEDBACK CONTROL DURING A NOVEL WEIGHT BEARING TASK

INTRODUCTION

Feed-forward and feedback movement strategies are fundamental to optimal neuromuscular control in humans (Elliott, Helsen, & Chua, 2001; Woodworth, 1899). Altered neuromuscular control is associated with poor human performance across the spectrum of function: from elite athletes falling short of a record to the person with Parkinson's disease unable to ambulate a short distance to be independent. Typically, injury occurs when the central nervous system is fooled with an event that was not expected, relying entirely on a feedback response. The integration of the anticipatory commands and the feedback commands is well documented; however, our understanding of feed-forward and feedback control during functional weight bearing movements remains elusive. In this study we assess the effects of manipulating the speed, resistance, and unexpected events on error during a novel functional weight bearing task.

While there is limited information on how speed and resistance cause the CNS to scale neuromuscular responses during weight bearing tasks, there are rich resources guiding us from the upper extremity literature. Feed-forward control of the upper extremity reflects the open-loop plan of movement, and has been shown to decrease in accuracy with increase in speed (Fitts, 1954; Fitts & Peterson, 1964; Woodworth, 1899), and resistance (Levin, Lamarre, & Feldman, 1995; Muehlbauer, Panzer, & Shea, 2007). Feedback control, however, is the closed-loop, error driven change in movement. Reaching experiments have provided evidence that unexpected acceleration/deceleration induced by mid-movement changes in speed (P. Cordo, Carlton, Bevan, Carlton, & Kerr, 1994; P. J. Cordo, 1990) and resistance (Cluff & Scott, 2013; Gottlieb, Song, Almeida, Hong, & Corcos, 1997), also diminish movement accuracy. Because whole body unexpected events involve the vestibular, visual, and somatosensory systems, the findings may vary from reports for upper extremity perturbations.

Our initial investigation of a single limb squat as a visuomotor task revealed that a fixed level of difficulty changes modulates the feed-forward and feedback control strategies as supported by changes in muscle activity about the knee. Improvements in performance can be achieved even under conditions where a person is denied visual feedback (Madhavan & Shields, 2007, 2009)**,** is fatigued (Ballantyne & Shields, 2010), older (Madhavan et al., 2009), or post-surgical (Abode-Iyamah et al., 2016; Madhavan & Shields, 2011). A limitation of our previous reports is that only a single level of resistance and speed was assessed during the weight bearing task, suggesting that the assessment would show ceiling or floor effects in other populations.

During routine clinical assessment, we typically measure impairments with a vast range of techniques (e.g. muscle testing, gross motor function exams, range of motion testing, sensory testing, timed standing balance, coordination, reflexes, and quality and endurance of gait). Testing how healthy people scale lower extremity movement and perturbation responses during a range of difficulty will provide insights into control of weight bearing functional movement. We believe that this is important in order to assess the integration of movement systems and strategies, and may provide a rapid method to characterize impairment, and, presumably, disability.

The purpose of this study was to determine if changes in speed, resistance, and unexpected acceleration either independently or in combination leads to reduced movement accuracy in a hierarchical pattern (greater error with greater resistance and/or greater speed). We hypothesize that an increase in speed and resistance would yield a linear decrease in movement accuracy, while unexpected perturbations would lead to a velocity-dependent and resistance dependent decrease in movement accuracy.

METHODS

Subjects

A total of 26 healthy adults aged 19 - 45 years (mean(standard deviation), 27.7(6.7) years; nine females and seventeen males) participated in the study. All subjects enrolled in the study had no acute or ongoing orthopedic, neuromuscular, or neurological deficits or disorders. Each individual gave informed consent before participation and our institution's Human Subjects Institutional Review Board approved the study.

Paradigm

The study involved a single session using a previously developed therapeutic exercise system (Shields, 2006) to deliver nine testing conditions: three movement speeds (0.2, 0.4, and 0.6 Hz) in combination with three levels of brake resistance (5%, 10%, and 15% of individual's body weight). Only the dominate leg was tested, as was defined as the side with which one would kick a ball. Each testing condition was separated by a one-minute rest period. The order of testing condition is fixed across all subjects: medium, light, then heavy resistance for the medium speed, followed by the same resistance order at the slow speed, and lastly the fast speed (Top panel, Figure 1A). Each subject was asked to track a computer generated sinusoidal target consisting of five cycles as they performed a single limb squat exercise (Figure 1B). Even though the movement speeds varied across nine testing conditions, the individual's body position and the required knee angular control remained constant. Specifically, the target trajectory is always fixed across all speeds, corresponding to a range of knee motion of approximately 30 degrees of knee flexion to full knee extension. Instantaneous visual feedback of actual knee position (black sinusoidal line, Figure 1C) was provided to subjects on the same monitor as the target trace (gray sinusoidal line, Figure 1C). No further knowledge of results was given other than instantaneous visual feedback.

Within each testing condition, the brake resistance was programmed to be removed unexpectedly for a pre-determined time equivalent to approximately 10% of the cycle duration (200, 250, and 500 ms for 0.6, 0.4, and 0.2 Hz, respectively). The timing of brake release was randomly inserted in one cycle from 2 – 5, and always occurred during early knee flexion phase (i.e. 10 degrees of knee flexion) in order to perturb the ongoing knee flexion motion (the rectangle overlying the sinusoidal lines, Figure 1C). Before data collection, subjects performed two practice trials at the medium speed to familiarize themselves with the task apparatus.

Data Collection

At the beginning of each testing condition, subjects stood on a platform and were attached to the custom designed device with the hip and knee extended and the ankle in the neutral position. The brake system was programmed to control levels of resistance throughout the entire experiment. Our pilot studies showed a strong correlation between the angular and linear displacements of the knee ($R^2 = 0.97$). A 15-cm linear displacement corresponds to 30 degrees of knee flexion during single leg squatting. The testing leg was secured by a Velcro strap around the knee to maintain a fixed position on the force sensor attached to the device for force measurements (Figure 1C). To display real-time visual feedback, a computer monitor was positioned approximately 30 cm in front of the subject and was adjusted to the subject's body height. To indicate the start of each test, a visual countdown of five seconds to target tracking was given. There were nine trials in total (3 speeds × 3 resistances), one trial per testing condition per subject. Within each trial, there were five repeated cycles. Force and knee kinematic data were synchronized and recorded at 2000 Hz using custom LabVIEW software (National Instruments; Austin, TX).

Electromyography

In a subset of 10 subjects, electromyography of the recuts femoris, vastus lateralis, vastus medialis and lateral hamstrings was collected. Surface electrodes (Ag/AgCl; 8 mm diameter; 20 mm inter-electrode distance) were placed over the muscle belly of each muscle (Koh & Grabiner, 1992; Rochette, Hunter, Place, & Lepers, 2003). All electrodes were secured with pre-wrap to minimize movement of the electrodes during testing.

Once electrodes were securely placed, each subject was seated in the chair of a Kin-Com isokinetic dynamometer (Chattex Corp.; Chattanooga, TN), with the knee joint positioned at 90 degrees. Subjects were then instructed to perform three maximum volitional isometric contractions in both knee flexion and knee extension. Subjects were given one-minute rest between each contraction to avoid fatigue. Verbal encouragement was given during each of the contractions. The mean of the maximum activity was then used to normalize all electromyographic data for each respective muscle. All EMG sampling during MVC and visuomotor task was performed using LabVIEW software (National Instruments; Austin, TX) and sampled at 2000 Hz.

Data Analysis

All analyses were conducted using Custom Matlab software (MathWorks, Natick, MA). In each trial, the onset of each cycle was first identified. Movement error was then quantified as the difference between target and user's signals at each time point within each cycle. Root-mean-square (RMS) of errors across all time points in each cycle was calculated to represent the average error performance for each cycle. We separated the “perturbed” cycle from the other four “non-perturbed” cycles for subsequent analyses. The RMS was calculated for all EMG data for the time period of 50-200 ms after the start of where the brake would be released (unperturbed) or was released (perturbed). All EMG for the perturbed condition was normalized to the EMG during the unperturbed condition.

Non-perturbed cycles**.** To track the cycle-by-cycle improvement in single-leg squat performance, we examined the reduction of movement errors by comparing RMS errors across five consecutive cycles. To determine whether performance of a single-leg squat is velocity-dependent and/or resistance-dependent, RMS errors were averaged across all non-perturbed cycles within each individual at each velocity, at each level of resistance, and in each condition. Group means of RMS errors were first calculated by averaging across all subjects and then were compared across different velocities, different levels of resistance, and different conditions.

Perturbed cycles**.** To investigate the “reactive feedback control” in response to an unexpected perturbation (i.e. release of the brake resistance) during single-leg squatting, we examined perturbation- evoked changes in errors and force. We quantified rates of error and force changes by dividing absolute values of error and force changes to its corresponding perturbation time period. In order to examine perturbation effects across different conditions, we normalized rate of error and force changes to the average of absolute change of error and of force during the non-perturbed cycles in each condition. All variables then were averaged over all subjects to create group means for each condition. The change in electromyography of each muscle during the long latency period of the perturbation (50-200 ms) was calculated relative to the muscle activity of the same time of a cycle without a perturbation. Percent change was calculated by dividing the difference between the perturbed and unperturbed activity by the unperturbed activity. Activation of each muscle was normalized to the activity of the maximum volitional isometric contraction to enable averaging across subjects.

Statistical Analysis

Statistical comparisons were made using SAS/STAT software (SAS, Cary, NC, USA). A two-way mixed model ANOVA with repeated measures for velocity and resistance, and a one-way mixed model ANOVA with repeated measures for cycle and condition was used to assess significant changes in errors and/or forces with/without the perturbation, and for percent change electromyography of the lateral hamstrings. Electromyography data for the quadriceps muscles was analyzed using a two-way mixed model ANOVA with repeated measure of condition. When the ANOVA was significant, post hoc analyses were performed using Tukey's honest significant difference test. For models using an ANOVA, the effect size is determined by η^2, where follow up tests using Tukey's, effect size was determined by Cohen's d. The level for statistical significance was set at $P < 0.05$.

RESULTS

General Error Analysis

Individual traces of target and user's signals across nine testing conditions (3 speeds × 3 resistances) are depicted in Figure 2 from a typical subject (upper panels; Figure 2A- 2C). Reproducible force profiles, characterized by the smallest amplitude at the lowest resistance (5% of body weight) and the highest amplitude at the highest resistance (15% of body weight), were observed throughout the entire test. This supports that the brake resistance is precisely controlled at a pre-determined level as movement speeds were changed from 0.2 Hz to 0.6 Hz. In addition, a general trend is observed: that is, greater discrepancies between target and user's signals (gray and black traces, respectively) were observed in conditions with higher speeds and/or resistances as compared to conditions with lower speeds/resistances. It is also noteworthy to mention that the perturbation triggered by the unexpected brake release has a significant impact on ongoing knee motion and force output (rectangles; Figure 2A- 2C). It is clear that the user's signal (black trace) was significantly deviated from the target signal (gray trace) during the perturbation period, especially in conditions with the highest resistance (Figure 2C). Accordingly, the force exerted by the subject dropped sharply during the perturbation period due to an abrupt removal of the brake resistance.

Movement Speed (Velocity) and Resistance

Similar findings were also observed in group averages of RMS errors across non-perturbed cycles (cycle 1- 5) for each condition. Overall, errors increase as movement speed or resistance increases (Figure 3A). There is a clear pattern showing that healthy adults significantly improved movement accuracy after the third repetition (i.e. cycle 3). The RMS error is significantly lower in cycle 3 to cycle 5 as compared to cycle 1 (post-hoc, all *P*s < 0.0001, *d*=2.8, 2.7, 2.8, respectively) or cycle 2 (post-hoc, *P* =0.02, 0.005, 0.001; d=1.1, 0.9, 1.0, respectively Figure 3B - Cycle). In addition, a progressive increase in speed resulted in a linear increase in RMS error (P<0.0001, η^2=0.50; Figure 3B - Velocity). A progressive increase in resistance also resulted in increased error (p<0.0001, η^2=0.01, post hoc, 5% versus 10% or 15% sig. different; Figure 3B - Resistance). There was an interaction of speed and resistance (*P*=0.0011) where at the highest speed error increases at each increment in resistance (P<0.0001, η^2=0.24), but at the slow and medium speed, the lowest resistance is different from the medium and high resistance. A hierarchical order of RMS errors was illustrated when averaging across all available cycles within each condition and across all subjects to yield the overall group means for nine conditions (3 speeds × 3 resistances; Figure 3C). There was a main effect of condition (P < 0.0001, η^2=0.60) and post hoc analysis revealed significant differences in RMS errors based on this hierarchy (post-hoc, all *P*s < 0.05). The hierarchical model illustrates the amplitude of the RMS error as a linear function of velocity. It suggests that the higher the velocity, the greater RMS error produced by the individual. It appears that altering resistance has minimal effects on error performance especially at the slow velocity; while the effect of resistance on error performance becomes more prominent at the higher velocity. This again suggests that, in the absence of the perturbation, the amplitude of movement error is highly correlated with the movement speed, but minimally affected by the level of force exertion.

Unexpected Perturbation Analysis (error)

In the presence of the unexpected force perturbation, the degree of the evoked response is scaled to the level of force exertion prior to the perturbation as well as movement speed. The analysis of rates of absolute error and force changes confirmed that the perturbation-induced changes in errors and forces are both velocity- and resistance- dependent (upper panels, Figure 4A and 4B). That is, a progressive increase in either velocity or resistance would result in a linear increase in error and force changes per unit of time (main effects of velocity P=.0014, 0.0029 η^2=0.08,0.057; and resistance P<.0001, 0.0011 η^2=0.11, 0.039 respectively). Post-hoc analyses showed significant increases in rate of error and force changes observed at fast speed (0.6 Hz) compared to slow speed (0.2 Hz) or at high resistance (15% BW) as compared to low resistance (5% BW; all $Ps \leq 0.003$). We also observed a similar trend when comparing rates of error and force changes across nine conditions (3 speeds × 3 resistances; Figure 4A and 4B; lower panels). The hierarchies for perturbation-induced rate of error and force changes demonstrated similar changes due to resistance at each velocity (interaction: P=0.056, 0.7076, respectively). Given a velocity or resistance, the perturbation-induced rates of error and force changes were largest at the highest resistance or the highest velocity. Therefore, in the presence of the unexpected perturbation, the degree of the reactive response necessary for regaining dynamic control is crucially determined by the movement speed and resistance applied to the knee movement (force from the brake).

Perturbation Analysis (EMG)

The change in electromyography of each muscle during the long latency period of the perturbation (50-200 ms) was calculated relative to the muscle activity of a cycle without a perturbation. The vastus medialis, rectus femoris, and vastus lateralis all increased in muscle activity as a function of resistance (all $P<0.05$, $\eta 2=0.17$, 0.24, 0.38 respectively). The response of the quadriceps EMG at each resistance was similar as velocity increased (velocity all $Ps>0.05$, all $\eta 2<0.03$, interaction all $Ps>0.05$). Due to motor equivalence across synergists of the quadriceps, all three were averaged together, demonstrating a step wise pattern increasing approximately 60% from lowest to highest resistance in the slow and medium velocities, and increasing nearly 100% from the lowest to highest resistance in the fast velocity (Figure 5B). Taken together, these findings illustrate that the quadriceps muscles exhibit a doubling of activity within 200 ms in response to an unexpected event that occurs under conditions of high velocity and high resistance. As expected, there was a reciprocal decrease in lateral hamstrings activity as compared to the knee extension muscles ($P=0.03$) but no statistical difference was with change in resistance ($P=0.242$) and velocity ($P=0.1887$, interaction $P=0.923$). The reduction in lateral hamstrings EMG compared to the knee extension complex EMG supports an inhibition of the knee flexors within 200 ms in order to reduce the acceleration of the limb after the perturbation (Figure 5B). This inhibition coupled with the excitation to the quadriceps creates the "optimal" force couple to negate the free fall induced by the unexpected release of the brake.

DISCUSSION

In this study, we found that a progressive increase in speed and/or resistance resulted in an increase in movement error. Likewise, during unexpected perturbations, the error was high when resistance and speed were set at the highest levels (i.e. the condition with the speed at 0.6 Hz and the resistance at 15% body weight). To our knowledge, this study is the first that provides a hierarchical framework (range of task difficulties) in order to quantify the feed-forward, feedback, and overall control of the knee during a functional weight bearing task.

Movement Speed (Velocity) and Resistance

In the absence of a random perturbation, it is clear that tracking a target at high speeds challenges the neuromuscular control system. Our findings are concordant with Fitts's law [3, 4] in that as the difficulty of the motor task increased the movement amplitude error increased. At a given level of task difficulty, faster responses tended to produce more errors. In this case, the level of task difficulty was increased in increments of movement amplitude per unit of time (i.e. increasing speed). Increased speed equating to increased difficulty has been supported in many motor control paradigms including: line tracing (Hocherman & Giladi, 1998), reciprocal motions (Fitts, 1954), and incident-anticipation (Duncan, Smith, & Lyons, 2013; Harrold & Kozar, 2002). The effects of resistance on motor tasks has been less definitive, where increased pen weight (resistance) increased the error of a reciprocal task (Fitts, 1954), though resistance did not influence the error of a complex repeated motion (Muehlbauer et al., 2007). Simply increasing the resistance, however, may not necessarily become more challenging. The average error at the fast speed was two times greater than the error at the slower speed, however, the average error at the highest resistance was only 50% greater than the error at the lowest resistance. Accordingly, velocity is a larger determinant in the difficulty of a weight-bearing visuomotor task, and creates a linear increase in difficulty (RMS error).

Perturbation Analysis (error)

During one of the flexion phases of each condition, a perturbation was delivered by releasing the brake of the apparatus for a short period of time. Unexpected perturbations are differentially challenging to the nervous system depending on the degree of resistance and speed of the task. During the unexpected perturbation, the difference in response (rate of error and rate of force) is due to purely non-volitional feedback (Crago, Houk, & Hasan, 1976b; Marsden, Merton, & Morton, 1976; Matthews, 1986). It is interesting to note that unlike error of the mixed feed-forward and feedback (unperturbed) portion, resistance and velocity have an equal weight in increasing difficulty during feedback response (perturbed portion). The error rate approximately doubles when incrementing from the slowest to fastest velocity, and from the lowest to highest resistance. Similarly, the force rate increases by approximately 70% when incrementing from slow to fast, and light to heavy resistance (Fig. 4A,B top panel). When examining the progression of the combination of velocity and resistance, instead of a completely linear nature, there is a step-wise increase of error and force rate. The bottom panels of Fig. 4 A and B demonstrate that the least resistance (5% BW) of each velocity condition provides slightly less impact on the error and force rate than the highest resistance (15% BW) of the speed just below it.

Perturbation Analysis (EMG)

Electromyography of the three quadriceps muscles during the long latency reflex demonstrated an increase in activity compared to the state of the unperturbed central set. At larger resistances, the muscles are increasingly elicited in a step-wise pattern that differs from the unperturbed. These findings are in support of previous literature (Matthews, 1986; Mrachacz-Kersting, Grey, & Sinkjaer, 2006; Petersen, Christensen, Morita, Sinkjaer, & Nielsen, 1998; J. Andrew Pruszynski & Scott, 2012; Welgampola & Colebatch, 2001). Although our study suggests equivalent supra spinal influence of all three muscles, one study suggests that the rectus femoris is the only quadriceps muscle with supra spinal contributions to the long latency component (Mrachacz-Kersting et al., 2006). The difference in findings is most likely due to the fact that our study involves a weight bearing visuomotor task compared to a seated, open chain movement. This suggests that the integration of vestibular, somatosensory, and visual feedback is an important determinant of the magnitude of the long latency reflex during upright stance.

During the lowest resistance conditions (5% BW) activity tends to be slightly increased in the lateral hamstrings. However, the same muscle group is inhibited in all other conditions (Fig. 5B). This indicates that when resistance is low a slight increase in joint stiffness may be the optimal strategy to prevent further error, and indeed does provide the least error within each velocity (Fig. 4A). As resistance increases, however, stiffening is no longer an optimal strategy thus the hamstrings demonstrate increasing inhibition, allowing the increasing activity of the quadriceps to slow (or reverse) the fall of the individual. Previous investigations have discussed the multi-system nature of both spinal and supra spinal inhibition during the long latency period of a perturbation (Cheney & Fetz, 1984; Leonard, Sandholdt, & McMillan, 1999; Manning, McDonald, Murnaghan, & Bawa, 2013; Matthews & Miles, 1988). Our study is consistent in that there is a clear trend of antagonist inhibition scaled with resistance (muscle activation) of both the agonist and antagonist during the stretch response.

The presented testing paradigm demonstrates that under each testing condition, learning occurs very rapidly (Figure 3B). This is advantageous to achieve an accurate measure of an individual's ability to perform in a short time, allowing for a potentially clinically feasible assessment. Currently in the clinic, a combination of multiple tests is necessary to predict disability, e.g. falls in the elderly (Billington, Fahey, & Galvin, 2012; Morris, 2007), or return to play in the ACL reconstructed athlete (Barber-Westin & Noyes, 2011; Cascio, Culp, & Cosgarea, 2004; van Grinsven, van Cingel, Holla, & van Loon, 2010). In this testing paradigm, the shortest testing condition (0.6 Hz) lasts 8.3 s and the longest (0.2 Hz) 25 s; allowing collection of all nine conditions in under 10 minutes. This novel weight bearing test provides a quantitative assessment of both feed-forward and feedback control (motor function) of the lower extremity through a range of conditions in a very short amount of time.

CONCLUSIONS

In this study we have presented a hierarchical framework (range of task difficulties) to assess feed-forward and feedback control during a functional weight-bearing, visuomotor task. The rapid ability to achieve intra-individual proficiency (within 3 cycles), speed of testing (each condition in under 30 s), and the ubiquitous nature of the partial single limb squat, provides the prospect of a framework to measure feed-forward and feedback control in people with and without gait and posture impairments.

