When motor control hangs in the balance: Sensorimotor learning during balance-challenging conditions

by

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Abstract

Maintaining balance while moving is fundamental for safe and successful motor performance. However, this aspect of daily movement is often overlooked in experimental paradigms that assess adaptation during constrained and/or isolated tasks. Consequently, we cannot easily extrapolate the results from these studies to naturalistic motor behaviours. The goal of this thesis is to determine how the necessity to maintain balance during unconstrained movement affects sensorimotor learning. For my first study, I assessed how challenging balance during adaptation affects generalization of learning. Four groups of participants adapted to a new visuomotor mapping induced by prism lenses while performing either a standing-based reaching or walking task, with or without a manipulation that challenged balance. To assess generalization, participants performed a single trial of each of the other group's tasks without the prisms. I found that both the reaching and walking balance-challenged groups showed greater generalization to their equivalent, non-adapted task compared to the balance-unchallenged groups. I also found that challenging balance modulated generalization across the reaching and walking tasks. For my second study, I tested how challenging balance affected motor memory retention. To do this, the same four groups of participants returned to the lab and repeated their adaptation protocol one week later. I found that only the walking groups demonstrated faster relearning (or savings) during re-exposure to the prisms. Crucially, I found that challenging balance significantly enhanced savings during walking. In my third study, I determined how a stability consequence associated with movement errors affected sensorimotor learning. Two groups of participants adapted to a new visuomotor mapping while performing a precision walking task either with or without the possibility of experiencing a slip perturbation when making errors. I assessed generalization of learning across two visually guided walking tasks and motor memory consolidation. To assess consolidation, I introduced an opposite direction visuomotor mapping following adaptation and evaluated relearning one week later. I found that the experiencing a physical consequence when making errors enhanced generalization and motor memory consolidation. Overall, this thesis provides a novel perspective on how the necessity for balance control contributes to sensorimotor learning, which has intriguing implications for the development of rehabilitation interventions.

Keywords: adaptation; generalization; retention; balance control; postural threat

To my parents:

You gave me roots to know where home is

And wings to chase my dreams

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List of Acronyms

ACC	Anterior cingulate cortex
ANOVA	Analysis of variance
AP	Anterior posterior
APA	Anticipatory postural adjustment
BC	Balance-challenged
BF	Biceps Femoris
BOS	Base of support
BU	Balance-unchallenged
COM	Center of mass
COP	Center of pressure
EMG	Electromyography
HAT	Head, arms, and trunk
MA	Muscle activation
MG	Medial Gastrocnemius
ML	Medial Lateral
ns	Not significant
rTMS	Repetitive transcranial magnetic stimulation
SD	Standard deviation
SE	Standard error
SRT	Seated reaching task
TA	Tibialis Anterior
tDCS	Transcranial direct current stimulation
TMA	Total muscle activation
VL	Vastus Lateralis

Published studies

Research contained in this thesis has been published, or is in revision, in the following peer- reviewed journals:

Chapter 2	**Bakkum A, Donelan JM, Marigold DS.** Challenging balance during sensorimotor adaptation increases generalization. J Neurophysiol 123: 1342-54 (2020).
Chapter 3	**Bakkum A, Donelan JM, Marigold DS.** Savings in sensorimotor learning during balance-challenged walking but not reaching. Under review.

Chapter 1.

Introduction

> *"We have a brain for one reason and one reason only - and that's to produce adaptable and complex movements."*
>
> *(Daniel Wolpert)*

Our nervous system has a remarkable ability to adapt how we move in response to the changing world around us, and it does so with seemingly little effort. It is often only when we experience a significant change that affects or impairs our movement that we become aware of the inherent challenges to motor control. These changes may stem from the environment or the body itself (e.g., age-related changes or injury) and cause errors in movement by altering the normal relationship (or mapping) between sensory input and motor output. In normal circumstances, we are able to rapidly adapt in these situations and return to a previous level of performance as we learn a new sensorimotor mapping. Furthermore, we are able to retain what is learned and apply, or generalize, this learning to make predictions (or facilitate performance) in new contexts. Taken together, sensorimotor learning improves our ability to move within our environment.