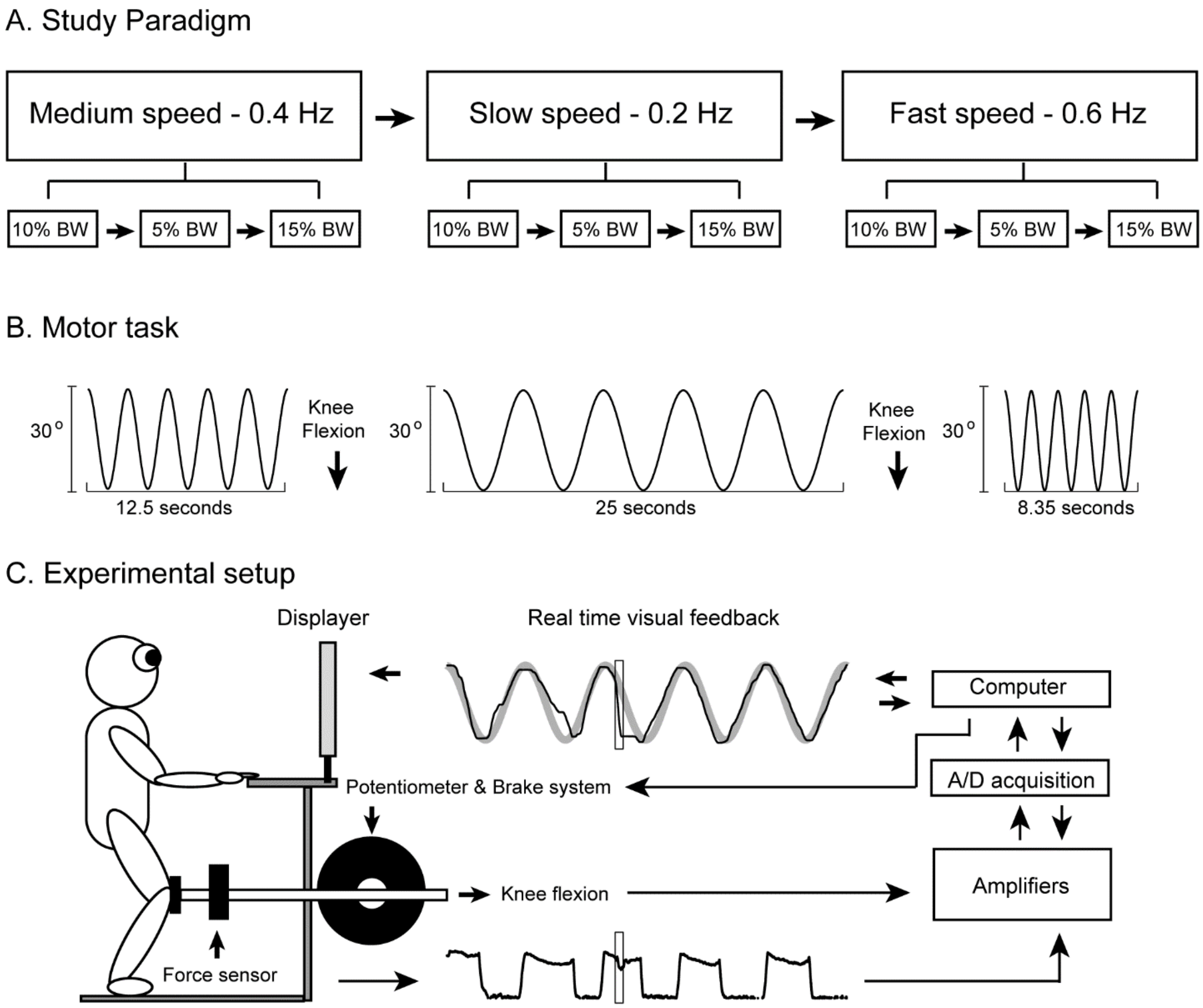


Figure 2.1 Illustrations of Study Paradigms (A), motor tasks (B), and experimental setup (C). Nine testing conditions (3 speeds × 3 resistance levels) were assigned to each subject in order: the medium speed in combination with three levels of resistance, the slow speed in combination with three levels of resistance, and the fast speed in combination with three levels of resistance (A). The motor task consists of five cycles of the sinusoidal waveforms (i.e. target signal) set at three pre-determined frequencies: 0.2, 0.4, and 0.6 Hz, corresponding to slow, medium, and fast movement speeds (B). The target signal corresponded to ~ 30 degrees of knee flexion and knee extension. Subjects were instructed to track computer generated sinusoidal targets as they performed a single limb squat exercise (C). Instantaneous visual feedback of actual knee position (the black trace) was provided to subjects on the same monitor as the target trace (the gray trace) (C). The brake system was turned off for a pre-determined period of time within a cycle to produce a perturbation. The rectangle overlaid on sinusoidal signals indicated the time period when the resistance was released. The bottom traces depicted force readings over time (C). BW: body weight.

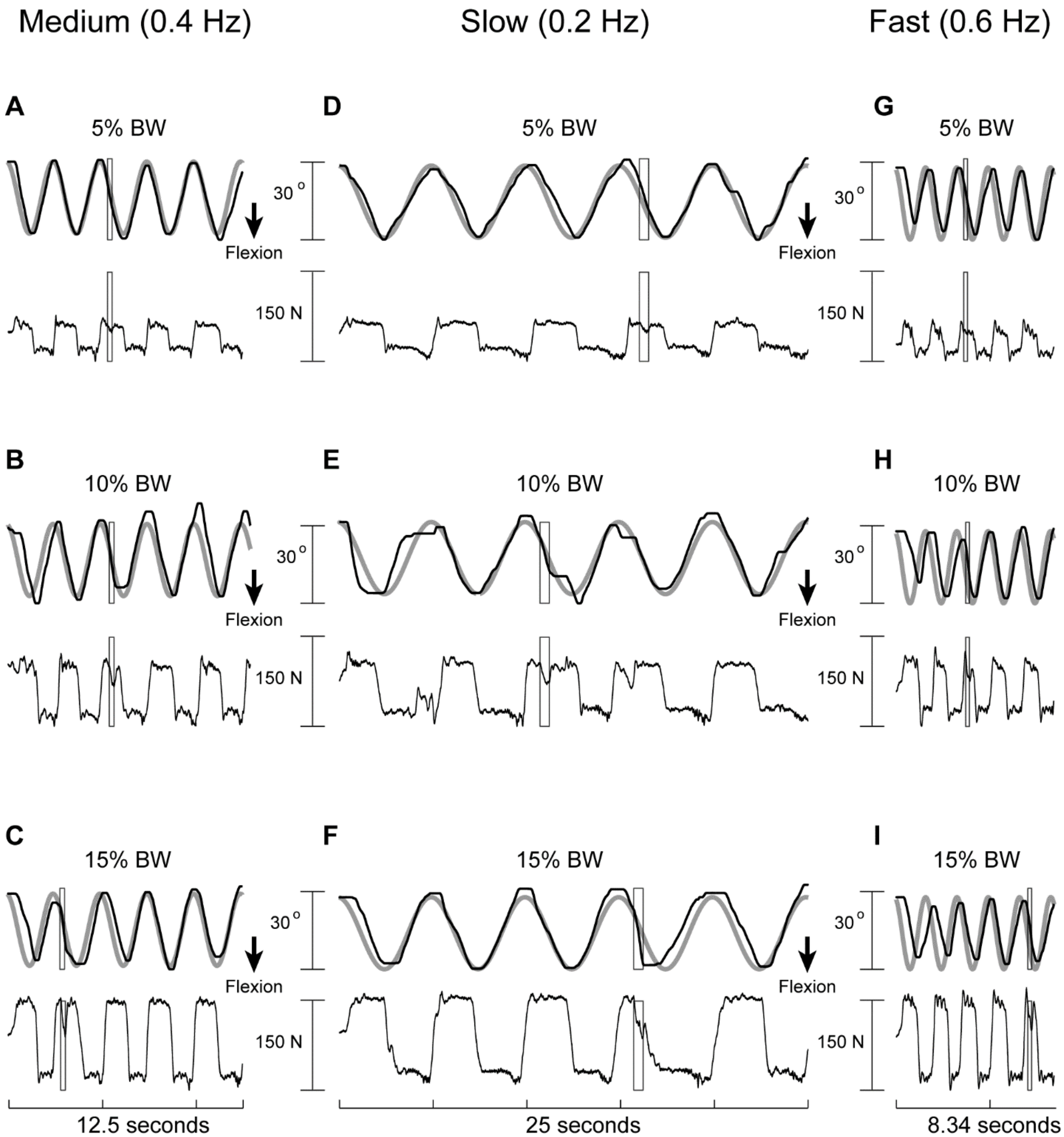


Figure 2.2 Motor Performance from a Typical Participant Across Nine Testing Conditions. Time series data of user's signals (black traces) overlaid with target signals (gray traces) across three speeds (slow, medium, and fast), with three levels of resistance (5%, 10%, and 15% BW) in each (Upper traces in **A- I**). The peak-to-peak amplitude of target signal corresponded to 30 degree of knee flexion to full knee extension and was consistent across all testing conditions; whereas the amplitude of force was scaled to the level of brake resistance (lower traces in **A- I**). Accordingly, the greatest force amplitudes were observed during conditions with the 15% of BW resistance (**C**, **F**, **I**). Rectangles indicate the time periods when the break resistance was removed. Note that the break release perturbed ongoing knee motion and force production. BW: body weight.

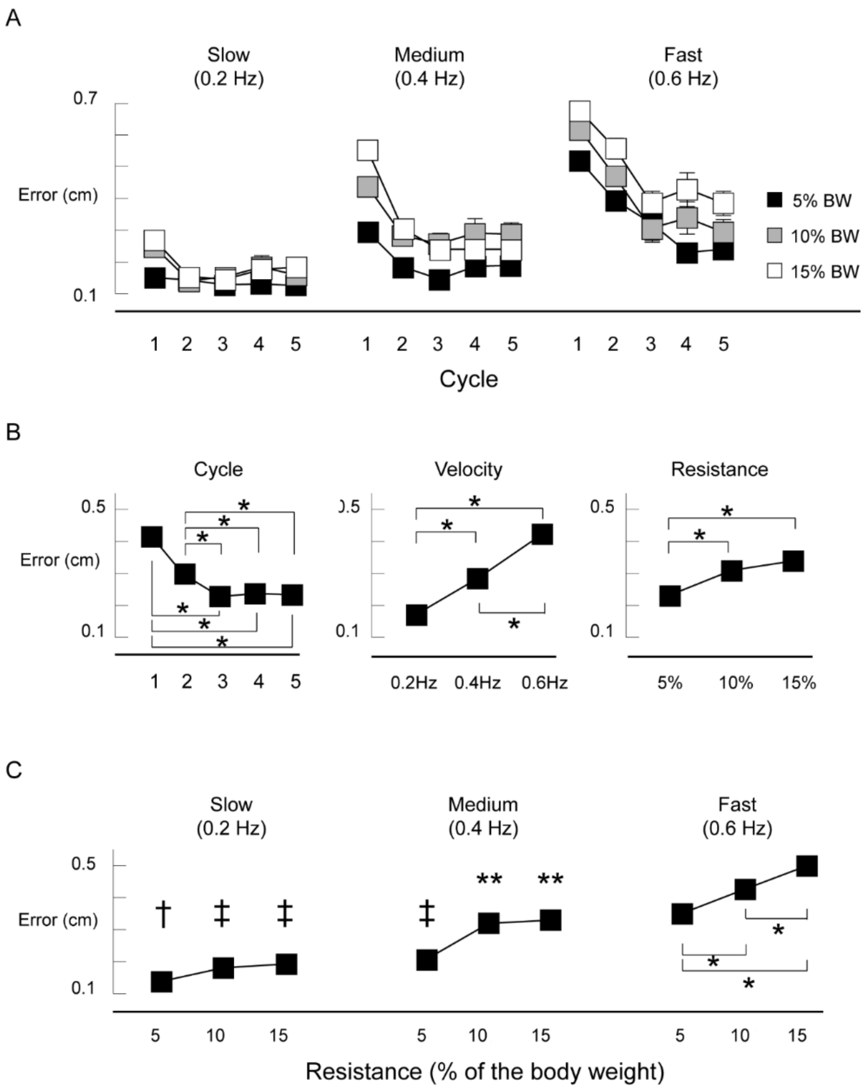


Figure 2.3 Group Averages of Root-Mean-Square (RMS) of Errors During Non-Perturbed Cycles. RMS errors were averaged over all subjects for each non-perturbed cycle within each condition (**A**). Recall that there were nine conditions, five cycles per condition. To determine factors that might influence movement accuracy, RMS errors were averaged across cycles, velocity, and resistance (**B**). In order to quantify the combination effect of velocity and resistance on movement accuracy, RMS errors were averaged across all non-perturbed cycles in each condition for each subject, and were then averaged over all subjects for statistical comparisons (**C**). Error bars, ± 1 SEM. BW: body weight. *: significant post-hoc differences between pairs of comparisons. †: significant post-hoc differences between the denoted condition (i.e. 0.2Hz, 5% BW) and all conditions at the medium and fast speeds. ‡: significant post-hoc differences between each denoted condition and conditions at the medium speed with 10% and 15% BW resistance, and all conditions at fast speeds. **: significant post-hoc differences between each denoted condition and conditions at the fast speed with 10% and 15% BW resistance.

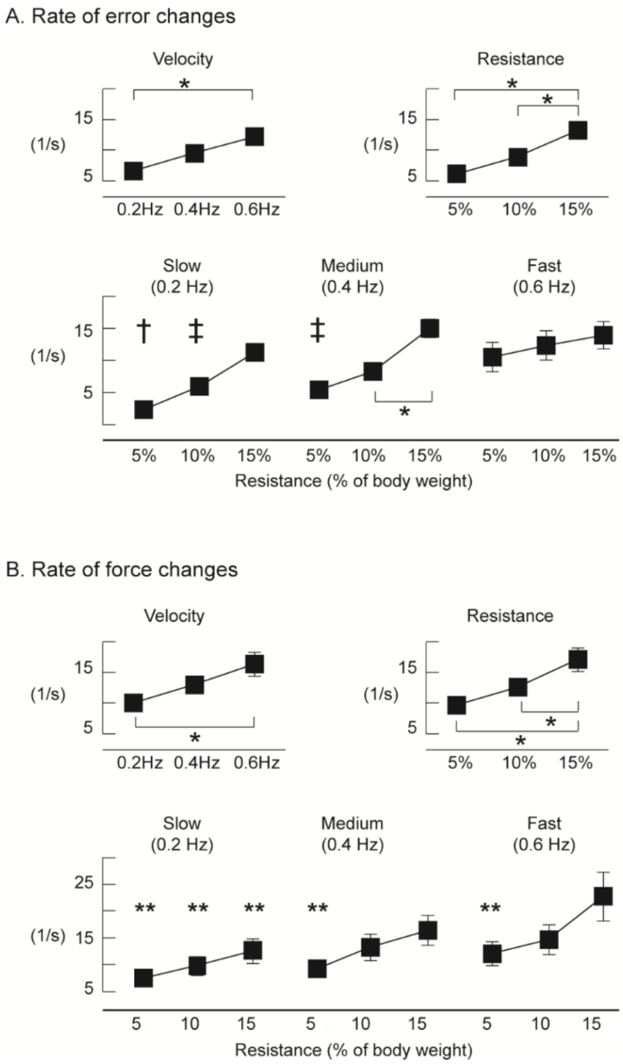


Figure 2.4 Group Averages of Rates of Error and Force Changes Across All Perturbed Cycles. Each data point is expressed as the rate of error change (**A**) and rate of force change (**B**) during the perturbation (i.e. time period of break release). Notice that absolute changes in error and force obtained during the perturbation period were divided to its corresponding perturbation duration and expressed as rates of error or force changes. To examine perturbation effects across different conditions, we normalized rate of error and force changes to the average of absolute change of error and of force during the non-perturbed cycles in each condition (lower panels in **A** and **B**). To determine factors that might influence movement accuracy, rate of error and force changes were averaged across velocity and resistance (upper panels in **A** and **B**). Error bars, ± 1 SEM. *: significant post-hoc differences between pairs of comparisons. †: significant post-hoc differences between the denoted condition (i.e. 0.2Hz, 5% BW) and all other conditions. ‡: significant post-hoc differences between each denoted condition and all conditions with 15% BW resistance. **: significant post-hoc differences between each denoted condition and the condition at the fast speed with 15% BW resistance. BW: body weight.

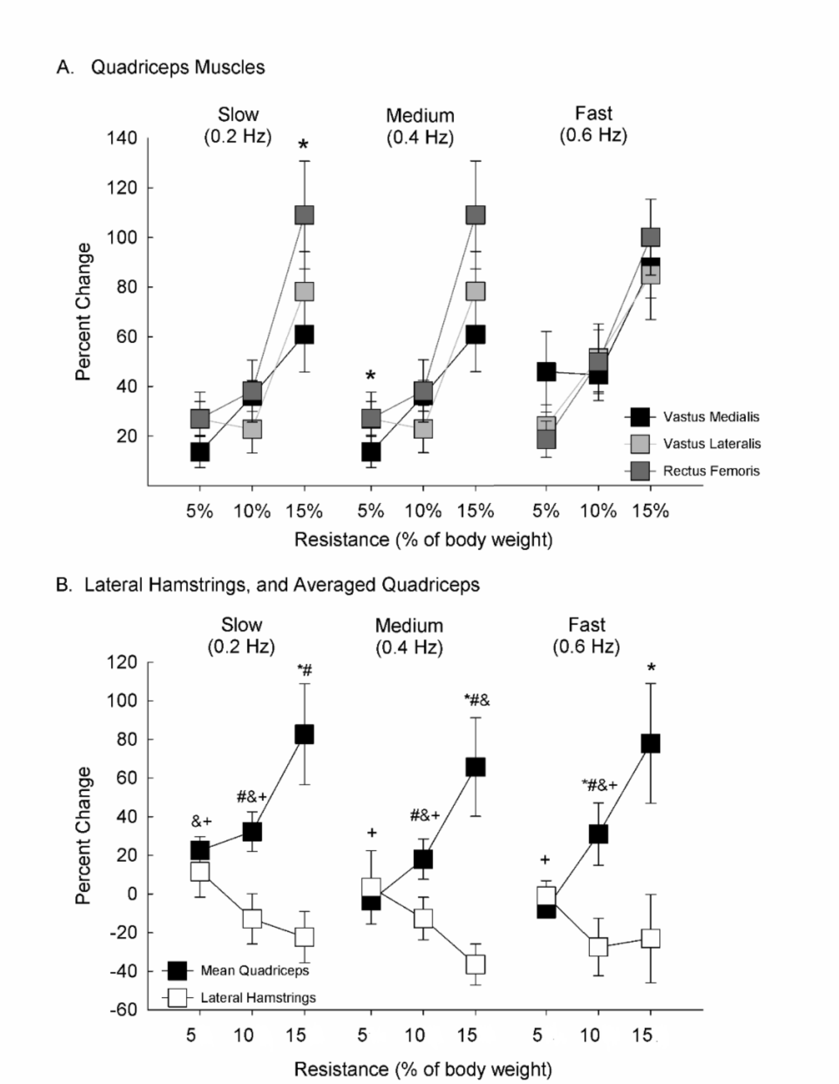


Figure 2.5 Percent Increase of the Perturbed from the Non-Perturbed Electromyography of the Agonists and Antagonists. Percent change of the electromyography of the long latency period of the perturbed cycle vs the equivalent time period of the non-perturbed cycle. Three of the quadriceps muscles were measured (**A**) including the Vastus Medialis (black square), Vastus Lateralis (Light gray square), and the Rectus Femoris (dark gray square). Due to motor equivalence of the quadriceps, activity from all three muscles was averaged (black square) and represented with the lateral hamstrings (white square) (**B**). The symbol '*' denotes significant differences between rectus femoris and vastus lateralis ($p<0.05$). In panel B, symbols (*, #, &, +) represent post hoc groupings of conditions. For example, * represents that electromyography activity under combinations of speed + percent body weight resistance of: 0.2Hz + 15%, 0.4Hz + 15% BW, 0.6Hz + 10% BW, and 0.6 Hz + 15% BW are significantly different the other speed + resistance combinations ($p<.05$). There was no statistical difference between conditions of the lateral hamstrings ($p>0.05$).

CHAPTER 3: SPEED AND RESISTANCE IMPACTS PERFORMANCE IN OLDER ADULTS DURING A NOVEL WEIGHT-BEARING VISUOMOTOR TASK

INTRODUCTION

Injury to older adults during weight-bearing activities are estimated to account for over $18 billion in annual healthcare costs (Stevens et al., 2006). Injury occurs when the nervous system is perturbed and fails to predict the correct level of stiffness (muscles) to control the altered velocity of the movable parts (joints) during weight-bearing activity. Strategies for movement control consist of both a feedforward component and a feedback component. Most studies support that these two components work in concert to optimize movement control. Many studies on movement control are restricted to a single joint, open chain (non-weight-bearing) movement with primary somato-sensory feedback control. Under single joint, open chain movement the CNS uses feedforward and feedback control strategies to optimize movement. In this study, we examine if similar control strategies are deployed during a multi-segmental weight-bearing task and whether these strategies are influenced by age.

When we slowly move the upper extremity toward a target, the nervous system can rely on somato-sensory feedback (position sense) to update the feedforward plan; while during faster movements, because of conduction time constraints, reliable velocity information is extracted and used to predict a control strategy (P. Cordo et al., 1994). During a reaching task, velocity is modulated based on the ability to decelerate the limb in order to reach the target/object accurately (Cooke et al., 1989; Darling et al., 1989; Williams, Jasiewicz, & Simmons, 2001). As we age, our volitional peak velocity decreases, and the time for deceleration increases in order to be accurate with the movement (Cooke et al., 1989; Goggin & Meeuwsen, 1992; Ketcham, Seidler, Gemmert, & Stelmach, 2002). Importantly, it is not the ability to move fast that is driving the motor strategy, as older people can generate similar velocity movements as younger people. Rather, the goal to be accurate requires that the velocity of the movement be adjusted (N. Walker et al., 1997). When performing a non-linear task (unlike reaching to a single point), coherence is a measure of the ability to match the velocity component (sine wave frequency); while peak error, or the maximum difference between a known target and the actual movement, is indicative of when to change the direction of movement. Precise velocity control may still render imprecise peak error and vice-versa, prompting us to explore how these two components of movement control change with age.

During visuomotor tasks older individuals lose the ability to predict faster movements (Newell, Mayer-Kress, et al., 2009), and to accurately control single and multi-joint force production (Christou et al., 2003). Thus, varying both force and velocity of a movement creates several layers of task difficulty as we age. In support of this view, assessments of visuomotor error are used to determine damaged neural substrates associated with neurological disease (Hocherman, Alexandrovsky, Badarny, & Honigman, 1998; Inzelberg, Schechtman, & Hocherman, 2008). However, there is limited information regarding the extent to which these same principles apply to a weight-bearing task (non-postural) across the lifespan. Accordingly, we propose to examine young (20-39), middle (40-59), and older (60-79) adults in this study.

A final test of movement control pertains to the ability to respond to an unexpected event. The central nervous system uses initial task conditions and feedback to optimize movement, especially after unexpected events. For example, when we are stepping off of a curb and we predict the wrong height thus loading the leg earlier than predicted, the central nervous system responds before conscious volitional reaction time. The short latency response occurs in under 30-50ms (Burke et al., 1970); while a long-latency response occurs later (>50ms) but before a volitional reaction time (200ms) can influence the response (Matthews, 1986). Due to the long latency response occurring *before* the influence of volitional correction, the long latency response is a window into feedback control mechanism of the movement system. The long latency response is intricately linked to the intention of movement (Calancie & Bawa, 1985; Colebatch et al., 1979; Hammond, 1956; Nashed et al., 2015; Weiler et al., 2015), and is thought to involve trans-cortical pathways (Leukel, Taube, Lorch, & Gollhofer, 2012; Matthews, 1986; Zuur et al., 2010). Currently, few reports have addressed the effects of age on error associated with unexpected events during a weight-bearing task.