From lifting a heavy load to navigating a busy sidewalk, most real-life movements necessitate extensive muscle coordination across multiple body segments to maintain balance and ensure safe and successful task performance. Despite these complex motor control problems, we are able to produce smooth and accurate movements that allow us to meaningfully interact with the world—highlighting both the flexibility and sophistication of our sensorimotor system. However, the need for balance control during daily movement is often overlooked during experimental paradigms that focus predominantly on adaptation during constrained and/or isolated tasks, which fail to capture the complexity of real-life movements. Consequently, results from these studies cannot be easily extrapolated to naturalistic motor behaviours, as during the latter, the control problem is complicated by the necessity to maintain balance while moving through the environment.

The goal of this thesis is to determine how the necessity to maintain balance during unconstrained, whole-body tasks affects adaptation, generalization, and retention of newly learned movement patterns. In this general introduction, I will first outline the different components of sensorimotor learning and some of the factors that affect this process. I will then discuss the potential influence of balance control on sensorimotor learning, as well as how a perceived threat of falling might impact adaptation, generalization, and retention of learning during unconstrained, naturalistic behaviours.

1.1. The different aspects of sensorimotor learning

Human movement control is complex. Yet, we are able to produce an assortment of coordinated and accurate motor behaviours. This flexibility requires the nervous system to learn and modify motor commands that lead to desirable outcomes. To do this, the nervous system engages multiple learning processes to acquire the knowledge necessary to produce the appropriate motor commands in any given situation. These distinct forms of learning include both sensorimotor adaptation and motor skill acquisition (Kitago and Krakauer 2013; Wolpert et al. 2011). During sensorimotor adaptation, the nervous system modifies well-learned movements in response to changing physiological and environmental states to regain a former level of performance. In contrast, motor skill acquisition entails learning new patterns of muscle activation and enhancing motor performance by reducing movement errors without sacrificing movement speed. Both adaptation and motor skill learning improve our ability to maintain movement accuracy while moving in and through the environment.

Sensorimotor learning processes are typically categorized by the type of information the nervous system uses as a learning signal (Spampinato and Celnik 2020; Wolpert et al. 2011). During error-based learning, for example, the nervous system compares the actual and predicted movement outcome to identify errors in movement (Wolpert and Ghahramani 2000). This form of learning is the driving force behind most sensorimotor adaptation paradigms and is discussed in more detail below. In contrast, the nervous system can also use reinforcement-based learning signals, such as success or failure, to explore which actions lead to desirable outcomes (Huang et al. 2011; Izawa and Shadmehr 2011; Shmuelof et al. 2012). For example, motivational feedback in the form of rewards and punishment can shape sensorimotor learning (Galea et al. 2015). Use-dependent learning can also influence the state of the motor system, where repeated execution of a movement, such as reaching to a target, can bias the direction of future reaching movements (Classen et al. 1998; Diedrichsen et al. 2010). Finally, recent research also highlights the involvement of cognition during sensorimotor learning, where people use deliberate strategies to achieve movement goals (Mazzoni and Krakauer 2006; Taylor and Ivry 2011; Taylor et al. 2014). Though evidence suggests that different forms of learning involve separate neural mechanisms (Haith and Krakauer 2013; Krakauer and Mazzoni 2011; Shadmehr and Krakauer 2008), it is important to acknowledge that these learning processes are not necessarily functionally independent. Thus, we use the term sensorimotor learning to incorporate these diverse learning systems and to describe any experience-dependent improvements in motor performance (Krakauer et al. 2019). For this thesis, I focus primarily on aspects of sensorimotor learning that pertain to how the nervous system adapts, generalizes, and retains learned motor behaviours.

1.1.1. Sensorimotor adaptation

To safely and effectively navigate our surroundings, we must maintain accurate sensorimotor mappings despite changing physiological and environmental states. For instance, changes to musculoskeletal and sensory systems as a result of aging or injury can disrupt the normal relationship between sensory input and motor output, causing errors in goal-directed movement. As we learn the new mapping, we are able to regain movement accuracy—a process known as sensorimotor adaptation. Given that our bodies and the environment change all the time, the ability to reliably adapt our movement becomes critical for successful motor behaviour in everyday life. This is also pertinent for patient populations, as it allows for some degree of natural recovery of function following injury or disease.