Accordingly, the purpose of this study was to examine the effects of age on nervous system control during a functional weight-bearing task. By focusing on measures of velocity matching (coherence) and absolute error (peak and mean error) during both expected and unexpected events we predict that age leads to differential changes in each of these movement control systems. Specifically, we expect that velocity control, as measured by coherence, deteriorates before amplitude control as measured by peak error and mean error. This knowledge will assist us in delivering more precise rehabilitation interventions to delay age-related declines in movement control.

METHODS

Participants

Ninety-four subjects participated in this study. Subjects were between the ages of 20 and 80 years old and were divided into three age groups: 20-39 years old, 40-59 years old, and 60-80 years old. These ages represent young adult, middle-aged adult, and older adult, respectively. Both males and females were included in this study, with 23 males and 25 females in the 20-39 year old group, 6 males and 22 females in the 40-59 year old group, and 9 males and 9 females in the 60-80 year old group. Exclusion criteria were self-reported neurologic deficits, musculoskeletal disorders, knee pain in the last 6 months, and osteoarthritis of the knee. All subjects signed an informed consent document approved by The University of Iowa human subjects review board following an explanation of the experimental protocol.

Experimental Protocol and Instrumentation.

Custom designed hardware and software were used for this study and has been previously described (Ballantyne & Shields, 2010; Madhavan et al., 2009; Shields et al., 2005; Tseng et al., 2016). Briefly, a rack and pinion gear and braking device controlled by a microcomputer resists and records linear displacement of knee flexion and extension during a single limb stance. During the task, a sinusoid waveform is traced on a computer monitor at a speed according to software input, while concurrent display of the linear displacement of the knee provides real-time feedback. Knee flexion range of motion was approximately 0-25 degrees, with a linear translation at the knee of 9.7 cm. This, therefore, creates a visuomotor task of the lower extremity in a single limb squat. Computer controlled resistance and velocity then create different levels of difficulty of the visuomotor task. (Figure 1B)

To secure each patient into the apparatus, the right knee was strapped to a horizontal shaft that is connected to the braking mechanism. The patella was placed comfortably against a pad at the end of the shaft that allows for vertical translation associated with knee flexion and extension in a standing position during the task. The patient was instructed that even though this is a single limb task, they could use light finger-tip touch for balance. Previous studies have demonstrated that less than 2 N force is used by patients when allowing one finger-tip touch during a similar task (Madhavan et al., 2009).

Once secured into the apparatus, and a detailed explanation of the task was given, each subject was allowed no more than 5 trials to become accustomed with the visuomotor task and the instrumentation. These were similar to the testing protocol, in that it consisted of a 5-cycle sine wave, and always started in the knee flexion direction from full knee extension. All familiarization trials were performed at 0.4 Hz, and 10% of body weight (BW).

Once the subject reported understanding the task and being comfortable with the instrumentation, testing was initiated.

The testing protocol consisted of 9 different trials where during each trial a 5-cycle sine wave was projected onto a computer screen (Tseng et al., 2016). During each trial the conditions were changed, delivering different combinations of movement rate (target frequency) and resistance at the knee as a percentage of body weight (BW). Conditions consisted of all 9 combinations of three resistances (5% BW, 10% BW, and 15% BW) and three speeds (0.2 Hz, 0.4 Hz, and 0.6 Hz). (Figure 1A) The nine conditions were pseudo-randomly presented during testing to eliminate order effect of difficulty. During each of the 9 trials, resistance was constant according to the programmed percent body weight, though a perturbation was delivered during one cycle of each trial by momentarily dropping the resistance to 0% BW (the brake was released) with no cueing to the subject as to when this would occur. Duration of the perturbation depended on the speed of the task (400ms at 0.2Hz, 250ms at 0.4 Hz, and 200ms at 0.6 Hz). This allowed for an unexpected perturbation to knee flexion (downward) with a consistent displacement of the knee for each condition of testing.

Data Analysis

Data collection of the visuomotor task was first performed by sampling the user displacement and axial force in custom software at 2000 Hz. Files were transferred to a desktop computer, and analysis of the user performance was performed in DIAdem Software (Version 12.0). The performance of an entire trial was measured with metrics of peak error, mean absolute error, and coherence.

Peak error is defined as the maximum error occurring during the trial, and excludes the perturbation and first cycles to eliminate the effect of the perturbation and the ability to "get on track", from the visuomotor performance. Mean error is the absolute value of the difference between the user and target signals divided by the number of samples. Coherence between two signals x(t) and y(t) is defined as the equation:

$$|C_{xy}(f)|^2 = \frac{|G_{xy}(f)|^2}{G_{xx}(f)G_{yy}(f)}$$

Where $G_{xy}(\lambda)$ is the cross-spectral density between x and y, and $G_{xx}(f)\ and\ G_{yy}(f)$ are the auto-spectral density of x and y, respectively.

It is the magnitude squared of the cross spectrum of the user and target signals, divided by the autospectrum of the user signal multiplied by the autospectrum of the target signal (Halliday et al., 1995). The coherence is a value between 0 and 1, where 0 is a completely non-related signal, and 1 indicates a linearly matched signal. The coherence measure is used to represent the ability of the user to match the frequency of the sinusoidal task.

During the perturbation portion of each cycle, time bins were created according to physiologically relevant periods. The short latency reflex has been demonstrated to occur 0-50ms following a perturbation due to the stretch of the antagonist muscle, here the quadriceps, and the long latency has been demonstrated to occur between 50-200ms following a perturbation. The pre-perturbation period is associated with the motor plan of the individual right before the perturbation, whereas the volitional feedback portion occurs greater than

200ms after the perturbation. Time bins are thus defined as pre-perturbation: 50 to 0ms before release of the resistance, short-latency time period: 0 to 50ms after release of the resistance, long-latency time period: 50-200ms after release of resistance, and post-perturbation response time period: 0 to 150ms following cessation of the perturbation period by return of the resistance to the trial-determined percent body weight.

For each of the perturbation time bins described, variables were calculated including: Knee flexion rate, force rate, and error rate. The constant and absolute error is inherently flawed for these analyses, as the starting position will affect the magnitude of the error during the perturbation. To eliminate this, rates were utilized to determine the effect of the perturbation on the subject's performance. Knee flexion and force rate were calculated in DIAdem by the best fit line of the time bin defined (all lines r-squared > 0.9). The error rate was defined as the best fit line of the resultant signal from the target signal minus the user signal during the time period defined. Force rate was normalized by individual's mass to allow comparison between subjects.

Statistical Analysis

Variables of peak error, mean error, cycle error, and coherence were analyzed using a split-plot repeated measures analysis of variance. Variables of knee flexion rate, force rate, and error rate were analyzed using a split plot, nested, repeated measures design. Significance level was set to 0.05, and statistical analysis was performed using SAS ("SAS," 2010).

RESULTS

Overall Trial Performance

All ages demonstrated an increase in peak error from the lowest trial velocity and speed (condition 1) to the highest resistance and speed (condition 9; Figure 3A). This relative increase in peak error was similar across age groups (age by condition interaction: 0.7579). From youngest to oldest, however, each age group progressively demonstrated larger peak error at each condition ($p<0.0001$). The older group experienced peak error 149% that of the young individuals (Figure 3A). Mean error demonstrated a similar trend of having the same relative increase in difficulty from condition 1 to 9 for all age groups (Figure 3B), and increasing error with increased age ($p<0.0001$). The older age group experienced an increase in mean error of 70% from the younger age group.

The measure of coherence demonstrated a slightly different result, where older and middle-aged individuals had coherence levels approximately 67% that of the young adults ($p<0.05$). The relative effect of the progression from condition 1 to condition 9, however, was similar for all age groups (interaction: $p>0.05$), each having a 74% decrease in coherence from the slowest and lightest resistance to the fastest and heaviest (Figures 3C). Interestingly, the younger group demonstrated a higher coherence than the other ages ($p<0.0001$), though there was no difference between coherence levels of trials for the older and middle-aged groups (post-hoc $p<0.05$). To ensure that a systematic delay in the capacity of the older individuals to follow the target signal didn't contribute to increased error, cross correlation of the signal was also calculated. It was determined that there was no statistical difference between the time of the greatest correlation for all groups ($p=0.89$). There was a velocity effect on the time of greatest cross correlation where the mean of the 0.6 Hz conditions (0.33 seconds) was 10 times that of the slower conditions ($p=0.92$).

Perturbation Performance

The effect of a force perturbation (brake released unexpectedly) was analyzed using the variables of knee flexion rate, error rate, and force rate. A very similar trend is readily observed (Figure 4) for all variables, though each parameter resulted in slightly different outcomes. Knee flexion rate (velocity) during the pre-perturbation period (the time period of 50ms before the brake was released), the time period consistent with the short latency reflex (50ms after the brake was released), and volitional correction (200-250 ms following release of the brake) demonstrated no difference between age groups. Interestingly, however, 50-200ms following the perturbation older aged individuals were bending their knee at approximately 23% faster rate than the middle and young-aged adults (Figure 4A).

The rate of change in force during the perturbation was different in that the younger individuals were different from the older and middle-aged group. Here, differences occurred during the two periods of non-volitional feedback (0-200ms) following the perturbation (p's<0.05); younger adults demonstrated a greater reversal of force into flexion of 34% during 0-50ms, and 24% during 50-200 ms following perturbation delivery (Figure 4B). Force generation before and after the perturbation, however, was similar between all age groups (p's>0.05; Figure 4B).

The error rate demonstrated age difference during each time period of the perturbation, however. The pre-perturbation period and the 50ms after showed that older individuals perform with a higher error rate than the younger age group with nearly double the error rate (50-0ms: $p=0.0016$, 0-50ms: $p=0.0003$). During the 50-200ms time period, there was a difference between all age groups; error rate increased as age increased ($p<0.0001$). The older age group error was 119% and 157% that of the middle-aged and younger-aged groups, respectively (Figure 4C).

When examining the effects of the change in task resistance and velocity on the 50-200ms period following the force perturbation, each change in velocity and resistance has a similar effect on each age group (p's>0.05 for interactions for each of knee flexion rate, force rate, error rate). Higher velocities and larger resistances tend to produce larger error rates and higher knee flexion rates during the pre-volitional response of a force perturbation (Figure 5A and C). Interestingly, however, though there is a trend for increased age to have an incremental increase in force rate as trial resistance increases, no real statistical trend was discovered (Figure 5B).

Though we have presented data where an effect of age is suggested, results may be confounded by the effects of overall task performance on the perturbation responses. As previously discussed in this section, older adults consistently performed worse with increased peak and mean error, and decreased coherence. To determine the effects of age on perturbation responses without the interaction of visuomotor task performance, we stratified each individual trial by coherence and by mean error of the four cycles where a perturbation did not occur. Coherence was chosen as it is inherently an indication of linearity between the user signal and the target signal (Halliday et al., 1995). The 99% confidence level of coherence (0.4005) is used to separate trials with high and low coherence, termed ‘coherent’ (good performers) and ‘non-coherent’ (poor performers), respectively. This is calculated by the equation:

$$1-(1-\propto)^{1/(L-1)}$$

Where α is the probability of type I error (here, α=0.99), and L is the number of cycles analyzed. Figure 2 provides representative examples of a visual representation of how performance affects coherence and peak error.

Coherence may be biased toward the ability to match the velocity (frequency) component of the task as observed in representative examples of Figure 2. We therefore also stratified performers based on the 99% confidence interval of the mean of each of the conditions. Low error was determined to be those below the mean plus the confidence interval, whereas those above were determined to have high error. When stratifying performance of each age group by trial coherence and mean error, the perturbation bins were analyzed using the same dependent variables of knee flexion rate, error rate, and force rate. Due to increased incidence of coherent and low error trials during slower speeds (and non-coherent and high error during faster speeds), unweighted means are presented when averaging across conditions (Figures 6 and 7).

Using this stratification, error rates were greater for poor performers at every age group regardless of being stratified by unperturbed cycle error or coherence ($p<0.05$, Figures 6C and 7C). Further, during the 50-200 ms following a force perturbation, the older poor performers (stratified by both unperturbed error and coherence) demonstrated greater error rates than the young and middle-aged adults. Older adults experienced greater error rates during the 0-50 ms following perturbation only when stratified by coherence. Both performance metrics were also able to show that even older adults that were good performers continued to demonstrate greater error rates compared to young and middle-aged performers (p's<0.05, Figures 6C and 7C).

Knee flexion rates were only different between groups during the 50-200 ms following the onset of a perturbation. When stratifying by coherence, poor performers (non-coherent) always had greater knee flexion rates than good performers (coherent), with older performers experiencing the greatest flexion rates compared to younger adults. Older poor performers experienced the overall greatest knee flexion rates with 47% greater speed than the best performing group (Figure 6A). When defining trial performance by unperturbed cycle error, however, perturbation differences between good (low error) and poor (high error) did not exist between all groups (p's>0.05), though older aged individuals did experience greater knee bending rates than their younger counterparts in both the good and poor performing groups. Again, older poor performers experienced the greatest bending rates with 40% greater degrees per second of knee flexion compared to the best performers (Figure 7A).

Rate of change of force during the perturbation also reveals differences between groups only at the 50-200ms period following a force perturbation.

Negative force rates indicate that the individual is pulling into extension (the opposite of the flexion during the fall of the perturbation), thus a greater negative force rate indicates a greater ability to counteract the fall into flexion induced by release of the brake providing resistance at the knee. When stratifying by coherence, differences exist between good and poor performers at each age group, with the younger age demonstrating the largest force rates compared to the young and middle-aged adults (Figure 6B). When determining performance by unperturbed cycles, differences are not apparent based on performance level for any time period (p's>0.05). Younger adults do demonstrate greater force rates during both the 0-50ms and 50-200ms periods following a perturbation with 45 and 27% greater extension force compared to older subjects, respectively (Figure 7B).

Trial Cycle Error

When examining the mean error of each of the 5 cycles of each individual trial, the young and middle-aged groups continue to improve in performance until they plateau during the third cycle (Figure 7A). The older-aged individuals, however, appear to not improve at all during the course of the 5 cycles (p>0.05). When separating full trials by performance in each age group as mentioned previously in this section, we can examine the learning that occurs during each trial for those trials in which individuals perform well (coherent or low unperturbed trial error) and those trials in which individuals perform poorly (non-coherent or high unperturbed trial error). There is a distinct difference in performance between the two groups no matter which method is used to stratify overall trial performance (Figures 8 B and C). The younger age group regardless of good or poor performance improves in error until plateauing at the 3rd cycle, whereas the older aged good and poor performers demonstrate no improvement at all from the first to the last cycle ($p>0.05$). The middle-aged adults differ, however, where good performing middle-aged adults plateau after 2 cycles, and poor performers don't plateau in improvement until the third cycle of each trial. In each of the young, middle and older age groups, poor performers experience greater error from the first cycle (74%, 61%, 50% greater, respectively) to the last (44%, 79%, 110% greater, respectively).

DISCUSSION

The major findings of this study were that when performing a weight-bearing, lower-extremity, visuomotor task: 1. The ability to control accuracy (peak and mean error) continue to change as we age, while velocity matching (coherence) deficits plateau in middle age, 2. Age has no effect on the hierarchical difficulty of combinations of resistance and velocity on a single limb squat, 3. Those who perform poorly (as defined by velocity matching and trial error) have greater error rates throughout the entirety of a force perturbation, 4. During the 50-200ms period following the start of an unexpected event, subjects over 60 years old experience greater knee flexion rates regardless of performance, additionally, velocity matching of the task predicts those with faster-falling rates in all age groups, and 5. Older individuals lack the ability to improve error within a trial (5 cycles), while middle-aged and young adults demonstrate the ability to improve task error during a single trial.

In this study, we were able to determine that age affects performance measures of coherence (velocity matching), and mean and peak error (magnitude of error) differently. This suggests that the methods used by the nervous system to control the accuracy of movement may deteriorate at different rates. This finding is consistent with previous upper extremity studies discussed, where velocity and acceleration profiles are sacrificed to maintain accuracy during aging, until finally both accuracy and velocity are unable to be controlled (Cooke et al., 1989; Darling et al., 1989). This is also similar to an open chain, lower extremity study of the knee where younger and middle-aged adults were better performers than older adults, measured in absolute error during an open-chain, 0.43 Hz tracking task (Williamson & Marshall, 2009).

Age-related changes in the sensorimotor system contributing to this are many. In older age tactile sensitivity diminishes (Thornbury & Mistretta, 1981), type II muscle fibers decrease in cross-sectional area (Lexell, 1995; Lexell et al., 1983), degradation of the neuromuscular junction occurs (Jang & Van Remmen, 2011), and the ability to accurately produce and maintain isometric and isokinetic forces diminishes (Larsson et al., 2001; Newell, Liu, & Mayer-Kress, 2009; Tracy, Maluf, Stephenson, Hunter, & Enoka, 2005). Proprioception also diminishes where older adults have decreased static position sense, increased reaction time, and decreased processing time (Aparicio et al., 2002; Madhavan & Shields, 2005). It has been shown that when a movement requires faster velocities, the difficulty of a motor task increases. The increased difficulty is due to diminished ability of older adults to control deceleration of their limb to accurately reach the end-point (Cooke et al., 1989), and to anticipate the arrival of the visuomotor feedback of the target (Haywood, 1980). All of these factors contribute to the complexity of the age-related decrement in motor performance.

Interestingly, although age-related changes resulted in altered performance, there was no difference in the effect of altering velocity and resistance on the relative difficulty of the task between age groups. This was contrary to our hypothesis, though is most probably explained by the possibility that the three velocities (0.2 Hz, 0.4Hz, and 0.6 Hz) and resistances (5% body weight(BW), 10%BW, and 15%BW) chosen for the study are on a portion of the curve where older adults may not perform as well as younger individuals, though is not extreme enough to demonstrate a dramatic decrement in the velocity or error strategy. This is further supported by the slower speed of the target compared to age-related coincidence-anticipation studies. Typically, the visual target in these studies will be between 2 and 5 mph (Haywood, 1980; R. Kim, Nauhaus, Glazek, Young, & Lin, 2013; Millslagle, 2000; Williams & Jasiewicz, 2001; Williams et al., 2001; Wrisberg & Ragsdale, 1979), where maximum speed of the visual path in this study is only 0.5 mph. Further, force control studies in older adults are also primarily isometric in nature (Christou et al., 2003), not having the benefit of change in the gamma motor system and proprioception to update the control strategy. The additional gamma motor system input may provide enough information to create the relative similarity in difficulty provided by increases in velocity regardless of previously documents age-related slowing.

Force Perturbation

During this study, an unexpected force perturbation was delivered randomly during one of the knee flexion phases. We were able to show that the older age group experiences larger knee flexion and error rates during the 50-200ms period following the onset of the perturbation, thus having a faster fall and greater error than the 20-59 year-olds. This suggests that during the time period associated with the long latency response of the lower extremity, older individuals are less able to control the speed of fall than their younger cohorts. Previous studies have identified that context and pre-activation is a major driver of the long latency response (Crago, Houk, & Hasan, 1976a; Matthews & Miles, 1988; Rothwell, Traub, & Marsden, 1980). Though we are not measuring muscle activation, we show that older individuals may have a different mechanical response regardless of similar pre-perturbation knee flexion rates, and similar context of performing the tracking task at the same velocity and %BW resistance as the younger aged.

Trial performance (error and velocity matching) may, however, be enough of a contextual and muscle activation difference to confound the age-related findings. Muscle activation patterns in the lower extremity reflect the progression of motor learning where muscle activation is greater, creating joint stiffness (co-activation) at early stages of motor learning (Shields et al., 2005). Findings regarding upper extremity movement even suggest that different regions of the brain may preferentially control aspects of control; the supplementary motor cortex (Macar, Coull, & Vidal, 2006; Mita, Mushiake, Shima, Matsuzaka, & Tanji, 2009; Tanji, 1994; Tanji & Shima, 1996) contributing sequential movement and timing (velocity control), and the cerebellum controlling precision of force and kinematics (Laforce & Doyon, 2001; Orban et al., 2010; Penhune & Doyon, 2005; Seidler, Purushotham, et al., 2002; Spraker et al., 2012; Yoon, Vanden Noven, Nielson, & Hunter, 2014). We therefore stratified performance by both coherence and error to assess potential contributions of each type of movement control. The 99% confidence level of coherence (velocity matching) determined good (coherent) and poor (non-coherent) performers, and the 99% confidence level of mean trial performance determined good performers (low error) from poor (high error) performers.

Knee flexion rate during the period consistent with the long latency response was greater (faster fall) for good-performing older adults when stratified by both coherence and trial error. Only when stratifying by coherence, however, is the knee flexion rate different between good and poor performers for all age groups. The same pattern occurs when analyzing force rate; stratifying by coherence reveals differences in force rate between all age groups. Both performance determinants, however, reveal that the force rate for young good performers reverses the fall to a greater extent than middle and older adults. The feedback response measure of error rate differed, however, where good performers, as determined by both performance measures, had lower error rates compared to poor performers at all ages. Both measures were also able to identify a greater error rate in older individuals during the period consistent with the long-latency response similarly.

The measure of coherence may actually be an indication of supplementary motor area (SMA) function. As mentioned previously, the SMA has been identified in the control of movement velocity and timing; reflecting the ability of the subject to match the velocity components of the sinusoidal signal component of the task. Further, the SMA has also been indicated in affecting the gain of the long latency reflex by influencing the context or intended plan of movement (Spieser, Aubert, & Bonnard, 2013; Tanji & Taniguchi, 1978; Tanji, Taniguchi, & Saga, 1980). It has even been suggested that connections exist between the SMA and the primary motor cortex, as well as directly between the SMA and the corticospinal tract (Chen, Entakli, Bonnard, Berton, & De Graaf, 2013; Spieser et al., 2013), influencing the amplitude of muscle activity during a perturbation and allowing a path to rapidly express influence on motor output.

A plethora of other cerebral regions are identified in contributing to motor performance and are reflected in the general measure of overall trial error. Several of these brain regions are also implicated in affecting the capability to produce, and the gain of the muscle response during the long latency period including the primary motor cortex (Bonnard et al., 2004; Kimura, Haggard, & Gomi, 2006; Spieser, Meziane, & Bonnard, 2010), and the cerebellum (Claus, Schocklmann, & Dietrich, 1986; I. Kurtzer et al., 2013). In this study, however, we found that coherence of an individual trial was able to identify those who experienced faster falls during a perturbation at all ages where stratifying by overall trial error was not. This suggests that a motor plan that reflects greater accuracy regarding the velocity component of a movement, quite possibly involving SMA function, will result in improved control during an unexpected force perturbation.