To produce successful motor commands, the nervous system relies heavily on sensory feedback to provide precise information about the state of our body and the environment. However, sensory feedback is delayed, sensory receptors transmit noisy information, and our bodies and the environment are continuously changing; all of which can lead to uncertainty and movement variability (Van Beers et al. 2002). Consider, for example, walking across the street and stepping up onto the sidewalk, as illustrated in Figure 1.1. If we only use visual information about where the curb is relative to our stepping limb, our estimate of the current state of our body would be delayed by ~100 ms and therefore, be obsolete (Wolpert and Ghahramani 2000). To compensate for such delays, the nervous system is thought to use model-based strategies to construct an estimate of the body’s state based on a broad understanding of how the body and environment function (Kandel et al. 2013; Shadmehr et al. 2010; Wolpert et al. 2011). Internal models are neural circuits that represent the relationship between sensory input and motor output and can be subdivided into two main components—the forward model and the inverse model. Forward models make predictions about the sensory consequences of a movement based on a copy of the motor command (i.e., the efference copy) (Fig. 1.1A). These predictions are then combined with actual sensory feedback to better estimate the current state of the body. This updated state estimate is then used by an inverse model (Fig. 1B) to facilitate or correct motor performance. Here, the inverse model uses feedforward control to generate the appropriate motor command based on the desired state (Shadmehr and Wise 2005; Wolpert and Ghahramani 2000). If the forward and inverse models are both accurate, their output (i.e., the predicted and actual movement) will be the same and there is no need to modify the motor command. In contrast, movement errors that occur as a result of discrepancies between the predicted and actual sensory consequences of a movement (i.e., a sensory prediction error) indicate that the initial motor command was not appropriate for the given task. For example, imagine you unexpectedly stub your toe on the curb. In this case, there is a mismatch between the predicted and actual consequences of the movement, resulting in a movement error. To correct for this error, the nervous system uses feedback control to account for such discrepancies between the desired and estimated states. The inverse model then modifies the motor command based on the updated state to, for example, increase flexion of the hip and foot of the stepping limb to clear the curb and prevent a fall. If movement errors persist, you may need to update the forward model to account for a recurring mismatch between the predicted and actual states. Taken together, the nervous system uses feedforward and feedback control to determine when and how to modify movement to regain movement accuracy—a process known as internal model recalibration (Wolpert and Flanagan 2016; Krakauer et al. 2019).

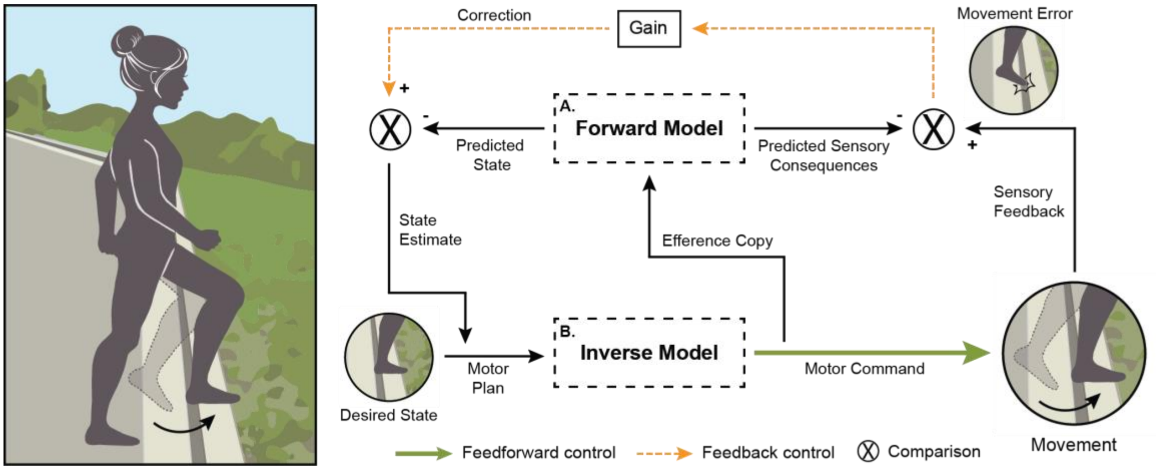

Figure 1.1 Internal model framework
Internal models represent the relationship between sensory input and motor output based on a broad understanding of how the environment and body function. ***A)*** Forward models make predictions about the sensory consequences of a movement based on an efference copy of the motor command. These predictions are then combined with actual sensory feedback to estimate the current state of the body. ***B)*** The inverse model uses the state estimate to generate the appropriate motor command (green arrow) based on the desired state using feedforward control. If both the forward and inverse models are accurate, the desired state will match the actual motor behaviour. In contrast, when movement errors occur, the nervous system uses feedback control (orange arrows) to correct for discrepancies between the desired and estimated states. See text for more details.

When we experience an error in movement, the nervous system must determine its source to correct for it—this is referred to as the credit assignment problem (Wolpert et al. 2001). Identifying the source of a movement error can be challenging, as the final outcome of most everyday movement is contingent on the interaction between multiple factors, such as the number of body parts involved and the desired limb trajectory. As a result of this complexity, we are not always successful in our movement and the reasons for why are often unclear. In this case, the nervous system needs to attribute the cause of the error to either internal (i.e., within the body) or external (i.e., environmental) factors. Internal factors, for example, may include deficits related to motor execution or altered sensorimotor mappings as a result of aging or injury. Furthermore, the nervous system must determine if the errors are temporary or are likely to persist, which will dictate whether and how we update our internal models. In the above example, there are several possibilities for why you may have kicked the curb, and the corrections required of the motor system would be different for each situation. For example, a momentary distraction, such as looking at your phone, may have caused you to miscalculate your foot trajectory relative to the height of the curb. In this case, any changes to your walking pattern would likely be temporary. Alternatively, if tiredness is to blame, you may choose to adjust your motor commands for the remainder of the day to account for such fatigue-induced errors. Consequently, solving the credit assignment problem is critical to determine whether internal model recalibration is necessary to regain movement accuracy for a given task.

Over the years, research across multiple adaptation paradigms has provided strong evidence for the use of internal models in motor control—though model-free mechanisms may also apply (Huang et al. 2011). We are able to study sensorimotor adaptation by systematically exposing the nervous system to perturbations, such as shifting the visual field using prism lenses (Alexander et al. 2011; Martin et al. 1996a; Redding and Wallace 2002) or rotating visual feedback (Krakauer et al. 2000; Krakauer et al. 2005; Krakauer 2009; Mazzoni and Krakauer 2006). We can also study how people adapt to more dynamic perturbations using robotic forcefields (Thoroughman and Shadmehr 2000; Shadmehr and Mussa-Ivaldi 1994; Shadmehr and Moussavi 2000) or split-belt treadmills (Morton and Bastian 2006; Choi and Bastian 2007) that physically perturb the limbs during movement. These techniques artificially disrupt the relationship between sensory input and motor output, causing errors in movement that result from the mismatch between the predicted and actual movement outcome. The resultant sensory prediction errors serve as a signal that something went wrong and over time, movement accuracy improves through a combination of error-based adaptation and other learning processes. For instance, error reduction can be achieved implicitly through cerebellum-dependent, internal model recalibration driven primarily by sensory predictions errors (Izawa et al. 2012; Mazzoni and Krakauer 2006; Morton and Bastian 2006; Synofzik et al. 2008; Tseng et al. 2007). Alternatively, recent research highlights the contribution of explicit strategic control during adaptation, demonstrating that deliberate strategies can also be employed to rapidly reduce movement errors (Mazzoni and Krakauer 2006; Redding et al. 2005; Taylor and Ivry 2011; Taylor et al. 2014). We can distinguish these two adaptative processes by measuring motor performance immediately after removing the perturbation, where an error in the opposite direction to the perturbation (i.e., a negative aftereffect) reflects implicit internal model recalibration (Redding and Wallace 1996). Furthermore, the timescales of implicit and explicit adaptation closely resemble two parallel processes involved in adaptation (McDougle et al. 2015; Smith et al. 2006). That is, a fast process that adapts and de-adapts rapidly and resembles explicit learning; and a slower process that adapts and de-adapts gradually over time and corresponds to implicit learning.