Aging, however, is associated with many peripheral and biomechanical changes. As humans age, there is a reduction in the number of motor units (Campbell, McComas, & Petito, 1973; Deschenes, 2011), decrease in stability of the neuromuscular junction (Deschenes, 2011; Hepple & Rice, 2016), slower cross-bridge dynamics (Hunter et al., 1999; Hunter, Todd, Butler, Gandevia, & Taylor, 2008; Vandervoort & Hayes, 1989), decreased Young's modulus of tendons (Narici, Maffulli, & Maganaris, 2008; Narici & Maganaris, 2007), fewer actin-myosin cross bridges (D'Antona et al., 2003), and reduction in fascicle length and pennation angle (Morse, Thom, Birch, & Narici, 2005; Scaglioni, Narici, Maffiuletti, Pensini, & Martin, 2003) all resulting in a possible delay in and/or diminished amplitude of corrective force production of the muscle. Again, it may be that those who have the least peripheral changes, or those that are more adequately able to compensate for or adapt to these changes are those that both perform better on the task and respond more like the younger cohort during a perturbation.

Regardless of performance, force rate was greater in the younger individuals compared to the middle and older adults, and knee flexion rates were greatest in the older adults. Seidler, Alberts, and Stelmach (2002) demonstrated that older individuals perform an upper extremity reaching task by using greater agonist and antagonist muscle activity (stiffness) to improve error during a single joint motion, though when a multi-joint movement is performed stiffness actually decreases. This would then potentially cause a response that is different than the younger groups during the time consistent with the long latency period due to altered pre-activation. Perhaps a more probable explanation lies in age-related changes that occur both in the neural substrate of the long-latency loop and the effector (muscle). Structural changes of the brain regions that affect motor control are well documented, including atrophy in the basal ganglia (Walhovd et al., 2011), and the cerebellum (Cavallari et al., 2013; Hoogendam et al., 2012; Sullivan, Deshmukh, Desmond, Lim, & Pfefferbaum, 2000), to name a few. Emerging research is even pointing to the possibility of age-related differences in the connectivity between brain regions causing altered control (Bernard et al., 2013; Ferreira & Busatto, 2013). Though we have not identified the source of the difference in age-related control strategies, we are able to identify that poorer performing older adults do experience greater error rate and knee velocity after an unexpected event, thus having a potentially greater risk for injury.

Within-Cycle Learning

Within trial error was also examined to determine the ability of each age group to improve their error during each of the 5 cycles. Initially, it appears that the younger and middle-aged groups plateau in learning during the third cycle of the task, while the older adults don’t actually improve at all. When stratifying by good and poor performers (coherence and full trial error), a slightly different result appears. All young adults plateaued in error during the third cycle, and all older adults had no improvement in error regardless of being a good performer or a bad performer. The middle-aged group was different in that the good performers plateaued in improvements in only two cycles, while the poor performers continued to improve throughout all five cycles of the trial. As previously discussed, velocity and acceleration profiles are slowed in order to maintain accuracy. It may be that good performers in the middle-aged group have not yet lost the speed response that their poor performing counterparts have. Further, the fact that poor middle-aged performers continue to improve (though not to the magnitude as the younger age group) indicates that their ability to alter the speed-accuracy relationship has not completely deteriorated. The lack of improvement in the older age group, however, indicates that those over 60 remain with the inability to alter the speed-accuracy relationship in a short time scale.

Limitations and Future Directions

In this study, we did not account for body mass, fitness level, or functional status of participants. Even though only healthy individuals were included in this study, it may be that body mass or body fat percentage may have an effect on the performance due to the weight-bearing nature of the task. Future study directions may also determine what dose of training will lower the knee flexion rate of the non-volitional perturbation response, and if a lower knee flexion rate actually correlates with decreased injury rates of the knee.

CONCLUSIONS

In this study, we were able to demonstrate that both the velocity and trial error change with older age while performing a single-limb squat (0-25 degrees) to a visuomotor task. We demonstrated that differences in the velocity component of the control strategy plateau at middle age (40-59), while peak and mean error continue to increase with age. Altering the resistance and velocity of the task did create a variety of difficulty, though the relative effect on difficulty did not change between age groups. We also demonstrated that when an unexpected perturbation occurs during the flexion phase of motion, error and speed of knee flexion was much higher in those with poor trial accuracy at all ages. This means that when someone is fooled while performing a task poorly, they pay a price. Further, even older good performers experience greater error and knee flexion rates during the period consistent with the long latency reflex, meaning that when an older adult is fooled, they may have a greater risk of injury. This suggests that when performing rehabilitation or teaching a new skill, clinicians should ensure that a patient can perform a skill well before incorporating perturbations; specially to take extra caution with older adults. Further studies should be performed to determine the effects of training, activity level, and pathology on performance, injury, and age.

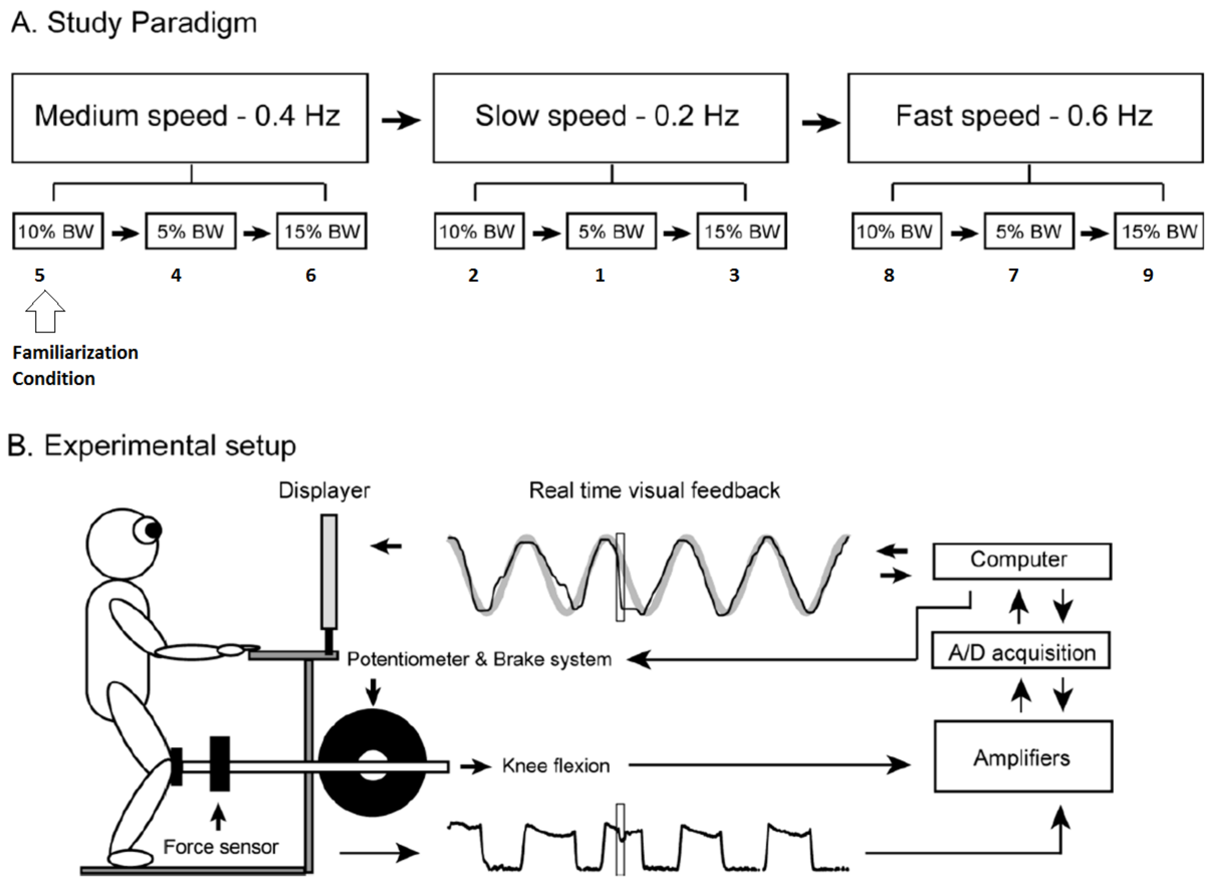
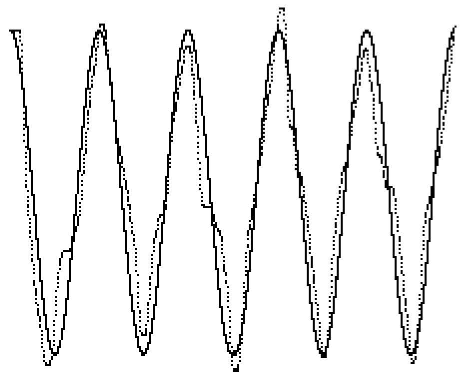
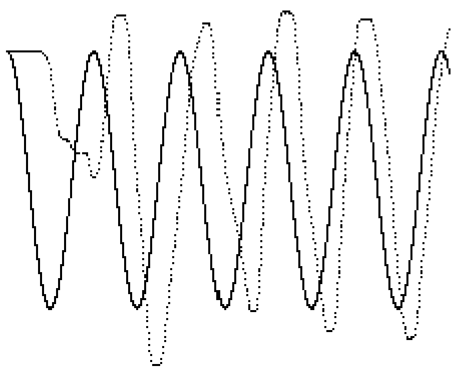


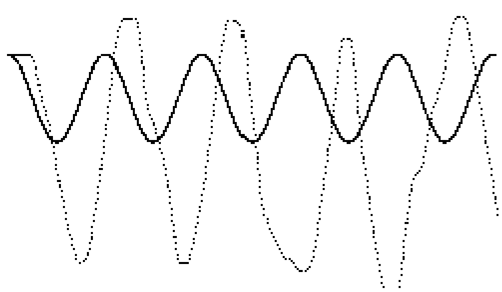
Figure 3.1 Visuomotor Task Experimental Setup. (A) Study paradigm of 9 difference testing conditions based on a combination of movement frequency (0.2 Hz, 0.4 Hz, and 0.6 Hz) and resistance as a percentage of body weight (BW; 5%BW, 10%BW, and 15%BW). Familiarization trials are performed at the medium frequency and medium body weight condition (condition 5). (B). Experimental set up of the visuomotor task. Real-time feedback regarding knee displacement of a single limb squat is provided concurrently with a computer-generated task according to the study paradigm.



A. High Coherence, Low Peak Error



B. Low Coherence, Low Peak Error



C. Low Coherence, High Peak Error

Figure 3.2 Representative Example of Coherence Levels: High coherence with low peak error (A), low coherence with low peak error (B), and low coherence with high peak error (C). For A-C, solid line is the computer generated target signal, dotted line is the user knee displacement, and the vertical dashed line denotes the start and end of the unexpected perturbation period.

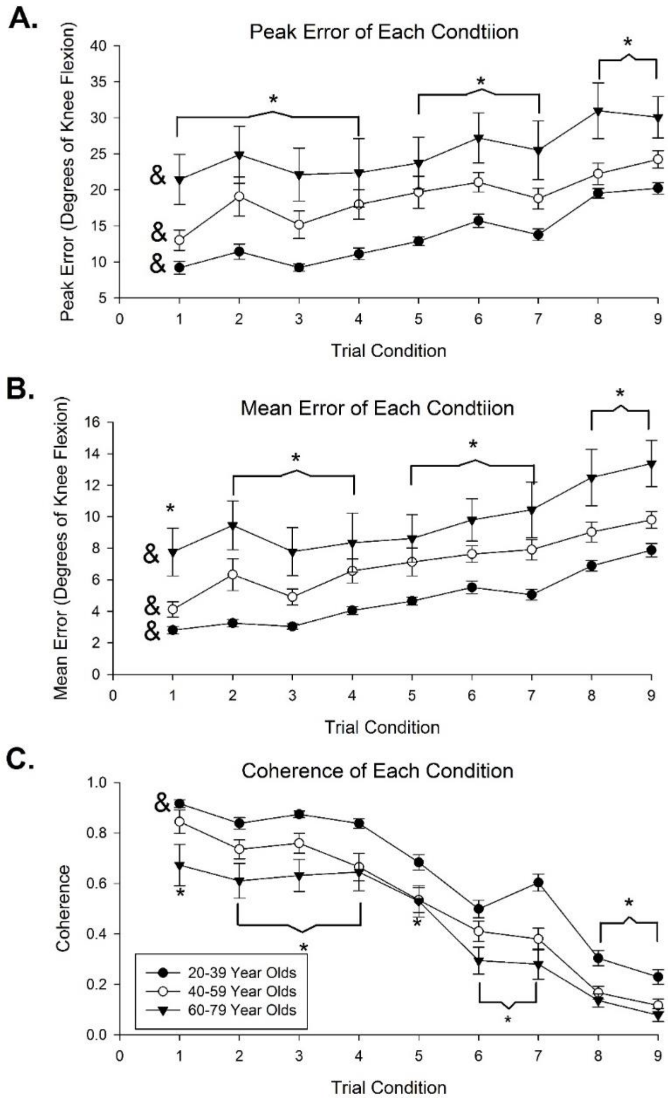


Figure 3.3 The Effects of Age on Performance During Each Testing Condition. Graphical representations of peak trial error (A), mean trial error (B), and mean coherence (C) of each age group at each testing condition. Closed circle represents the 20-39 year olds, open circle the 40-59 year olds and closed triangle the 60-79 year olds. Asterisk represents that the results of the condition are significantly different from the other conditions not included in the bracket ($p<0.05$). Ampersand indicates that the age group is significantly different from the others. Note that there is no interaction effect for AgeGroup x Condition ($p>0.05$) indicating that significant differences between conditions hold true for all age groups.

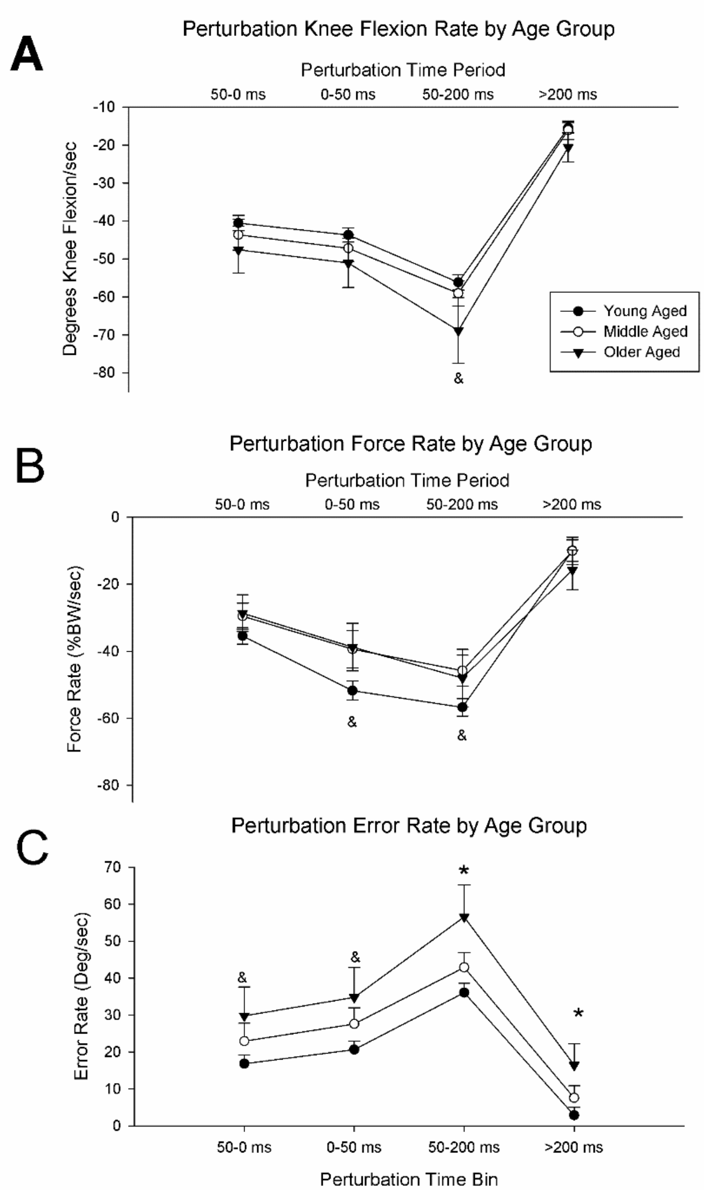


Figure 3.4 The Effects of Age on a Force Perturbation. Knee flexion rate (A), Force rate (B), and error rate (C) during physiologically defined time bins during a force perturbation. The x-axis denotes the time bins of 50-0ms before the onset of the perturbation, 0-50ms following the perturbation, 50-150ms following the perturbation, and 200-350ms following the perturbation (>200ms). Three age groups are represented in each graph with closed circle representing the 20-39 year olds, open circle the 40-59 year olds and closed triangle the 60-79 year olds. Asterisk denotes that each age group is statistically different from each other; ampersand denotes that the older age group is significantly different from the younger age, and the cross indicates that the young and middle-aged are statistically different (significance level set at 0.05).

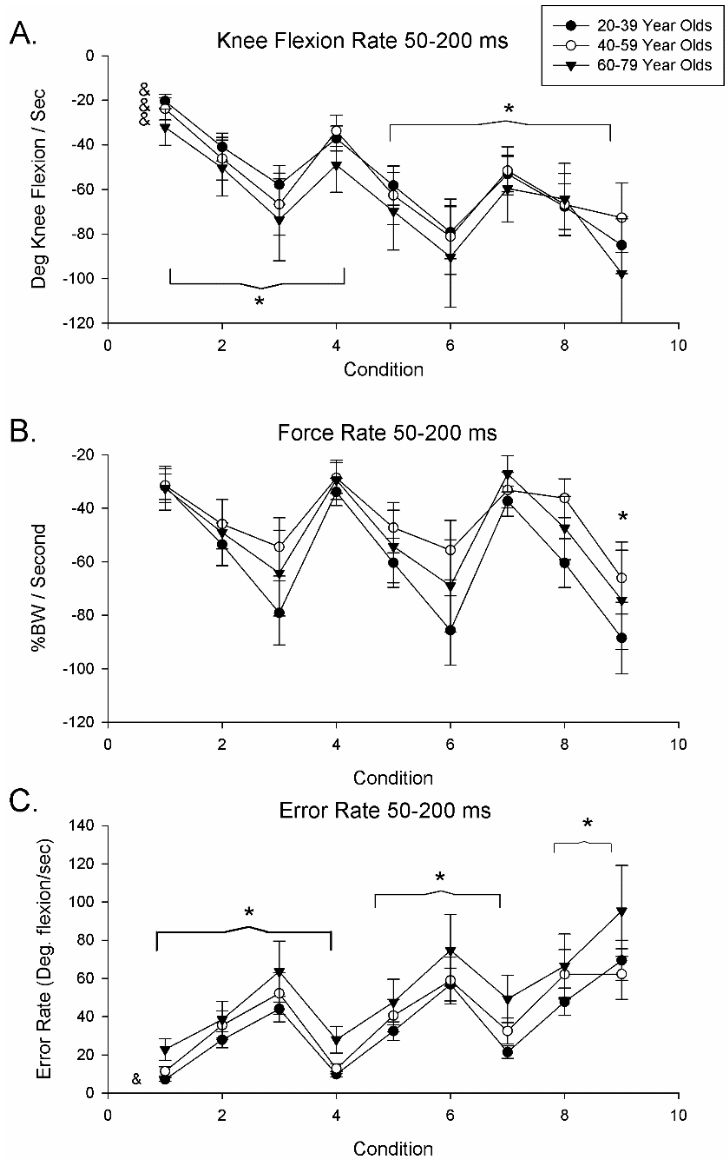


Figure 3.5 The Influence of Trial Resistance and Velocity on the Time Bin Consistent with the Long Latency Response. Knee flexion rate (A), force rate (B), and error rate (C) during the 50-200ms following a force perturbation. The x-axis shows the nine trial conditions composed of a combination of three resistances (5, 10, and 15% body weight) and three velocities (0.2, 0.4 and 0.6 Hz), where the slowest and lightest resistance is condition 1, and the fastest and heaviest resistance is condition 9. Three age groups are represented in each graph with closed circle representing the 20-39 year olds, open circle the 40-59 year olds and closed triangle the 60-79 year olds. Asterisk denotes the condition is different from all others not within the same bracket; ampersand denotes that the age group is statistically different from the other age groups (significance level set to 0.05). Note that the interaction of age and condition is >0.05 for all parameters indicating a similar effect of velocity and resistance across ages for each rate variable.

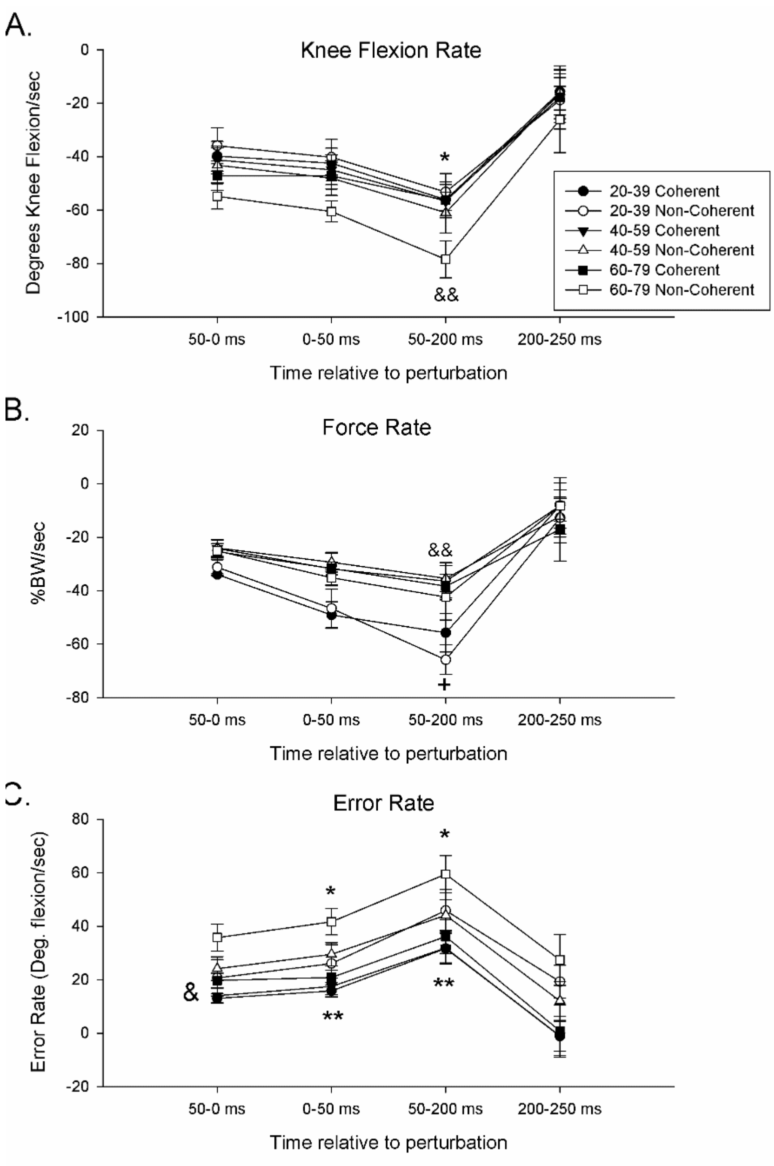


Figure 3.6 The Effects of a Force Perturbation on Good and Poor Task Performers as Defined by Coherence. Knee flexion rate (A), force rate (B), and error rate (C) for young (circle), middle-aged (triangle), and older aged (square) subjects during time bins associated with a force perturbation. Performance is stratified by the 99% confidence interval level of coherence, with good performers (closed shape) having a trial coherence above the 99% CI level, and poor performers (open shape) having a trial performance below the 99% CI. Double asterisk (**) indicates older aged good performers different from young. Single Asterisk (*) indicates older aged poor performers different from young. Cross (+) indicates young adult performers significantly different from middle-aged and old. Ampersand (&) indicates significant different between coherent and non-coherent for all time bins. Double ampersand (&&) indicates significant difference between coherent and non-coherent for indicated time bin. Significance level set at 0.05.