Sensory prediction error is a driving force for sensorimotor adaptation (Wallman and Fuchs 1998; Mazzoni and Krakauer 2006; Tseng et al. 2007). However, the extent to which internal models are updated is largely dependent on the conditions under which initial learning takes place (Kagerer et al. 1997; Criscimagna-Hemminger et al. 2010; Schlerf et al. 2013; Gibo et al. 2013). During adaptation studies, for example, participants may experience a sudden and abrupt perturbation that causes large initial errors in movement. Here, participants may engage more explicit strategies to rapidly reduce movement errors and compensate for the large perturbations. In contrast, if the perturbation is introduced gradually over multiple trials such that the movement errors are small, participants may be less aware of an environmental disturbance and learning may be more implicit. Consequently, error size can affect adaptation by engaging distinct learning processes that may adapt over different timescales. Young, healthy adults, for instance, show comparable learning in response to large and small errors, while older adults and patients with severe degeneration of the cerebellum are better able to learn from gradual perturbations (Buch et al. 2003; Criscimagna-Hemminger et al. 2010). This also suggests that gradual and sudden perturbations do not engage the same neural mechanisms. Error variability can also influence sensorimotor adaptation, as identifying the source of the error to correct for it becomes more challenging. This may result in delayed error reduction and impair overall adaptation (Howard et al. 2017). Alternatively, recent studies suggest that movement variability may serve to prime the nervous system, effectively guiding exploration to facilitate sensorimotor learning (Dhawale et al. 2017; Seidler 2004; Wu et al. 2014).

Taken together, identifying the source of the sensory prediction error is critical for sensorimotor adaptation. Furthermore, the presentation of such errors dictates how and when the nervous system updates its internal model to regain movement accuracy. In the following section, I will discuss aspects of sensorimotor learning that pertain to the transfer, or generalization, of learned movement patterns beyond training.

1.1.2. Generalization of sensorimotor adaptation

Human motor control is impressively versatile in that elements of learned movement patterns can be transferred beyond training and applied in new situations—a concept known as generalization (Poggio and Bizzi 2004). This requires the nervous system to make predictions about new situations based on past experiences. Rather than using a simple look-up table to map a specific consequence with the appropriate action, the nervous system adapts acquired motor skills to meet the demands of the new task or environment (Mussa-Ivaldi 1999; Poggio and Bizzi 2004). Consider, for example, learning to play tennis. While you may at first focus on your forehand stroke, ultimately you want to execute all tennis strokes effectively. As no two shots are the same, you must also adapt each stroke to changing conditions, such as the speed and direction of the ball. Fortunately, learning to execute one tennis stroke can improve your ability to perform others, especially those similar to the ones well-practised. While performance may still be imperfect, this prior experience can facilitate subsequent learning.

Sensorimotor adaptation, like motor skill learning, is not confined to the exact movement patterns acquired during training, but instead generalizes to unlearned movement directions (Krakauer et al. 2000; Thoroughman and Shadmehr 2000), amplitudes (Krakauer et al. 2000; Mattar and Ostry 2010) and workspace locations (Malfait et al. 2005; Wang and Sainburg 2005; Lei et al. 2013). Similarly, adapted movements can generalize beyond training to different limbs (Morton et al. 2001; Sainburg and Wang 2002; Savin and Morton 2008; Wang and Sainburg 2003; 2004) and in some instances, across different movement categories or tasks (Abeele and Bock 2003; Alexander et al. 2011; 2013; Morton and Bastian 2004). For instance, visuomotor adaptation during reaching with one arm can facilitate subsequent performance using the other arm (Sainburg and Wang 2002) and even the leg (Savin and Morton 2008). Additionally, visuomotor adaptation generalizes between a target tracking and a centre-out pointing task (Abeele and Bock 2003). However, the extent to which this generalization occurs varies widely and is often limited (Balitsky Thompson and Henriques 2010; Carroll et al. 2014; Ghahramani et al. 1996; Krakauer et al. 2000; Morton et al. 2001; Wang 2008; Wang and Sainburg 2004). Interlimb generalization, for example, is often asymmetric with some studies reporting unidirectional generalization from the nondominant to the dominant arm (Wang and Sainburg 2003; 2004) or vice versa (Balitsky Thompson and Henriques 2010). Similarly, the magnitude of generalization from the arm to the leg is far greater than that from the leg to the arm following prism adaptation (Savin and Morton 2008). Thus, adapted movements can generalize across a variety of tasks, although the degree to which generalization occurs appears largely dependent on the nature of tasks being assessed.

Generalization following sensorimotor adaptation is reflected by the degree to which naïve motor performance is impacted by past experience. In research, this is often demonstrated by motor performance that is biased towards the adapted state—also known as an aftereffect—indicating that the learned motor behaviour was applied to the new setting. Research examining generalization provides insight into the neural mechanisms underlying sensorimotor adaptation. For example, research shows generalization following adaptation to abrupt versus gradual perturbations likely engage distinct neural mechanisms (Berniker and Kording 2008; Fercho and Baugh 2014; Kluzik et al. 2008; Torres-Oviedo and Bastian 2012; Wilke et al. 2013). These studies highlight the significance of attributing movement error experienced during adaptation to either internal or external sources and the influence of this credit assignment on sensorimotor generalization. For example, gradual perturbations that produce small movement errors during adaptation may enhance generalization, as smaller errors are more likely attributed to the internal sources (i.e., produced by the body). In contrast, sudden perturbations that produce large and unusual movement errors are typically assigned to the training environment and are largely context dependent. This is evident following split-belt treadmill adaptation whereby the gradual introduction of a new walking pattern produced greater generalization to overground walking compared to an abrupt perturbation schedule (Torres-Oviedo and Bastian 2012).

Research exploring generalization may also inform the development of more effective rehabilitation protocols that promote the transfer of learning to real-world settings. For instance, “device-induced” learning via robots or treadmills can be used to facilitate rehabilitation (Bastian 2008), though it is imperative for this learning to generalize to real-world settings for it to be meaningful. Studies show, however, that generalization to natural movement following “device-induced” adaptation is limited and short-lasting (Cothros et al. 2006; Reisman et al. 2009; Reynolds and Bronstein 2004). For example, Reisman et al. (2009) demonstrated that split-belt treadmill adaptation generalizes to overground walking in persons post stroke, though not completely. These authors used an abrupt perturbation protocol where participants had large and variable movement errors. However, a gradual introduction of the new walking pattern, such as the protocol used in Torres-Oviedo and Bastian (2012), may enhance generalization, as the restriction of movement error to the body’s natural range promotes general adjustments that transfer across contexts. Thus, generalization patterns help us gain insight into how sensorimotor learning is controlled and the strategies that can be used to enhance generalization beyond a clinical setting.

Altogether, generalization allows us to capitalize on past experience to facilitate subsequent learning, though the extent of generalization depends largely on the tasks being assessed and the training conditions. Research exploring generalization provides valuable insight into the mechanisms underlying adaptive behaviour which may inform the design of effective rehabilitation interventions aimed at promoting recovery following neurological injury and disease. In the following section, I will discuss how the nervous systems retains and recalls motor memories formed during adaptation and the factors that influence this motor memory retention.

1.1.3. Motor memory retention

From tying shoelaces to riding a bicycle, people are able to retain learned motor skills for prolonged periods of time despite inconsistent practice. This motor memory allows us to rapidly meet the demands of familiar tasks and environments and increases the likelihood of future task success. Given that we are likely to encounter familiar motor tasks on a daily basis, the ability to store and quickly recall previously learned movement patterns is important for everyday motor control. This is also beneficial following physical rehabilitation, as it allows patients to build on what has been learned in successive therapy sessions.