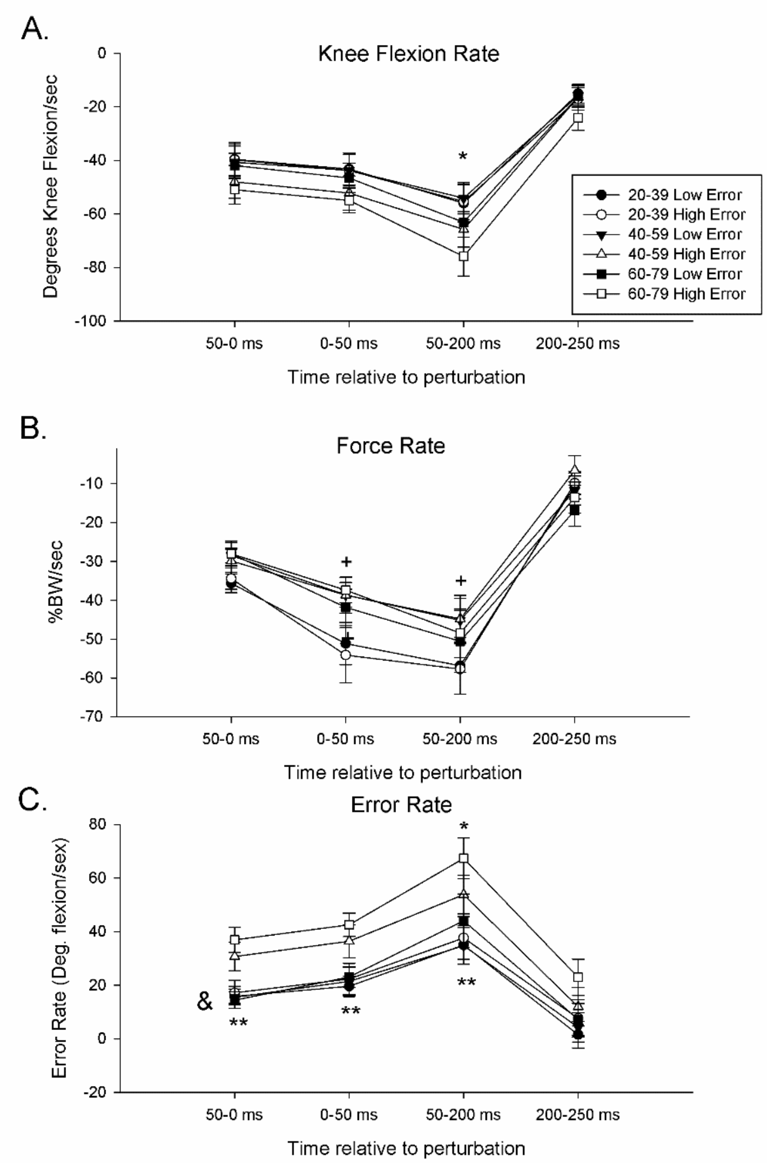


Figure 3.7 The Effects of a Force Perturbation on Good and Poor Task Performers as Defined by Mean Trial Error. Knee flexion rate (A), force rate (B), and error rate (C) for young (circle), middle-aged (triangle), and older aged (square) subjects during time bins associated with a force perturbation. Performance is stratified by the 99% confidence interval (CI) level of the mean error of each condition, with good performers (closed shape) having a trial coherence less than mean+CI, and poor performers (open shape) having a trial performance above mean+CI. Double asterisk (**) indicates older aged good performers different from young. Single Asterisk (*) indicates older aged poor performers different from young. Cross (+) indicates young adult performers significantly different from middle-aged and old. Ampersand (&) indicates significant different between coherent and non-coherent for all time bins. Double ampersand (&&) indicates significant difference between coherent and non-coherent for indicated time bin. Significance level set at 0.05.

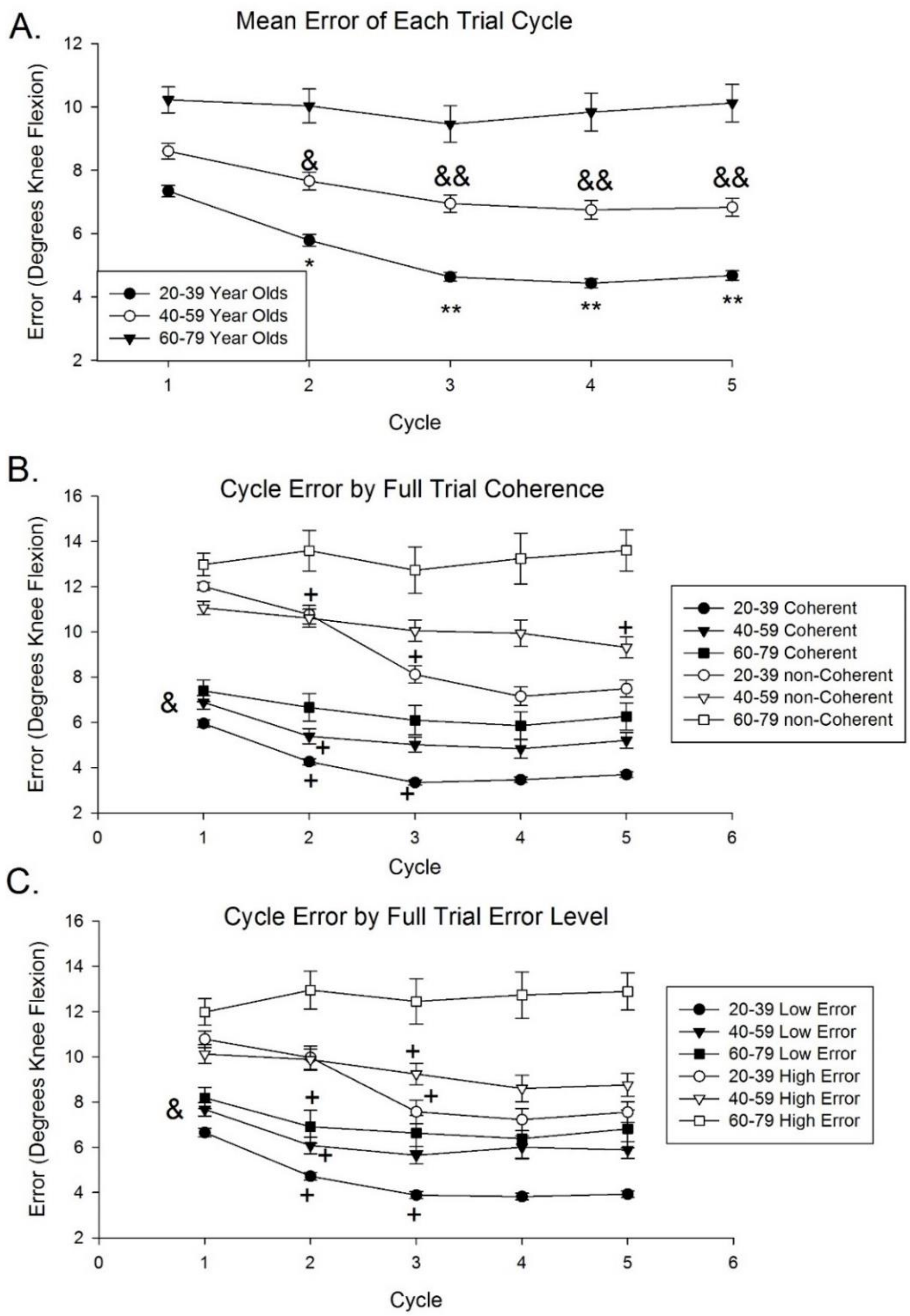


Figure 3.8 Within Trial Improvement in Error. Figure A demonstrates error of each cycle (5 total) for each age group of young (closed circle), middle-aged (open circle) and older (closed triangle). Figure B represents the within trial cycle error of the same three age groups (young: circle, middle-aged: triangle, older adult: square). The three age groups are divided into good performers (closed shape) and poor performers (open shape), as defined by the 99% confidence interval of the trial coherence. The cross (+) indicates the designated cycle is different from the previous cycle in the same age and performance group ($p<0.05$).

CHAPTER 4: COGNITIVE STRESS COMBINED WITH A NOVEL WEIGHT-BEARING VISUOMOTOR TASK IMPACTS MOTOR LEARNING AND PERFORMANCE IN OLDER ADULTS

INTRODUCTION

In order to navigate one's community, it's necessary to be able to perform simultaneous motor and cognitive tasks. This allows one to talk to a companion, or to think about a grocery list, all while walking through an uncertain and changing environment. Unfortunately, the ability to perform simultaneous tasks is diminished in older adults, and can lead to potentially serious injuries. Attention distracting influences on a motor task are more thoroughly investigated in the upper extremity, during ambulation, and during static balance tasks. Limited generalizability of upper extremity control to lower extremity movement, a large number of continuous steps required to detect gait differences, and different motor planning during static balance compared to weight-bearing movement are all limitations in our understanding of simultaneous cognitive and motor control of functional weight-bearing movement. In this study, we aim to investigate the extent to which a dual cognitive and weight-bearing movement can be learned, remembered, transferred to new conditions, and be controlled during unexpected events.

The ability to perform both a cognitive attention-demanding task and a motor task well involves the automaticity of the motor task. Automaticity of a motor task is characterized by requiring minimal cognitive attention to carry out the task, and is measured by the difference between dual-task and single-task performance of the motor task, termed dual-task cost (Nordin, Moe-Nilssen, Ramnemark, & Lundin-Olsson, 2010; Somberg & Salthouse, 1982; L. Yang, Liao, Lam, He, & Pang, 2015). Unfortunately, automaticity of movement is impaired in older adults, requiring increased cognitive resources to perform a previously automatic task such as walking (Whitman et al., 1999; W. L. Wong, Masters, Maxwell, & Abernethy, 2008; Woollacott & Shumway-Cook, 2002). This was classically observed by Lundin-Olsson et al (1997), where older individuals would stop walking when asked a question, not having the ability to perform both a cognitive and a motor task simultaneously (Lundin-Olsson, Nyberg, & Gustafson, 1997). A number of subsequent studies revealed that postural and movement stability is prioritized over a cognitive task (Li, Lindenberger, Freund, & Baltes, 2001; Nnodim et al., 2015; Schrodt, Mercer, Giuliani, & Hartman, 2004), and that indeed gait parameters are affected by a simultaneous task in older adults (Beauchet et al., 2003; Coppin et al., 2006; Yogev-Seligmann, Hausdorff, & Giladi, 2008). Unfortunately, in order to have adequate predictability and detection of changes in gait parameters, at least 30 (Galna, Lord, & Rochester, 2013) to 40 (Marques et al., 2016) continuous steps is required, and shows limited capability to actually predict those who will have injuries (Montero-Odasso, Muir, & Speechley, 2012) (Mortaza, Abu Osman, & Mehdikhani, 2014). This number of continuous steps would then require time-consuming testing and post-analysis, rendering distracted gait analysis not very feasible in the standard clinic.

Using dual-task walking as an actual intervention is attractive, as it appears to be intervening at the source of the inability to ambulate in the community. Dual-task ambulation training has been recently reviewed in those with neurologic impairment (Fritz et al., 2015; Wajda, Mirelman, Hausdorff, & Sosnoff, 2016), showing modest improvements in spatio-temporal parameters of gait. Commonly, gait testing is performed in a safe and predictable environment; walking over level ground and without obstacles to navigate. Recently, a visually rotated reaching task that is trained while performing a simultaneous visual discrimination task, showed a narrower generalizability of movement to new reaching directions and new contexts (Bedard & Song, 2013; Song, Im, & Bedard, 2015). To our knowledge, this has not been studied during a weight-bearing lower extremity task and may be important in the transfer of movement control to new contexts outside of the clinic.

Age associated declines in cognition has also been linked to deterioration of mobility. Probably the most studied indices of cognition are executive function (inhibitory control, mental set shifting, and updating task demands), and working memory capacity (maintenance and manipulation of information over brief time periods) (McCabe, Roediger, McDaniel, Balota, & Hambrick, 2010). A systematic review determined that even subtle declines in executive function related to a one-year history of falls in healthy community-dwelling adults (Muir, Gopaul, & Montero Odasso, 2012). Further, one study found that in 179 older adults, baseline executive function determined by the Flanker Task and Wisconsin Card Sort Test actually predicted outcomes of an intervention aimed at improving mobility (N. P. Gothe et al., 2014). Working memory capacity, however, is directly related to the rate at which younger adults learn a new motor skill, though is less clear for older adults (Anguera, Reuter-Lorenz, Willingham, & Seidler, 2010; Bo et al., 2009). The complexity of cognition and learning a motor task while distracted (dual-task) may be much more nuanced. One study found that dual-task cost (dual-task compared to single-task performance) was greater in those with lower working memory capacity but was not related to disease severity of people with Multiple Sclerosis (Hamilton et al., 2009). This result was similar to dual-task ambulation in subjects with mild cognitive impairment (Montero-Odasso, Verghese, Beauchet, & Hausdorff, 2012). Another group found that working memory capacity and single-task gait parameters *independently* predicted dual-task performance rather than relying on each other (Motl et al., 2014; Sosnoff et al., 2014). Although in a rehabilitation setting it is natural to emphasize interventions on motor skill deficits causing impairment, it appears that both interventions of cognitive training alone as well as dual-task training may have beneficial effects on mobility (Azadian et al., 2016; Mirelman et al., 2011; Silsupadol, Siu, Shumway-Cook, & Woollacott, 2006).

Distractions during an unexpected event while moving through the community (e.g. obstacle in the way, or mis-predicting the height of a step) is also of recent interest. This has been investigated during goal-directed upper extremity reaching (Cheng et al., 2013; Taylor & Thoroughman, 2007), or a sliding platform to induce a slip while standing (Bhatt, Yang, & Pai, 2012; Nnodim et al., 2015; P. J. Patel & Bhatt, 2015; Pavol, Runtz, Edwards, & Pai, 2002; Zettel, McIlroy, & Maki, 2008). These studies provide a basis for our understanding of feedback control, though again is difficult to generalize to weight-bearing movement. Upper extremity reaching incorporates fewer sensory inputs due to no influence from the vestibular system, and slip platforms have little reproducibility in testing due to increased muscle stiffness to prevent falling (no longer unexpected) after only one slip. Further, the large number of repetitions thought to detect true differences in gait renders some studies regarding gait perturbations questionable. Our lab has, however, been able to safely and reliably detect the behavioral response to an unexpected perturbation in a weight-bearing lower extremity visuomotor task in young and older individuals (Madhavan et al., 2009; Madhavan & Shields, 2009).

We have recently modified our system to include a visual discrimination task (see supplemental video). With this modified system, we will be able to determine the ability of individuals to learn, transfer, and remember a weight-bearing motor task with and without distraction. A visual discrimination task was chosen for this study due to previous evidence that dual-task learning is enhanced if similar central resources are used in the motor and the cognitive tasks (Goh et al., 2012; Hemond, Brown, & Robertson, 2010). Previous upper extremity visuomotor studies have determined that a similar visual discrimination task paradigm does indeed induce a cognitive-motor interference effect (Im, Bedard, & Song, 2016; Song & Bedard, 2013, 2015) and will allow investigation of cognitive-motor dual-task investigation in the lower extremities.

By initially studying the differences between healthy younger and older subjects, we will identify early changes in the control system of functional movement even before impairment exists. This will aid in determining appropriate interventions to prevent further deterioration in movement control as the effects of aging or disease process continue.

METHODS

Subjects

Sixty-four total subjects participated in this study. Subjects are in two age groups where 40 subjects are between the age of 20-39 years old ("Young") and 24 subjects between the ages of 60-80 years old ("Older"). Subject numbers are based on an analysis to achieve greater than 0.80 power for variables of final training error and coherence, and testing error and coherence. Only healthy adults in each age range participated in this study. Exclusion criteria includes: self-reported history of any of: knee ligament reconstruction, current or recent (<3 mo) history knee pain, cardiovascular disease, known lower extremity osteoarthritis, rheumatoid arthritis, neurologic disease, and any movement impairment. Subjects were asked to attend three visits within 8 days, each visit lasting less than one hour, and were compensated for their time.

Experimental Design

Motor Task

Our group has designed a weight-bearing system that has the capacity to measure force and displacement at the knee while performing a game-based visuomotor task (Shields, 2006). In this manner, we can provide a hierarchy of task difficulty by varying force as a percentage of body weight, and adjusting the speed of the target line to follow. This system also has the capability to safely deliver an unexpected force perturbation during movement by rapidly decreasing the resistance delivered at the knee to null, and then rapidly returning the resistance to pre-perturbation levels. Perturbations are always performed during the flexion phase of knee motion at approximately 10 degrees of bending. The duration of the perturbation only lasts approximately 20% of the flexion cycle. This allows the investigation of feedback control during a weight-bearing movement in a safe and effective manner (Madhavan & Shields, 2009).

The motor task is the same for all groups of subjects. On Day 1, subjects will perform 20 training trials at a speed of 0.4 Hz and a resistance of 10% body weight (BW). After every trial, subjects are given feedback in the form of a percent error score calculated as the difference between the user's knee angle and the knee angle associated with the target line position, divided by the range of motion associated with the amplitude of the target signal (0-25 degrees knee flexion). After every 5 trials, subjects are asked their rate of perceived exertion on the Borg 15-pt scale as it has been previously validated for perceived muscle exertion (Gearhart et al., 2001; Lagally & Costigan, 2004). Subjects are offered a one-minute rest break following each exertion rating. Following twenty training trials, subjects are given a one-minute rest break. Subjects then perform a series of nine conditions of the visuomotor task now without feedback of percent error. The nine conditions consist of a combination of three target line speeds (0.2, 0.4, and 0.5 Hz), and three resistances (5%, 10%, and 15% body weight). This is not randomly delivered, though always in the order of Hz/%BW: 0.4/10, 0.4/5, 0.4/15, 0.2/10, 0.2/5, 0.2/15, 0.6/10, 0.6/5, and 0.6/15 (Fig. 1). Subjects are not explicitly told that there is a testing order. Subjects are told at the start of testing that they are allowed to take breaks at any time they request. Subjects are again asked their rate of perceived exertion on the Borg scale following all nine trials of testing.

Forty-eight hours later subjects return, starting with performing five training trials (reacquisition) again at 0.4 Hz speed and 10% body weight. Feedback in the form of percent error is again provided following each trial. After 5 trials, subjects are asked their rate of perceived exertion and issued a one-minute rest period. Following rest, nine conditions of testing are performed two additional times where subjects are asked their rate of perceived exertion following each combination of nine trials.

On the final day, seven days following the initial test day, subjects perform three sets of the nine testing conditions. Again, each subject is asked their rate of perceived exertion between each set of nine conditions, and rest breaks are allowed at each participant's preference.

Cognitive Task

Our system has most recently been modified to allow a simultaneous cognitive counting task while performing the visuomotor task. On the same screen as the projected motor task (target line), the letter “T” will flash for 0.5 seconds every 1.0 seconds. The letter, however, will be randomly selected from either upright or upside down, and one of four colors (orange, yellow, pink or white). The cognitive task then involves counting the number of pre-specified color(s) and orientation(s) of a letter that flashes on the screen. This method has been used by other researchers and has provided an effective cognitive load as part of a cognitive-visuomotor task (Song & Bedard, 2015). The combination of the visuo-cognitive and visuo-motor tasks provides an innovative method of measuring feedforward and feedback control while performing a simultaneous cognitive task and weight-bearing functional movement.

Subjects in each the Young and Older age groups are divided into four sub-groups. Two groups are considered control groups (CT1 and CT2), and two are intervention groups (DT1 and DT2). During Day 1 training and testing, the control groups will perform only the motor task. One intervention group (DT1) will be asked to simultaneously count the number of upright orange T’s that flash on the screen during the motor task (simple cognitive task), while the other intervention group (DT2) will be asked to count the total sum of the upright orange and upside down yellow T’s (complex cognitive task). On day 2 (48 hours later), the initial five training trials will again be performed under the same day 1 condition, but will be followed by testing under a “cross condition”. The cross condition for the dual-task performers will be performing solely the motor task (no cognitive task), while the control groups will now perform the dual-task where CT1 performs the simple cognitive task, and CT2 performs the complex cognitive task. During the second nine conditions of testing, subjects will again perform under their trained (day 1) conditions. On the final testing day, each subject performs the nine testing conditions first under day 1 conditions, while the second nine conditions of testing are performed again under the cross condition as previously described, and the last nine conditions testing performed under the previously untested dual-task condition.

Cognitive Testing

Cognitive domain testing is performed before visuomotor testing on the first and last days and is assessed using the NIH Toolbox Cognition Kit (Bernard et al., 2013). Only selected tests of List Sorting, Erikson Flanker, and Dimensional Change Card Sort will be performed. This is achieved by a user and a tester sitting in a quiet room at a computer, each with the ability to see their own screen. The tester then reads instructions and delivers the test according to the NIH Toolbox Guide. The List Sorting test is designed to obtain a general working memory capacity score rather than solely a verbal or spatial. This is achieved by the subject seeing a picture of the item, as well as hearing the name of the object (e.g. a speaker plays a voice saying “elephant”, as a picture of an elephant appears). This measure of the working memory capacity as delivered in the method of the NIH Toolbox is determined to have a good reliability coefficient of 0.77 (Tulsky et al., 2014). The same study also was able to demonstrate moderate convergent validity of 0.58 and divergent validity of 0.27. This indicates that this will provide a good measure of working memory capacity for our purposes.