In sensorimotor adaptation, motor memory retention is reflected by faster adaptation (or relearning) during re-exposure to a familiar perturbation—a phenomenon known as savings (Brashers-Krug et al. 1996; Krakauer et al. 2005). For example, people demonstrate faster adaptation (i.e., a faster reduction in movement error) upon re-exposure to a previously learned visuomotor mapping induced by prisms lenses (Bakkum et al. 2021; Maeda et al. 2017b; 2018; McGowan et al. 2017). Research suggests that a memory of errors, or experience with errors similar to those encountered during relearning, elicits savings (Herzfeld et al. 2014; Leow et al. 2016). Other studies, however, suggest that savings is achieved explicitly through the recall of a deliberate aiming strategy (Haith et al. 2015; Morehead et al. 2015; Nguyen et al. 2019). While the processes that underlie savings remain subject to debate, these performance improvements can be observed over extended periods of time and demonstrate the potential long-term benefits of prior learning on subsequent motor performance. For example, motor memories can be retained for hours, days, and even up to one year (Brashers-Krug et al. 1996; Day et al. 2018; Krakauer et al 2005; Maeda et al. 2017b; 2018). However, similar to generalization, the extent to which savings occur is largely dependent on the conditions of initial learning. For example, studies show that an abrupt perturbation schedule that elicits large movement errors results in greater savings (Leech et al. 2018; Morehead et al. 2015; Malone et al. 2011). Additionally, increasing the amount of exposure to the perturbation influences how quickly people recall a previously learned movement (Alhussein et al. 2019; Day et al. 2018; Nguyen et al. 2019; Roemmich and Bastian 2015). Taken together, these findings highlight the flexibility of motor memory formation and demonstrate that learning conditions can be manipulated and leveraged to elicit enhanced savings.

To retain a motor memory, the brain must transfer the memory from a short-term volatile state to a longer-term fixed state through the process of consolidation. Here we operationally define consolidation as the motor memory becoming stable over time and resistant to interference by competing mappings (Brashers-Krug et al. 1996; Krakauer et al. 2005; Krakauer and Shadmehr 2006; Shadmehr and Brashers-Krug 1997). Under appropriate conditions, consolidation begins with a short-term process where information is bound into memory traces and stored within the hippocampus and related medial temporal lobe structures for retrieval (Alvarez and Squire 1994; Squire 1992). Over time, repeated retrieval of the memory trace strengthens the connections between these structures and the neocortex through synaptic plasticity (Dudai 2004), eventually eliminating the need for hippocampus as the neocortex alone is capable of sustaining the memory for long periods of time. This standard model of memory consolidation is supported by studies demonstrating that lesions to the hippocampus of humans and other animals generally impair memories of recently learned information (i.e., short-term memories), though older memories are preserved (Squire 1992). However, learning new material shortly after initial learning can disrupt or interfere with consolidation of short-term memories. For example, learning a new *mapping B* soon after learning *mapping A* can disrupt the consolidation of *mapping A* and impair motor memory retention—a process known as retrograde interreference (Goedert and Willingham 2002; Krakauer et al. 1999; Krakauer et al. 2005; Wigmore et al. 2002). Prior learning can also negatively impact subsequent learning where there is a marked decrease in initial performance during *mapping B* following adaptation to *mapping A*. This is defined as anterograde interference, where performance is biased towards a previously adapted state (i.e., *mapping A*) such that any observable performance improvements during relearning of *mapping B* may be masked (Brashers-Krug et al. 1996; Hinder et al. 2007; Krakauer et al. 2005; Lerner et al.