When developing measures of executive function, the NIH aimed to generate tools that work across a broad range of ages to enhance generalizability. They therefore adopted the Dimensional Change Card Sort as a measure of set shifting and task switching, and the Erikson Flanker test as a measure of inhibition control and executive attention (Zelazo et al., 2014). Both tests were revealed to have a re-test reliability of approximately 0.85, and an age correlation of approximately -0.6 for the ages of 25-85 (Zelazo et al., 2014).

Physical Activity Assessment

The International Physical Activity Questionnaire Short Form (IPAQ-SF) was delivered on the last day of testing to estimate the physical activity of subjects in the past week. The seven day time frame of the questionnaire captures the testing duration presented in this methodology. Previous unpublished data from our laboratory demonstrates a moderate correlation (R=0.594) between IPAQ-SF score and mean activity as rated by an Actigraph™.

Data Analysis

Custom software using LabView is used to collect knee displacement data as well as axial force data sampled at 2000 Hz. Files were then analyzed by using customized analysis in DIAdem Software (Version 12.0). Whole trial performance was assessed using variables of absolute error (root mean square error), and coherence. During the perturbation portion of each cycle, time bins were created according to physiologically relevant periods. The short latency reflex has been demonstrated to occur 0-50ms following a perturbation due to the stretch of the antagonist muscle, here the quadriceps; the long latency has been demonstrated to occur between 50-200ms following a perturbation. Just prior to release of the resistance, 50ms is used as the pre-perturbation period. For each of the perturbation and pre-perturbation time bins described, variables were calculated including: knee flexion rate, and error rate. The constant and absolute error is inherently flawed for these analyses, as the starting position will affect the magnitude of the error during the perturbation. To eliminate this, the knee flexion rate and error rate was utilized to determine the effect of the perturbation on the subject's performance. Knee flexion rate was calculated in DIAdem by the best fit line of the time bin defined (all lines r-squared > 0.9). The error rate was defined as the best fit line of the resultant signal from the target signal minus the user signal during the time period defined.

Dual-task cost is used as a measure of the difference in motor performance between a dual-task trial and a single-task trial. This difference between the distracted and undistracted performance is an indicator of automaticity of the motor task. Dual-task cost is calculated for both full trial variables, as well as variables used to analyze described time periods of the perturbation.

Statistical Analysis

Variables of mean error and coherence will be analyzed using a split plot repeated measures analysis of variance. Variables of knee flexion rate, force rate, and error rate will be analyzed using a split-plot repeated measures design. Follow-up tests will be performed using Tukey's HSD Test. Changes in performance during training and second day resting will be performed using an

ANCOVA to account for the variability in each subject's first trial performance and last training trial, respectively. Differences in IPAQ-SF between groups will be determined using a one-way ANOVA. Differences in cognitive test results will be performed using Student's t-test. The significance level for all tests is set to 0.05, and statistical analysis will be performed using SAS ("SAS," 2010).

RESULTS

Activity and Cognitive Characteristics

No statistical difference in self-reported activity (International Physical Activity Questionnaire-Short Form) was determined via a one-way ANOVA between each group ($p=0.912$). The average continuous score for all groups was 4434 MET-min/week.

Cognitive assessment results were significantly different (all p's < 0.0001) where older adults earned lower scores than younger adults on Card Sorting (mean ± standard deviation; young: 125.8 ± 7.8, old: 113.5 ± 8.2), Flanker Test (young: 115.0 ± 5.9, old: 106.2 ± 4.6), and Dimensional Change (young: 118.3 ± 8.8, old: 107.0 ± 10.4).

Skill Acquisition and Retention

On the first day of testing, everyone underwent training of the visuomotor task by performing 20 trials at the medium resistance and medium frequency condition (Fig. 2 left side). By the end of training, younger individuals reached a similar level of error (Fig. 2A) and coherence (Fig. 2C) regardless of performing a simultaneous cognitive task (Dual-Task 1 and 2) or only performing the motor task (Control). An asymptote in learning was achieved at increasing trials for increasing cognitive task complexity with control, simple cognitive task, and complex cognitive task groups achieving the asymptote in motor performance at trial 8, 12 and 17, respectively. Older adults, however, demonstrated similar learning of the visuomotor task between those performing a simple cognitive task and no cognitive task, achieving an asymptote in error by the 8th trial (Fig. 2B), and coherence by the 12th trial (Fig. 2D). Older adults learning the visuomotor task while performing a complex cognitive task on the other hand, demonstrated little improvement in both error and coherence with much greater variability. Younger and older groups achieved similar final training performance except for older subjects tasked with a complex cognitive task performing at 3 times the error (p=0.0038) and half the coherence (p=0.0117). Although not depicted, when stratifying visuomotor performance by accuracy of the cognitive task, when cognitive task error was high visuomotor task error was high, and conversely when cognitive task error was low visuomotor task error was low. During first day training, cognitive task error decreased from approximately 125% ([user count – actual count]/actual count) to approximately 10% (see Figure 2 insert).

Forty-eight hours following the first day of testing, subjects returned; performing five additional training trials under the same conditions in which they trained the first day Fig 2. Right panel). Older individuals demonstrated less retention of learning compared to day 1 final training (p=0.0003), though within each age group, retention of learning was similar across intervention groups (all p’s > 0.05)**.** Younger adults returned on the second day of testing with only a 12% increase in error and a 7% decrease in coherence compared to final training error. Although older adults performing the complex cognitive task continued to perform more poorly compared to all other groups (coherence: p=0.017; trial mean: p=0.0004), retention of the motor task continued to be similar across groups, with an increase in error by approximately 20% and decrease in coherence by 25% compared to final training performance on the first day of testing. Following five training trials on the second day of testing, those performing a complex cognitive task did not achieve the same level of performance on the motor task as the control and simple cognitive task groups (Fig. 2 right side). Interestingly, a similar coherence (post hoc, p=0.1171) and error (post hoc, p=0.0601) was achieved between younger and older adult groups only in the dual-task 1 group (simple cognitive task). Error remained larger in control (p=0.0007) and dual-task 2 (p=0.0038) groups for older compared to younger adults.

Transfer of Learning

Transfer of learning is the application of a learned movement to new conditions. Here we tested a combination of three resistances as a percentage of body weight and three speeds of the line across the screen; the medium resistance and speed was the trained condition, the other 8 combinations newly introduced after training (Fig. 3). Younger adults demonstrated a progressive increase in error (Fig. 3A) and decrease in coherence (Fig. 3C) with increasing resistance and velocity (all p's < 0.05). The relative effect of altering task conditions was similar across younger adult groups (interaction: coherence p=0.8569, trial error p=0.5910), though error was on average 1.1 degrees knee flexion lower in the control group compared to those performing a simple and complex cognitive task (coherence p=0.0020; trial error p=0.0048).

Older adults performed differently when tasked with new conditions (age*condition interaction: both coherence and trial error p<0.0001), although continued to be similar across groups (interaction: coherence p=0.2069; trial mean p=0.0692). Older adults experienced similar error and coherence across new conditions with the exception of an approximate 93% increase error and 65% decrease in coherence at 0.6 Hz compared to 0.2 and 0.4 Hz (p's<0.0001). Interestingly, older adults in the control and simple cognitive task groups had similar error and coherence on new task conditions, where those performing the complex cognitive task consistently experienced greater error and decreased coherence (p=0.0023 and p=0.0018, respectively). Post-hoc testing of cross-correlation analysis revealed no difference in time of best correlation between all groups of all ages (p=0.780) indicating no systematic delay of tracking by the older compared the younger group. Time of best correlation ranged from 0.022 seconds at 0.2 and 0.4 Hz to 0.23 seconds at 0.6 Hz. This is consistent with the previous chapter, where the highest rate of movement is approximately 10 times the delay as the slower two frequencies.

Non-Volitional Feedback

Error rate and knee flexion rate was analyzed during the period consistent with the long-latency response was determined for each of the nine testing conditions. This was determined as the time following the period consistent with the short latency spinal reflex though before volitional correction (50-200ms);

depicted in Figure 4. Both younger and older adults reveal an effect of resistance and velocity resulting in increased error rate and knee flexion rate with increase in both task resistance and task velocity (all p's>0.05). Although no difference in non-volitional response is determined between groups within each age for knee flexion rate ($p=0.0516$), error rate reveals a lower error rate for controls compared to dual-task groups for both younger and older adults ($p<0.0001$). Interestingly, older adults experience slower knee flexion rates compared to younger adults ($p=0.0003$), experiencing 22 and 18 degrees knee flexion per second less knee flexion rate at the highest task resistance and velocity, respectively.

Dual-Task Cost

Dual-task cost, an indication of the automaticity of the motor task, is defined as the motor performance subtracted from the motor performance while performing a simultaneous cognitive task (Nordin et al., 2010; Somberg & Salthouse, 1982; L. Yang et al., 2015). Younger adults demonstrate dual-task cost closer to null for both error (Fig. 5A) and coherence (Fig. 5C) when exposed to a cognitive task during training compared to those who trained without a cognitive task ($p<0.0001$ for both coherence and trial error). Interestingly, dual-task trained even demonstrate better performance when there is a cognitive task compared to only performing the motor task. Older adults show a different pattern, demonstrating similar dual-task cost between the dual-task trained groups and the control group tasked with a simple cognitive task. The Control 2 group (training with only the motor task then asked to perform a complex cognitive task), however, demonstrates significantly poorer dual-task cost compared to all other groups ($p<0.0001$ for both coherence and trial error).

One week following the first training sessions, each subject performed all testing conditions under the same dual- and single-task conditions as performed on the second day of testing. Dual-task cost for younger adults (Fig. 6A,C) demonstrates a continued trend at the trained condition (medium speed and resistance); dual-task trained continue to have a dual-task cost error and coherence closer to null than the control subjects ($p=0.0252$). At all non-trained conditions, dual-task cost is similar across groups (post hoc, $p>0.05$). Interestingly, the older adults demonstrate a different trend. Older adults exposed to a complex cognitive task, be it during training or day 2 testing, have a poorer dual-task cost compared to those exposed to a simple cognitive task ($p=0.0003$). This difference is maintained not only at the trained condition, but at all resistances and velocities (interaction $p=0.9965$). Interestingly, older adults also demonstrated similar dual-task cost within each group across all conditions (trial mean: $p=0.2800$; coherence: $p=0.1827$)

Cognition and Motor Performance Correlations

Correlations were performed to determine the relationship between motor performance and cognition (Table 2). Working memory capacity was only able to explain 28.3% of the variability of the rate of learning on day 1 for the control group younger adults. Working memory capacity was not correlated with rate of learning for all dual-task groups and the older adult control groups. Executive function as measured by the Flanker test, however, explained between 71.9 and

89.5 percent of the variability in final day, trained condition motor performance of both younger and older adult dual-task trained groups. Executive function, though, did not correlate with final performance of the control groups in both age groups.

DISCUSSION

The major findings of this study were: 1) a simultaneous cognitive task increases the number of training trials required to reach an asymptote in visuomotor task learning for all adults, with a complex cognitive task inhibiting acquisition of the motor task in older adults; 2) Consolidation of motor learning was not affected by the presence of a cognitive task during learning; 3) Transfer of the learned visuomotor task to new conditions of resistance and rate of movement is diminished by the presence of a cognitive task; 4) Error rate during the non-volitional time following a force perturbation is greater in both younger and older adults when there is a simultaneous cognitive task; 5) Automaticity of the motor task is improved when training is performed simultaneously with a cognitive task, where the least achievement of automaticity is observed in older adults who were asked to perform a complex cognitive dual-task following training with only the motor task; and 6) Executive function explained approximately 80% of the variability in final day, trained condition, visuomotor performance in those performing the dual-task; though working memory capacity accounted for only 28% of the variability of the rate of learning in only the younger adults forming solely a visuomotor task.

Skill Acquisition and Retention

All groups, with the exception of older adults performing a simultaneous complex cognitive task (DT2), demonstrated acquisition of the visuomotor task. Both trial error and coherence were reduced to a stable performance with a similar proficiency achieved by all groups. As cognitive task difficulty increased from no, to a simple, to a complex cognitive task; the rate of learning slowed, increasing the number of trials required to achieve an asymptote in motor task performance. In the older adult group the complex cognitive task decreased the rate of learning so much so that in the twenty training trials it appears that no acquisition of the motor task occurred.

Our findings that cognitive load affects rate of learning is consistent with volumes of previous studies (Malone & Bastian, 2010; M. Patel, Kaski, & Bronstein, 2014; Taylor & Thoroughman, 2007, 2008). Of note, several studies also showed that at the end of practice, final performance of a motor task is similar regardless of the presence of a cognitive task (Montero-Odasso, Muir, et al., 2012; Noble, Trumbo, & Fowler, 1967; Song & Bedard, 2015; Strobach, Frensch, Soutschek, et al., 2012). Interestingly, our older group that performed the complex cognitive task (DT2) showed little improvement during acquisition of the motor task. This is similar with few studies that show that older adults don't achieve the same performance while dual-tasking as younger adults even with extra practice (McDowd & Craik, 1988; Strobach, Frensch, Muller, & Schubert, 2012; Tsang & Shaner, 1998). It is likely, though, that the level of concurrent task difficulty continues to be influential on the capacity to improve in error during a single session of practice. A study by Schwenk and colleagues (2010) showed similar results where individuals with dementia continued to show a reduced capacity to perform a dual-task compared to controls under a complex, though not simple, cognitive load even after 12 weeks of practice (Schwenk et al., 2010). Although subjects in our study were not identified as having dementia, it appears that the same trend holds (although in this study for only one session) even with the normal effects of aging.

Discrepancies in older and younger adult dual-task capability may be due to differences in neural substrate activation. Although dual-task performance for younger and older adults may activate similar brain regions (Al-Yahya et al., 2015; Erickson et al., 2007a, 2007b; Godde & Voelcker-Rehage, 2017; N. P. Gothe et al., 2014), there is evidence that activation is more distributed through the frontal cortex in older compared to younger adults (Erickson et al., 2007b; Hartley et al., 2011; Reuter-Lorenz & Lustig, 2005). This is suggested as a possibly compensatory mechanism for altered function of isolated structures associated with aging.

The frontal cortex is identified as a major contributor to dual-task performance due to involvement in both motor planning (Poldrack et al., 2005) and rule-set shifting (McCabe et al., 2010); though the cerebellum (Lang & Bastian, 2002; Wu, Liu, Hallett, Zheng, & Chan, 2013), and dorsal pre-motor cortex (Goh et al., 2013) may also play critical roles. Many of these regions also play an intricate role in executive function and working memory capacity which has also been shown to decline with older age (Tulsky et al., 2014; Zelazo et al., 2014), and as demonstrated by lower mean Card Sorting and Flanker task in our older age group compared to younger. The complex cognitive task in our study is probably more difficult than our simple cognitive task in two different dimensions. During the complex task, subjects must maintain and switch between two rule sets thus increasing demand on the central executive, and must count potentially larger numbers of objects thus increasing demand on the working memory. This additive difficulty of both systems may saturate the processing capability of older adults, resulting in decreased ability to improve performance on the motor task.

Previous dual-task learning studies have shown both improvements in (An et al., 2014; Goh et al., 2012; G. Y. Kim, Han, & Lee, 2014; Raisbeck, Regal, Diekfuss, Rhea, & Ward, 2015) and impaired (K. Gothe, Oberauer, & Kliegl, 2007; Makizako et al., 2012) delayed (>24 hours) retesting performance. Here we actually showed that there was no effect on motor performance regardless of cognitive task complexity or age. This is interesting, considering our study employed motor and cognitive tasks that share central processing resources, which is posited to facilitate consolidation of learning (Goh et al., 2012). This differential finding may be related to the fact that in our study, the processing of both the cognitive and motor task was continuous over a period time, while Goh and others (2012) determined the benefit of central process sharing between the motor and cognitive tasks during the discrete time period related to planning of movement, or the execution of reaching. Another aspect of potential confounding is related to a lack of considering factors that influence consolidation such as sleep or motor cortex activation during training. It may also be that there exists an optimal difficulty level of the cognitive task in order to enhance motor task consolidation that was not achieved in this study.

For most participants in our study, both motor and cognitive task error started high, and was gradually improved simultaneously. This is similar to previous upper extremity studies (Song & Bedard, 2013), asserting that attention is delivered to *both* visuomotor and visuo-cognitive tasks equally as opposed to allocating increased resources to just one of the tasks. If the latter were true, then we would expect either the cognitive or the motor error to improve before the other. Song & Bedard (2013) further proved this concept using a novel approach where subjects were asked to reach toward a target that was either in a different location or the same location as a visual cognitive task. In this study, subjects achieved similar reaching errors whether or not the visuo-cognitive task was in the location of the goal-directed movement. This supports that subjects in this study were most likely able to allocate attention to both the visuomotor and the visuo-cognitive tasks presented.

The exception to this equivalent cognitive-motor interference in our study is the older adult group performing the complex cognitive task (DT2). The older DT2 group significantly reduced cognitive task error by the end of training, though motor error and variability remained high. This may indicate that when older adults are presented with a difficult cognitive task, priority is differentially allocated to the cognitive task vs the motor task, perhaps being a major factor in the limited motor learning in this group. The possible choice of older adults to prioritize the cognitive task is interesting, considering previous studies have shown that when not specifically directed to focus on one task or the other, subjects will adopt a "posture-first" strategy (Nnodim et al., 2015; Shumway-Cook, Woollacott, Kerns, & Baldwin, 1997; Sun & Shea, 2015), focusing on the motor task rather than the cognitive task. In this experiment, we allowed all subjects to have light touch on the testing frame, and have external support at the knee by the rack and pinion system constraining movement to the sagittal plane. This may have provided sufficient postural support to eliminate fear of instability or falling, decreasing need for postural protection strategies and thus allowing the choice to concentrate on the complex cognitive task.

Transfer of Learning

In this study, all individuals were tested under 8 novel conditions as combinations of three resistances and rates of movements (the medium resistance and frequency is the trained condition and thus not novel) immediately after practice on both the first and second (48 hours later) days of the study. Younger individuals continued to scale performance of new task conditions by resistance and velocity as seen in Chapter 3, though a learning effect is noted as the error and coherence curves have shifted downward and upward, respectively. Younger adults show a similar pattern of transfer of learning (no group by condition interaction), though greater error and lower coherence is noted at each condition for those with a dual-task compared to single task. Older adults on the other hand, show a flattening of the resulting difficulty curve that was determined in Chapter 3, showing similar performance at the three resistances during the 0.2 and 0.4 Hz frequencies (conditions 1-6). Transfer to novel conditions is greater due to decreased presence of the hierarchy of difficulty except at the highest velocity. Although motor task performance in DT2, a similar performance effect of resistance/frequency continues to be present, indicating possible implicit learning that did not result in motor error reductions during training (Jimenez & Vazquez, 2005; Vandenbossche, Coomans, Homble, & Deroost, 2014).

Few studies have attempted to identify the ability to transfer a motor skill that was acquired under a cognitive-motor dual task. Of these studies, methodologies differ substantially and provide varying results. One study attempted to transfer a visual adaptation of reaching to new reaching positions. They were able to show that as the distance of the new reaching position relative to the trained position increased, the transfer of learning (reaching performance) decreased (Bedard & Song, 2013). Interestingly, training of an upper extremity coordination task (spooning beans between cups; "feeding") resulted in improvement in an unrelated upper extremity task (fastening buttons with the non-dominate hand; "dressing") (Schaefer & Lang, 2012). Although the mechanism and neural basis of transfer in this study was not suggested, it does reveal that dual-task training may provide improvements not only in the trained task, but to motor tasks using similar effectors. We add to this knowledge, showing that both older and younger adults can transfer a dual-task learned weight-bearing movement of the same muscles to novel task conditions, though as complexity of the cognitive task increases, transfer of the motor task decreases. This is a beneficial finding due to the need of older and younger individuals alike to be able to vary speed of movement to meet situational demands regardless of carrying various types and numbers of objects (resistance). Further, the transfer of one movement to a completely different movement using the same limbs may indicate that by starting a rehabilitation program with a more isolated repeated movement such as our single limb squat, may transfer to improvements in gait and other functional movements necessary for accomplishing activities of daily living.

Although not studied here, there is interesting evidence that transfer of the cognitive task may also occur. When seven patients with Parkinson's Disease were tested under a non-trained cognitive-gait dual-task (associated listing) following four weeks of dual-task training (serial 3's), training, gait parameters were improved compared to no dual-task training (Yogev-Seligmann, Giladi, Brozgol, & Hausdorff, 2012). Similarly, when performing a reaching adaptation, training with a visual discrimination task (such as in this experiment) resulted in increased savings when performing the reaching motion with a high load auditory task (Song & Bedard, 2015). Future investigations may determine if such transfer occurs when altering sensory systems responsible for detecting or responding to the second task in weight-bearing movements. This may provide insights into mechanisms to decrease lower extremity injuries when moving through a constantly changing environment.

Non-Volitional Feedback

During one of the five cycles of each trial, a force perturbation was elicited by rapidly reducing the resistance to null for less than a second. Following training, the perturbation response was assessed under the nine conditions paradigm. Young adults continue to experience a systematic increase in error rate and knee flexion rate with increase in resistance and frequency. This increase in error and knee flexion rate is similar to non-trained, age-matched performers in the previous chapter, though shifted downward as would be expected with improvements due to learning. Here we found that younger single-task and dual-task trained subjects experience similar effects of the perturbation except for an increase in error rate in the dual-taskers when moving against the highest resistance and velocity condition. This is similar to a previous study where an auditory stimulus was presented before, during, or after a force perturbation during an adapted reaching motion. Here they found that regardless of the timing of the presentation of the auditory stimulus, there was no effect on the feedback response of the reaching motion, though did slow reaching adaption (Taylor & Thoroughman, 2007). Interestingly, static postural studies have found that as postural demand increases, visual working memory decreases (Elaine Little & Woollacott, 2014), and that when a postural perturbation is elicited, the EEG response (N1) is diminished while dual-tasking, resulting in greater changes in center of pressure movement (Little & Woollacott, 2015). This provides potential further evidence that upper extremity somatosensory aid and external support at the knee provided during testing generates enough postural stability that our results deviate from that of static postural studies.

In this experiment, older individuals performing the complex cognitive task (DT2) experience greater error and knee flexion rates than controls. This may, at least in part, be due to the fact that older individuals never achieved the same level of performance during training as the control and simple cognitive task performers. As presented in chapter 3, there is a strong influence of motor performance on the feedback response to a perturbation during a weight-bearing movement and may account for the difference in this study. Interestingly, older individuals experienced lower error and knee flexion rates, especially at the 0.6 Hz conditions. One previous study actually showed that older adults performing a cognitive-gait dual-task adopted a more “cautious gait” strategy than younger individuals, resulting in decreased risk of falls (Soangra & Lockhart, 2017). The analogue in this study may be a “stiffer knee joint” strategy that may account for a more cautious movement that would diminish the kinematic response of the perturbation. This may be resolved in future studies by electromyography of muscles about the knee to determine if greater co-activation occurs with increased age and cognitive load. Interestingly, when a postural perturbation during gait is delivered via an instrumented orthotic, no gait differences are noted following the perturbation, but there is an increase in response delay to the cognitive task (Nnodim et al., 2015). This “posture-first” strategy most probably did not occur in our study due to the subtle nature of the perturbation, allowing subjects to have light touch support to decrease the postural aspect the visuomotor task, and as previously described a possible increase in attention to the cognitive task compared to the motor task in older DT2 subjects.

A significant limitation of our investigation of feedback response during dual-tasking is the lack of standardizing the appearance of the cognitive task (letter flashing on the screen) relative to the perturbation. This may have allowed insights into the effects of cognitive tasks on the processing and or the execution of a feedback response by altering the timing of the presentation of a cognitive task to a postural perturbation during a functional movement. Although upper extremity reaching research indicates there is no effect on feedback response of when the cognitive task is presented (Taylor & Thoroughman, 2007), this may not generalize to weight-bearing, lower-extremity movements.

Dual-Task Cost

The difference between dual-task and single-task performance is termed dual-task cost (Nordin et al., 2010; Somberg & Salthouse, 1982; L. Yang et al., 2015). Dual-task cost allows insight into the capability of an individual to automatize the motor task, allowing attentional resources to the cognitive task. An automatized movement would result in a dual-task cost of null, not having a difference in motor performance regardless of the presence of a cognitive task. Here, nine testing conditions of the visuomotor task were delivered under both single and dual-task conditions on both the second and third days of testing. We show that 48 hours after training, younger adults that are trained with a dual-task have a dual-task cost closer to null compared to those who trained with the single motor task. This is similar to previous studies where reaching adaptation is best performed under the attentional context with which they learned the task both with immediate (Song & Bedard, 2015) and delayed recall (Im et al., 2016).

Interestingly, older adults were slightly different where dual-task cost was similar between both dual-task trained groups (DT1 and DT2) and the single-task trained group that was then tasked with a simple cognitive task (CT1); though the single-task trained group asked to perform a complex cognitive task (CT2) showed a dual-task cost deviating greater from null for both trial error and coherence. Like previous studies (Canning, Ada, & Paul, 2006; Y. R. Yang, Chen, Lee, Cheng, & Wang, 2007), dual-task cost was significantly greater for all older aged groups, indicating that the decreased ability to automatize the visuomotor task resulted in similar dual-task cost when the cognitive task is simple. It may be that the simple cognitive task continued to allow enough attentional resources for the CT1 older adults to perform similarly to the less automatized dual-task trained, while the complex cognitive task both achieved a high enough attentional demand to detract from the motor task. Interestingly, the fact that the older DT2 group showed little acquisition of the task during training, and that dual-task cost was no different from DT1 and CT1 groups, further suggests that implicit learning may have actually occurred for the older DT2 group.

Upon return seven days after initial training (Day 3 of testing), younger adults revealed an effect of training on dual-task cost solely on the trained condition (medium speed and resistance). Control subjects actually showed *better* performance on the dual-task condition compared to their trained single-task condition. Interestingly, dual-task trained subjects had dual-task cost an equivalent distance from null in the opposite direction from the controls, performing better on the single-task condition by the same magnitude as the single-task trained performed on the dual-task. This might be due to training order, as single-task trained performed nine conditions of the visuomotor task without a cognitive task, followed by nine conditions of a dual-task. Another possible explanation may be the benefit of hybrid training (Buraggada, 2004; Silsupadol et al., 2006; Song et al., 2015; Strobach, Frensch, Soutschek, et al., 2012). Although inconsistent results, it may be that training first with a single-task, and then being exposed to several trials of a dual-task (nine conditions on the second day), enhances automaticity of the motor task.

On the final testing day, older adults again revealed a different dual-task cost compared to younger adults where those exposed to the simple cognitive task, whether during training or testing (CT1 and DT1), had improved automaticity compared to those exposed to the complex dual-task (CT2 and DT2). It appears that while simple cognitive task performers could continue to improve with repeated exposure to the task, complex task performers continued to be unable to improve in motor performance while performing such a difficult distractor. Interestingly, dual-task cost remained greater for older adults compared to younger adults, even for the simple cognitive task group. This is consistent with a study showing that older adults don't achieve the same dual-task cost as younger adults when performing a coordination task, even with extra practice (Strobach, Frensch, Soutschek, et al., 2012). It may be that with a substantial distraction, older adults need substantially greater practice, or that automatization of a coordination or weight-bearing movement may be impaired with older age.

Cognition and Motor Performance

In the recent decade, evidence is starting to accumulate regarding the relationship of motor performance and cognition. In this study, we attempted to correlate cognitive performance measures of working memory capacity and executive function to motor learning and performance of the single motor and cognitive-motor tasks. Here we found that the greatest predictor of delayed retesting of trial error on the final day of testing was the Flanker Test executive function measure. Executive function explained 72-90% of the variability of error while dual-tasking for older and younger adults. Executive function did moderately predict final day coherence, though only for young adult controls and simple cognitive task performers and older adults performing a complex cognitive task.

Gothe and colleagues (2014) determined that starting executive function (Flanker Task) predicted mobility outcomes (8ft walk test, timed stair up test, timed stair down test) after 12 months in healthy, community dwelling older adults. The amount of error that was attributed due executive function was much lower in their study, however, accounting for only approximately 6% of the variance. This may be due to clumping generalized gross motor function rather than precisely measuring error of a movement as in this study. It is interesting that executive function correlated to coherence and error differently. A previous dual-task gait training study in 228 healthy, older adults determined that executive function predicted change in swing time, though not gait speed for dual-task walking (Hausdorff, Schweiger, Herman, Yogev-Seligmann, & Giladi, 2008). They explain this finding by positing that different components of functional movement may be controlled by systems that are differentially affected by executive function. This may indeed be the case in our study as well, where matching the rate of movement is controlled by different central networks than error of movement.

Working memory capacity in our subjects was only able to explain approximately 30% of the variability in the rate of learning for both coherence and trial error in only the young adults performing only the motor task (controls). Working memory capacity did not significantly correlate with all other groups. Previous studies have shown that working memory capacity correlates to undistracted motor learning in younger adults (Bo & Seidler, 2009), though is more complex in older adults (Anguera et al., 2010, 2011). Although working memory capacity has also been shown to be related to dual-task cost of walking in those with Multiple Sclerosis (Hamilton et al., 2009) and older adults (Montero-Odasso, Muir, et al., 2012), we did not find the same correlation for dual-task cost during our prescribed movement. A limitation may be the low subject numbers, especially in each older group. It may also be that the working memory capacity test as part of the NIH Toolbox incorporates both auditory and visual working memory capacity, as both a picture is displayed on the screen while a speaker plays a vocalization of the presented object. This may allow auditory system compensation during cognitive testing, while only visual working memory capacity is able to be employed during the visuo-cognitive and motor testing.

Few studies have even started to attempt to determine the central structures and networks responsible for dual-tasking in older adults. While learning a new motor task, older adults activate the sensorimotor and frontal regions to a greater extent than younger adults (Heuninckx et al., 2008). Interestingly, dual-task regional activity is shifted to include the temporal and occipital lobes rather than only frontal and motor areas as in single-task activation (Bogost, Burgos, Little, Woollacott, & Dalton, 2016). This increase in resources to perform two tasks, presumably further complicates the ability to use cognitive measures to predict dual-task performance and learning capabilities.

Limitations

One major limitation of this study may actually be the visual nature of the cognitive task. Although the goal of a visual discrimination task was to utilize similar resources as the motor task to enhance learning (Goh et al., 2012), age is associated with decrements in visual saccades and searching capabilities and may have been an unaccounted for factor in decreased older adult performance. Interestingly, however, previous upper extremity research performed with a similar paradigm showed that retention of performance was relatively maintained even with a high load auditory stimulus indicating that the visual nature of the study may not have been necessary to induce a similar effect (Song & Bedard, 2015). And further, the location of the visual discrimination task relative to reaching goal did not affect performance on either task (Song & Bedard, 2013).

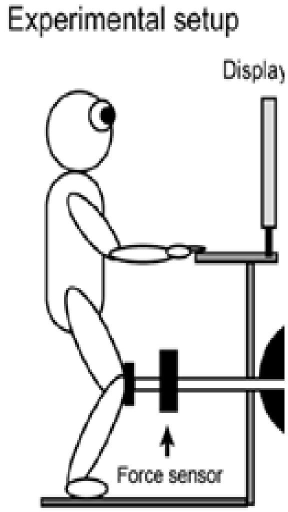
Unfortunately, the upper extremity paradigm was not used on older adults and do not aid in overcoming the aforementioned limitation. Further, no information was gained regarding the visual strategy of individuals, where future studies using eye tracking software may shed light in visual tracking and fixation related to performance on each task.

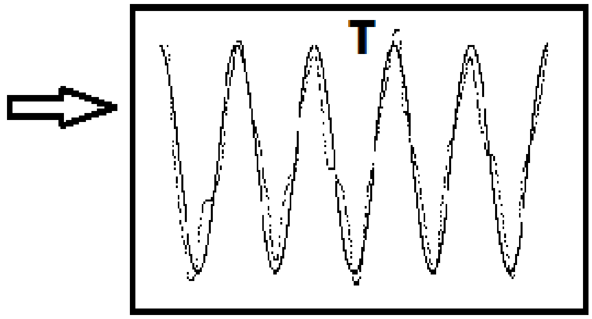
Consolidation of memory is affected by many factors including altered brain activity during sleep (Fogel et al., 2014), altered activation of the motor cortex (King et al., 2016), and interference from other memories following the motor task (Roig et al., 2014). Future studies may include imaging modalities of electroencephalography (EEG) during sleep and EEG or functional near-infrared spectroscopy during motor learning to assess factors that may contribute to consolidation of the motor task while performing another concurrent task.

Finally, results of older individuals in this study may only applied to “super-agers”, as self-reported selection criteria eliminated many common ailments of those over 60 years old such as knee pain, osteoarthritis, and neurologic disease.

CONCLUSION

Our results demonstrate that even in healthy, older adults without self-reported physical and cognitive deficits, differences exist in dual-task learning compared to younger adults. Dual-tasking with a complex cognitive task eliminates the ability of older adults to improve motor performance with a possible increased attention allotted to the cognitive task, while a simple task only slows the rate of learning. Older adults maintain the ability to transfer learning to new task conditions of resistance and rate of movement, though is worst at movement speeds. Dual-task cost of a complex cognitive task was also noted to be greatest in older adults that were trained without distraction, possibly benefiting from exposure to a simple cognitive task. Finally, executive function accounted for ~80% of error of final performance, possibly being a measure of prognosis for motor learning.





Testing Order	Low Resistance (5% Body Weight)	Medium Resistance (10% Body Weight)	High Resistance (15% Body Weight)
Slow Speed (0.2 Hz)	5	4	6
Medium Speed (0.4 Hz)	2	1	3
Fast Speed (0.6 Hz)	8	7	9

Figure 4.1 Experimental setup. Cartoon design of the standing frame, monitor, and rack and pinion delivery of resistance and the knee and detection of knee movement (top left). Representative example of user generated line (dashed) and target line (solid line) of the five-cycle sinusoid task (top left). Nine speed x resistance combinations of the testing paradigm. Training is performed under condition 5 (medium speed and medium resistance (bottom right).

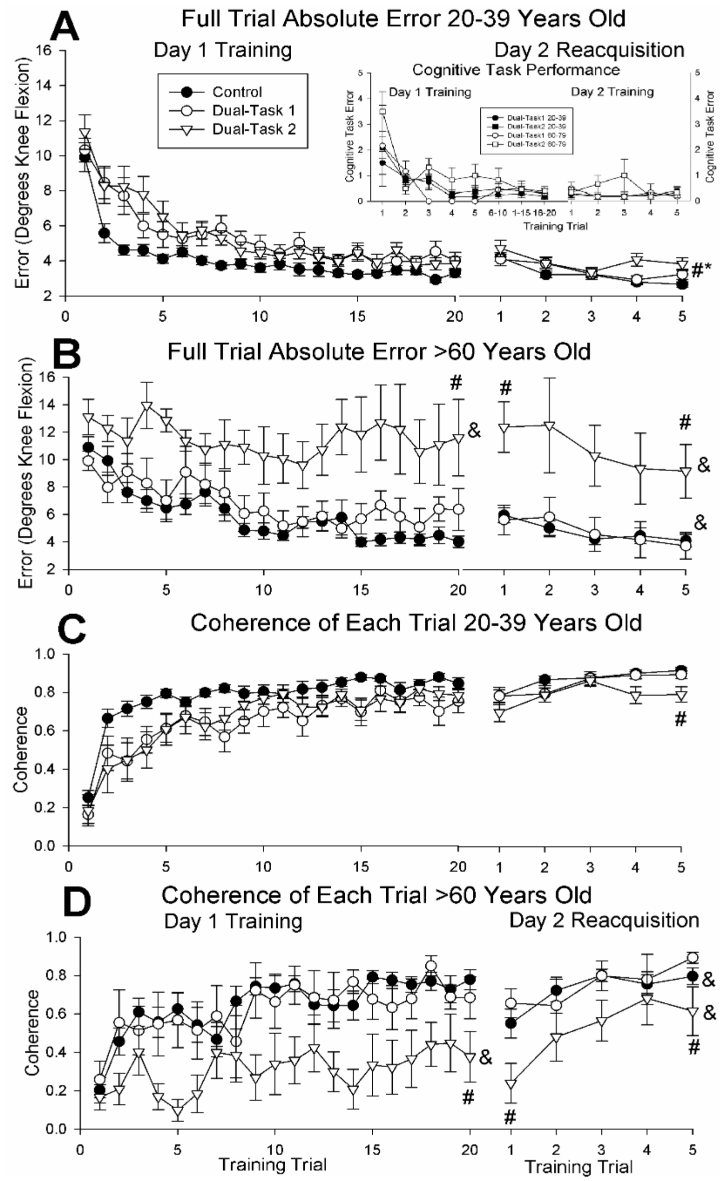


Figure 4.2 Skill Acquisition and Retention Full Trial Analysis. Twenty training trials on day 1, and 5 training trials 48 hours later were performed without distraction (closed circle: Control), a simple cognitive task (open circle: Dual-Task 1), and a complex cognitive task (open triangle: Dual-Task 2). Mean and standard deviation of the absolute value of trial mean (A,B), and Coherence (C,D) is presented. Older adults in the dual-task 2 group experienced greater error and lower coherence compared to all other groups on day 1 (#, hash), and in both younger and older adults on day 2. Although retention testing on day 2 revealed poorer performance in the older dual-task 2, performance compared to final day 1 training was similar across all ages and groups. Ampersand (&) indicates Older adults with higher error or lower coherence from younger adult for similar training group ($p<0.05$). Note dual-task 1 groups between ages achieve similar levels of error and coherence by final training trial on both day 1 and day 2.

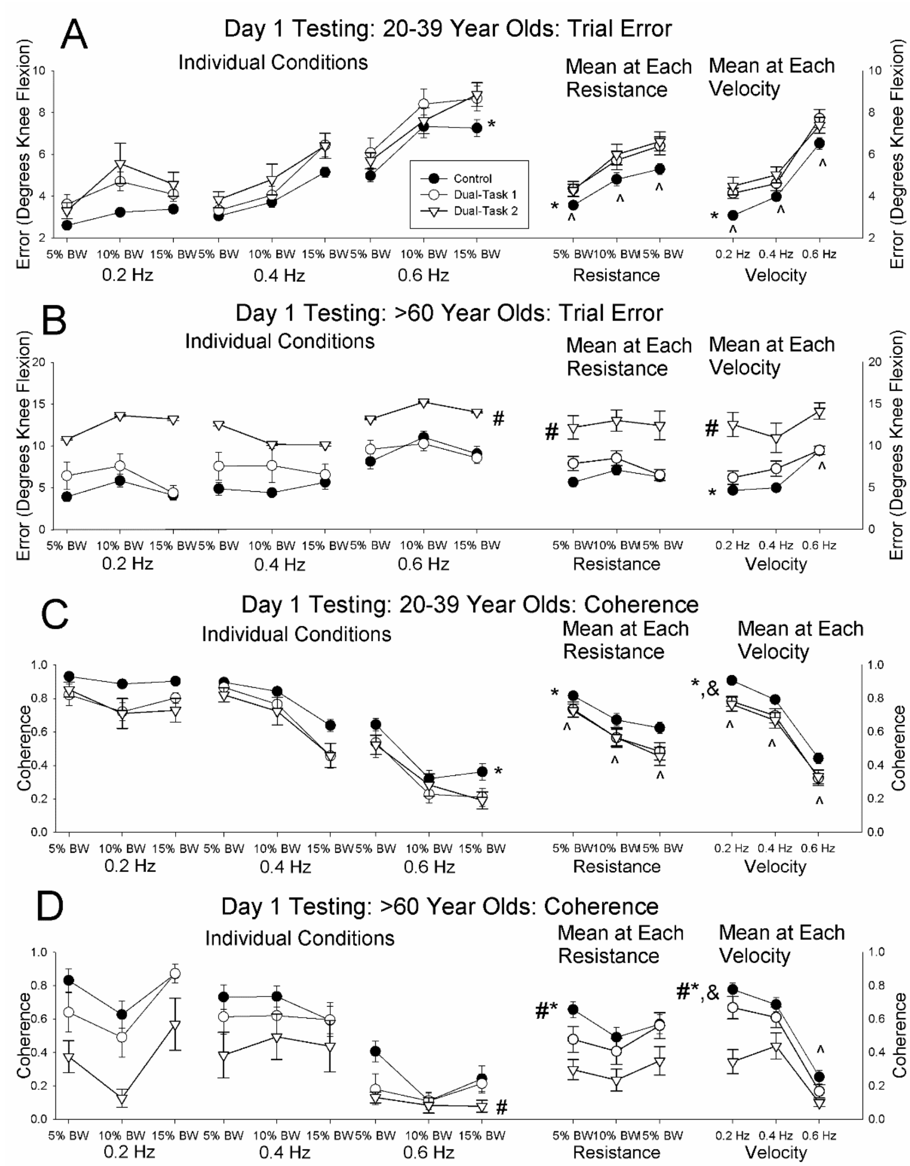


Figure 4.3 Transfer of Learning: Full Trial Variables. Trial Error (A,B) and Coherence (C,D) for younger (A,C) and older (B,D) adults, performing only the motor task (control, closed circle), and simultaneous motor, and simple (open circle) and comples (open triangle) cognitive tasks. Nine conditions were performed as a combination of three resistances as a percentage of body weight and three rates of the sinusoid to track on the screen. The left side depicts each indidual combination, where the right side depicts the mean of three trial of each resistance and velocity. Astrisk (*) indicates younger controls perform differently than dual-task groups. Carrot (^) indicates condition of resistance or velocity is signiticatly different from the others. Hash (#) indicates older dual-task 2 group different from other older groups, while hash with an asterisk (#*) indicates dual-task 2 group only different from the control group.

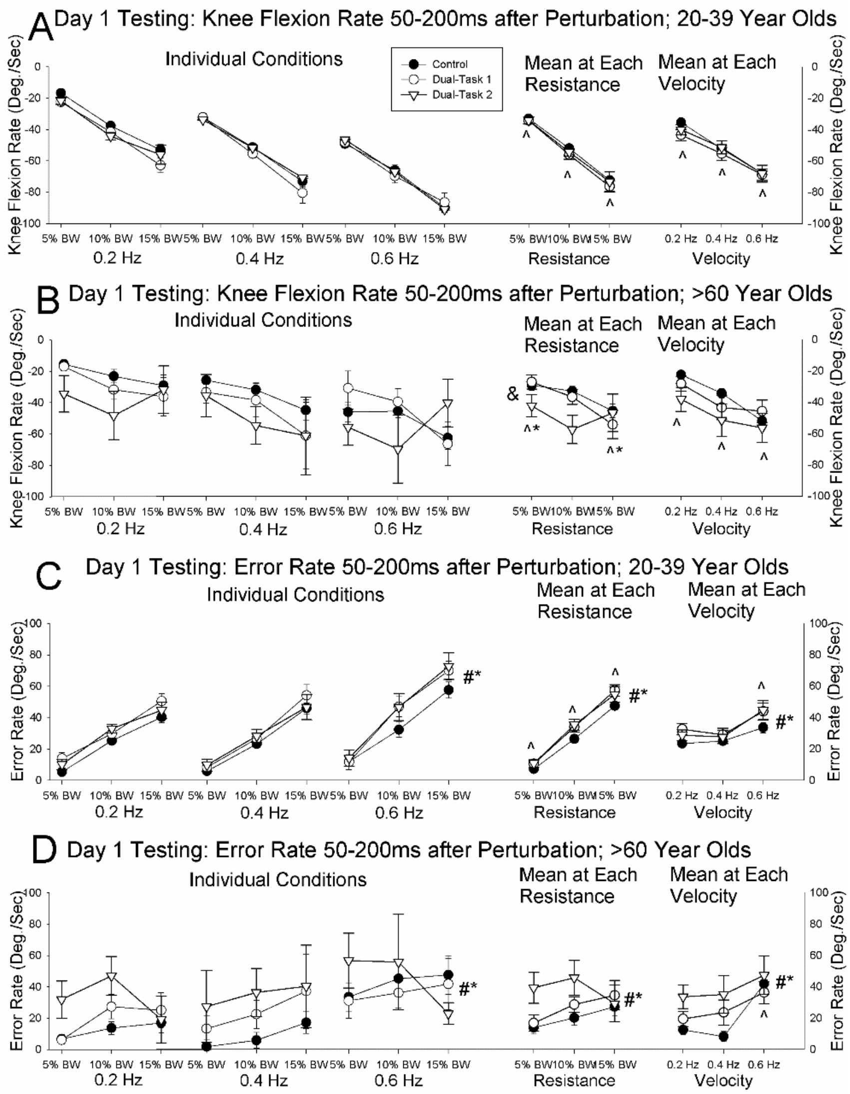


Figure 4.4 Transfer of Learning: Non-Volitional Feedback Variables. Knee flexion rate (A,B) and error rate (C,D) 50-200 ms following an unexpected force perturbation for younger (A,C) and older (B,D) adults, performing only the motor task (control, closed circle), and simultaneous motor, and simple (open circle) and comples (open triangle) cognitive tasks. Nine conditions were performed as a combination of three resistances as a percentage of body weight and three rates of the sinusoid to track on the screen. The left side depicts each indidual combination, where the right side depicts the mean of three trial of each resistance and velocity. Carrot (^) indicates condition of resistance or velocity is signiticatly different from the others. Carrot with an asterisk (^*) indicates condition different from each condition with the same symbol. Hash with an asterisk (#*) indicates dual-task 2 group only different from the control group. Ampersand (&) indicates all older adult groups different from the younger adult groups.

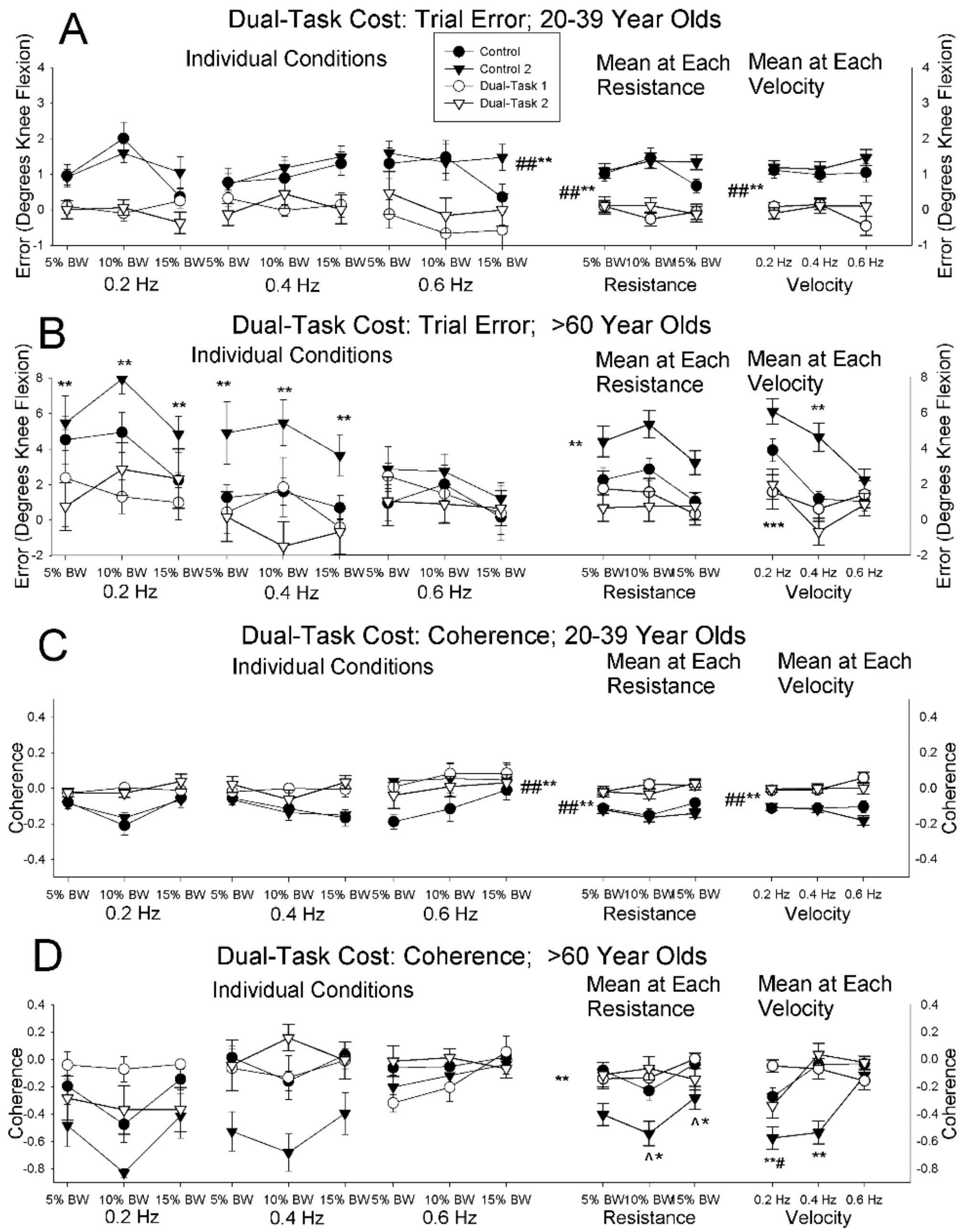


Figure 4.5 Dual-Task Cost: Day 2. Young (A,C) and Older (B,D) adults performed both a single motor (closed symbol) and dual cognitive-motor (open symbol) tasks. Presented is the difference in motor performance between single and dual-task conditions at each resistance and velocity. Double hash and double asterisk (##**) indicates dual-task groups different from control groups. Double asterisk (**) indicates CT2 group diferent from all other groups. Triple asterisk (***) indicates both CT2 and CT1 different and different from dual-task groups. Carrot with asterisk (^*) indicates different from other conditions with the same symbol.

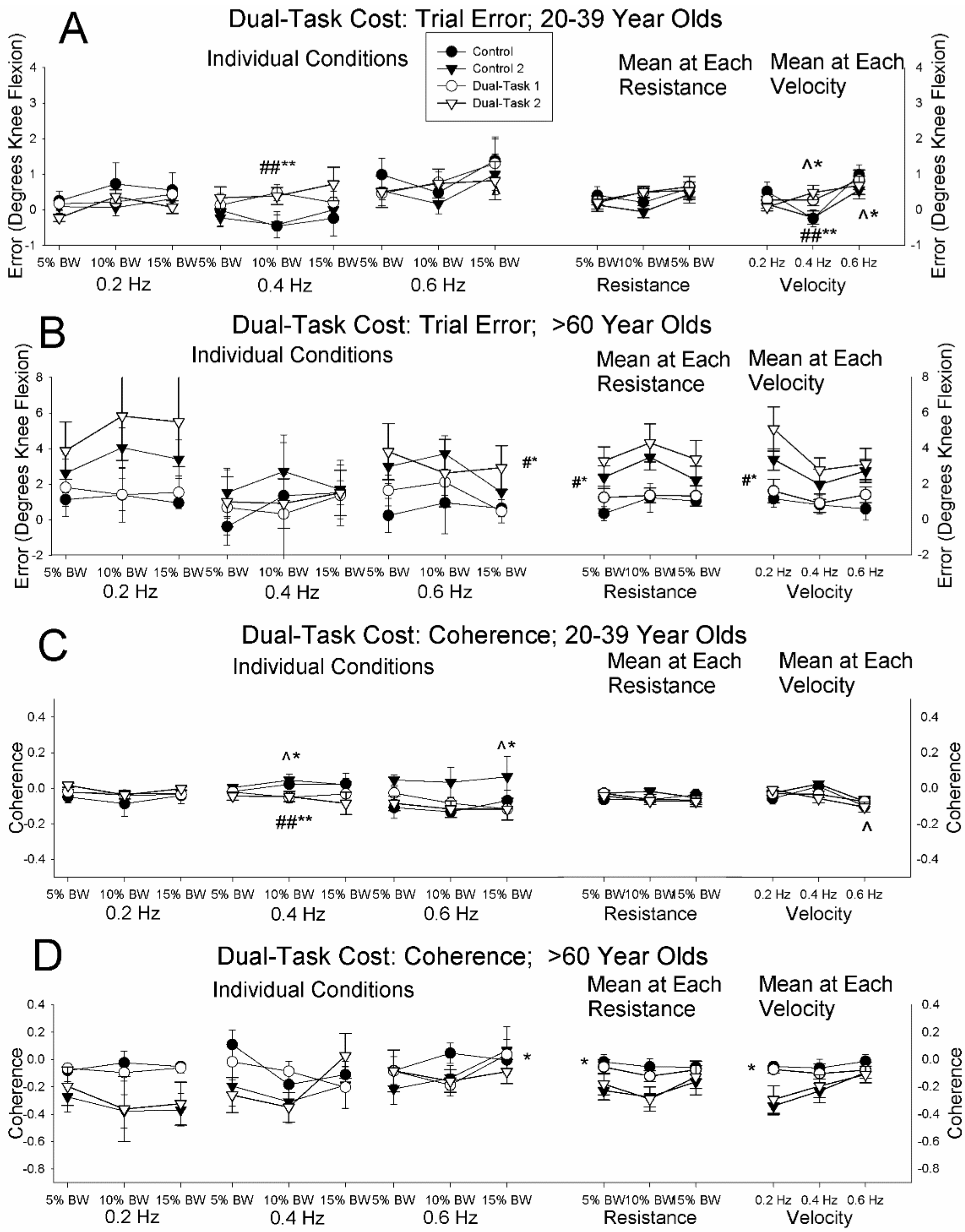


Figure 4.6 Dual-Task Cost: Day 3. Young (A,C) and Older (B,D) adults performed both a single motor (closed symbol) and dual cognitive-motor (open symbol) tasks. Presented is the difference in motor performance between single and dual-task conditions at each resistance and velocity. Double hash and double asterisk (##**) indicates dual-task groups different from control groups. Hash plus asterisk (#*) indicates CT1 and DT1 different from CT2 and DT2. Asterisk (*) indicates CT1 different from DT2. Carrot with asterisk (^*) indicates different from other conditions with the same symbol.

Table 4.1 Experimental Design. Testing conditions presented for four training groups on three different days (Day 1, Day 2, and Day 3). Testing flow begins at the top of each column (Day 1), continuing to the bottom of the same column (Day 3). Cognitive testing using the NIH Toolbox was also performed before testing on both Day 1 and Day 3 of testing.

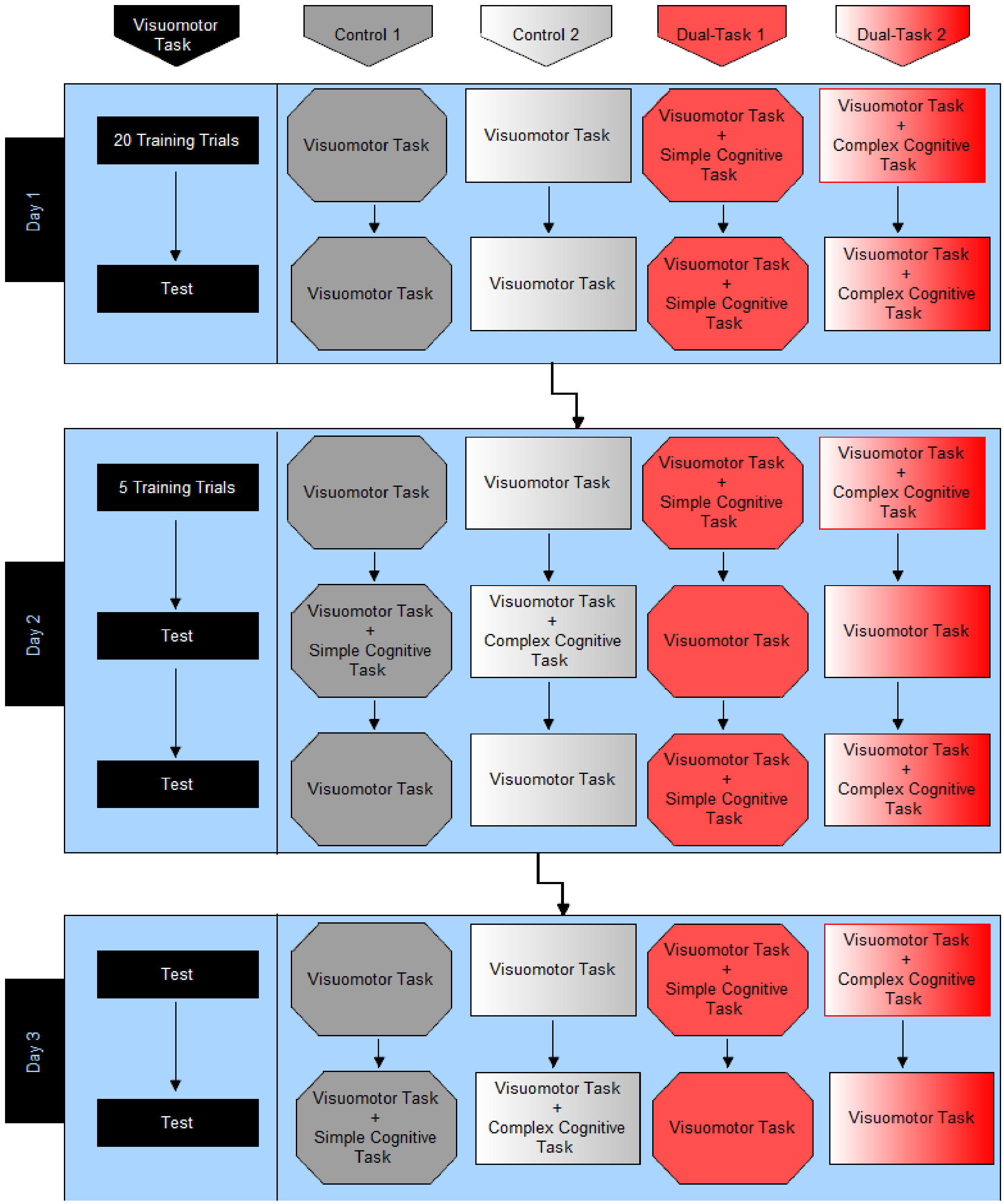


Table 4.2 Motor Task and Cognitive Test Performance Correlations. Working memory capacity correlates to the rate of motor error reduction in younger adult control groups only. Executive function highly correlated with the final day trial error of all dual-taskers in both age groups. There is a less clear relationship between executive function and final day coherence, correlating with young control and DT1 subjects, and only the DT2 older subjects. Bold and asterisk values indicate significant correlation using a critical value of 0.05.

Cognition Measure	Dependent Variable	Age Group	Patient Group	R-squared	p-value
Working Memory Capacity	Decay Exponent fit to *Trial Error* during 20 Training Trials	Younger Adults	Control	**0.283**	**0.017***
			DT1		0.512
			DT2		0.206
		Older Adults	Control		0.905
			DT1		0.422
			DT2		0.622
	Growth Exponent fit to *Coherence* during 20 Training Trials	Younger Adults	Control	**0.337**	**0.005***
			DT1		0.242
			DT2		0.554
		Older Adults	Control		0.085
			DT1		0.701
			DT2		0.541
	Final Day *Trial Error* on Trained Condition (Medium Speed and Resistance)	Younger Adults	Control		0.217
			DT1		0.449
			DT2		0.717
		Older Adults	Control		0.814
			DT1		0.643
			DT2		0.618
	Final Day *Coherence* on Trained Condition (Medium Speed and Resistance)	Younger Adults	Control		0.376
			DT1		0.407
			DT2		0.241
		Older Adults	Control		0.718
			DT1		0.900
			DT2		0.683

Table 4.2 Continued

Executive Function	Final Day *Trial Error* on Trained Condition (Medium Speed and Resistance)	Younger Adults	Control		0.591
			DT1	**0.755**	**0.024***
			DT2	**0.760**	**0.0236***
		Older Adults	Control		0.484
			DT1	**0.719**	**0.032***
			DT2	**0.895**	**0.004***
	Final Day *Coherence* on Trained Condition (Medium Speed and Resistance)	Younger Adults	Control	**0.327**	**0.008***
			DT1	**0.475**	**0.027***
			DT2		0.471
		Older Adults	Control		0.357
			DT1		0.137
			DT2	**0.889**	**0.014***
	Decay Exponent fit to *Trial Error* during 20 Training Trials	Younger Adults	Control		
			DT1		
			DT2		
		Older Adults	Control		
			DT1		
			DT2		
	Growth Exponent fit to *Coherence* during 20 Training Trials	Younger Adults	Control		0.0622
			DT1		0.635
			DT2		0.281
		Older Adults	Control		0.280
			DT1		0.106
			DT2		0.114

CHAPTER 5: CONCLUSIONS

A broad understanding of motor control has been achieved through research performed on upper extremity reaching, walking on level ground, and static balance. Though invaluable insights have been achieved under these testing paradigms, inherent limitations result in less being known regarding functional movement in weight-bearing. Gait studies require large numbers of consecutive steps in order to achieve high reliability, static balance is limited to the isometric goal of no movement, and upper extremity reaching lacks insights into feedback from the vestibular system. The purpose of this research was to 1) validate a combination of resistances and rates of movement that create a hierarchy of conditions with which to assess motor control during a weight-bearing visuomotor task, 2) to determine the effects of healthy aging on motor control during a weight-bearing visuomotor task, and 3) to determine the effects of healthy aging and cognitive distraction on weight-bearing motor learning.

SPECIFIC AIM 1

Hypothesis 1a

Resistance and movement rate will have a systematic effect on movement accuracy.

Supported: Increases in both resistance and movement rate (frequency of the visuomotor task) cause an increase in tracking error, and a decrease in matching the frequency of the task (coherence).

Hypothesis 1b

Unexpected changes in acceleration will have a velocity-dependent effect on movement accuracy.

Supported: Increase in movement rate of the task (higher frequency of the sinusoid) resulted in greater error and force rates during the pre-volitional response period after a perturbation. Interestingly, increase in resistance also resulted in greater error and force rates when increasing force from 5% to 15% of body weight. Resistance, however, reveals a much greater effect than velocity on mean electromyographic activity of the quadriceps and hamstrings muscles during the long-latency period following a perturbation.

SPECIFIC AIM 2

Hypothesis 2a

As age increases absolute error and peak error will increase, and velocity matching will decrease.

Supported: As age increases from young (20-39), middle (40-59), and older (60-79) adults, there is a step-wise increase in both mean trial error and peak trial error. Coherence (velocity matching) does decrease between the young and middle aged adults, though plateaus in decrement after middle age (there is no difference between middle and older age group coherence). This suggests a velocity-error tradeoff that is described in upper extremity movement control paradigms.

Hypothesis 2b

As age increases, an unexpected force perturbation will result in increased knee flexion rates, decreased knee extensor force rates, and increased error rates during the pre-volitional response.

Partially Supported: Although no difference is noted between age groups for the knee flexion rate during the 50ms after the perturbation, force rate and error rate are different between younger and older aged subjects. During the period consistent with the long-latency response (50-200ms), difference are only noted between younger and older aged groups for knee flexion rate and force rate; while error rate is progressively increased during this time period between each age group.

Hypothesis 2c

When normalizing non-volitional feedback responses to accuracy as measured by mean trial error and by coherence (velocity matching), older individuals will demonstrate faster falls and larger error rates regardless of mixed feedforward and feedback performance.

Supported: Knee flexion rate, force rate, and error rate were different for all age groups during the 50-200ms following a perturbation between those above (good performers) and below (poor performers) the 99% confidence interval level for coherence. In fact, older aged poor performer experienced the lowest knee extension force rates, and the greatest knee flexion and error rates.

SPECIFIC AIM 3

Hypothesis 3a

Increased cognitive task difficulty will decrease the rate of learning of a new motor task, with a greater reduction of the rate of learning in older compared to younger adults.

Partially Supported: Increase in cognitive task difficulty did decrease the rate of learning, increasing the number of trials before achieving an asymptote in acquisition of the motor task. Interestingly, when performing solely the motor task and when performing the motor task with a simple cognitive task, the number of trials to achieve a stable performance was the same in the older and younger adults. Although younger adults performing a simultaneous complex cognitive task could achieve error reduction, older adults in this group appeared to be unable to reduce motor errors consistently.

Hypothesis 3b

Increased cognitive task complexity will diminish consolidation of the motor task, with greater influence on older vs. younger individuals.

Not Supported: No difference was found for consolidation of the motor task regardless of cognitive task in each age group.

Hypothesis 3c

Increased cognitive task difficulty will result in increased error and decreased velocity matching under new motor task conditions of resistance and speed for both younger and older adults.

Partially supported: Younger adults revealed that a cognitive task decreased transfer of learning to new test conditions as demonstrated by increased error and decreased coherence for all conditions compared to single-task trained. Older adults, however, showed similar transfer between single-task trained and those performing a simple cognitive task. A complex cognitive task, however, demonstrated a similar transfer curve shape but with significant decrement in performance. Interestingly, the shape of the difficulty curve was maintained following training in young adults, though older adults had a flattening of the curve, performing similar on each condition with the exception of the highest rate of movement.

Hypothesis 3d

Increase in cognitive task difficulty will result in increased error rate and knee flexion rate during non-volitional responses to an unexpected perturbation, with a greater effect in older compared to younger individuals.

Partially Supported: Knee flexion rate was no different between single- and dual-task groups for both younger and older adults. Error rate, however, was greater in both younger and older adults performing the simultaneous complex cognitive task. The older adult group results may be confounded, however, due to not achieving the same level of performance as the other groups following training, as Chapter 3 revealed that full trial performance of the visuomotor task influences feedback control.

Hypothesis 3e

Dual-task training will decrease dual-task deficit for both older and younger adults.

Supported: Dual-task cost for both measures of coherence and trial error was lower for the dual-task trainers in both age groups. Upon retesting 7 days after training, however, younger adults had no difference in dual-task cost between dual-task and single-task trained, while older adults had lower dual-task cost after having been exposed to a simple cognitive task either in training or testing. Dual-task cost on the final day of testing is confounded, however, due to extended exposure to both single- and dual-task conditions most probably demonstrating the effects of hybrid practice rather than first day training.

Hypothesis 3f

Working memory capacity will predict rate of learning during both single and dual motor tasks in young but not in older subjects, while executive function will predict performance in both young and older groups.

Partially Supported: Working memory capacity was only moderately correlated with the learning rate of young adult single-task trainers, though no other group. Executive function, however, explained ~80% of the variability of final day performance for all dual-task groups, though not control groups, for both younger and older adults.

SUMMARY

In summary, we demonstrated that a combination of three resistances at the knee and three frequencies of movement generate a hierarchy of difficulty when performing a visuomotor task of a mini-squat according to a line on a screen. We then demonstrated that on this portion of the difficulty curve of a visuomotor task, differences in performance are detected even in healthy older adults without impairment. When performing a weight-bearing task, older adults show a velocity-accuracy trade off that is similar to upper extremity reaching studies. We also determined that pre-volitional feedback response to an unexpected force perturbation is altered with age and overall task performance; where older aged, poorer performers experience to poorest feedback response as measured by elevated error rates.

Finally, when examining the effects of a simultaneous cognitive task delivered to older and younger adults while learning the visuomotor task, principles of motor learning were effected. Rate of learning is increased in both older and younger adults as cognitive task difficulty increases, though in the older adult the complex cognitive task resulted in inability to improve visuomotor task performance within 20 training trials. Transfer of learning to new conditions was impaired in dual-task trained younger and older adults compared to single-task trained, though interestingly consolidation of learning was no different between single-task and dual-task trained for both age groups. Dual-task cost was lower in those that were dual-task trained revealing improved automatization of the motor task compared to single-task trained. Finally, executive function is strongly correlated with capability of both younger and older adults to perform a cognitive-visuomotor dual-task.

Future studies are necessary to determine if performance on this visuomotor task is correlated with the ability of older adults to perform other functional movements such as gait, or on clinical outcomes measures such as risk of lower extremity injury, risk of falling, or achieving community mobility. In this body of work, we have identified a quick and accurate method to assess the motor control system. This system has the precision to detect motor control differences even during healthy aging and may be a tool to both identify and to intervene to prevent injury.

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