2020; Miall et al. 2004). After repeated exposure, however, the effects of interference decrease, and we are able to learn and retain competing sensorimotor mappings—a concept known as dual adaptation (van Dam et al. 2013; Welch et al. 1993)

Research suggests that interference may be mitigated by prolonging the passage of time between different bouts of learning to allow for consolidation. For example, savings of force-field adaptation is evident during reaching movements when subsequent learning of a second, opposing force-field occurs ~4-6 hours after initial learning (Brashers-Krug et al. 1996; Shadmehr and Brashers-Krug 1997). This suggests that motor memories may be stable and less susceptible to retrograde interference after sufficient time has passed between learning sessions. However, the benefits of this approach are not always evident. Several studies have failed to demonstrate consolidation even with prolonged breaks between learning (Bock et al. 2001; Caithness et al. 2004; Goedert and Willingham 2002). Additionally, research suggests that the addition of so-called "washout" trials that serve to return performance to baseline levels prior to learning a new mapping can attenuate performance detriments due to anterograde interference (Krakauer et al. 2005), though the addition of washout trials is not always sufficient to unmask consolidation (Caithness et al. 2004). Evidently, much of the literature on motor memory consolidation is conflicting and has, understandably, resulted in great controversy. Still, the process of consolidation remains a critical component to how motor memories are formed and stored and as such, continues to be an important topic of research.

Overall, the ability to recall past experiences allows us to rapidly select appropriate motor commands to meet the demands of familiar tasks and environments. This motor memory is reflected by faster relearning, or savings, which is largely dictated by the conditions of initial learning. Research exploring motor memory retention and consolidation deepens our understanding of the mechanisms that underlie memory formation and interreference in sensorimotor learning. Ultimately, insight into how motor memories are formed and stored may improve the development of training and rehabilitation protocols that enhance savings and mitigate unwanted interference.

1.2. The influence of balance control on sensorimotor learning

Maintaining balance while moving is fundamental for safe and successful motor performance in everyday life. Even mundane tasks like washing the dishes or doing the laundry require extensive muscle coordination across multiple body segments to control balance while maintaining movement accuracy. Here, the nervous system must generate the appropriate motor commands to ensure task success while implementing effective postural control strategies to prevent falling and possible injury. This is undoubtedly a complex motor control problem, yet everyday experience demonstrates our ability to function and even thrive when confronted with these inherent movement challenges. Still, this aspect of daily motor control is often overlooked in experimental paradigms that focus predominantly on adaptation during seated, isolated upper limb movements where maintaining balance is not a major concern (Krakauer et al. 2000; Shadmehr and Mussa-Ivaldi 1994). Even studies exploring adaptation during walking are typically constrained by a treadmill and as a result, do not challenge balance to the same degree as real-life motor behaviours (e.g., Roemmich and Bastian 2015). Consequently, results from these studies fail to capture the complexity of naturalistic movements that necessitate balance control.

The human musculoskeletal system comprises over 600 muscles spanning 206 bones that provide both structure for the body and facilitate movement (Zatsiorsky and Prilutsky 2012). The interconnected nature of this system is such that it requires intricate coordination between multiple degrees of freedom in service of even the simplest of actions—just pointing your index finger requires coordinating activity across several muscles that determine the motion of many digits (Schieber 1995). During movement, the degrees of freedom can be defined as any factors that arise from the body’s biomechanics or physiology, such as additional body segments, joints, and muscles, that influence the body’s motion and/or state (Bernstein 1967). As movement becomes more elaborate and the degrees of freedom increase, multiple movement strategies can achieve the same movement goal. Bernstein (1976) referred to this redundancy as the “degrees of freedom problem” which states that the nervous system must learn to integrate and coordinate multiple degrees of freedom to reduce redundancy and achieve skilled motor performance. As most daily tasks make use of multiple body segments and limbs, real-world sensorimotor learning is complicated.

The ability to stand upright while interacting with the world is critical for everyday movement. Doing laundry, for example, requires widespread muscle coordination to maintain a stable, upright posture while handling different objects. Human standing is inherently unstable as the upper-body—comprised of the head, arms, and trunk (or the "HAT" segment)—makes up two-thirds of the body's mass, which lies above two-thirds of the body's height (Winter et al. 1990). This mass represents a large inertial load that needs to be regulated to maintain an upright standing posture and prevent falling. This requires the nervous system to stabilize the body's centre of mass (COM) against gravity and within the base of support (BOS), typically defined as the area of the body that is in contact with the support surface (Horak 2006; Winter 1995). This so-called "postural equilibrium" is achieved, in large part, using the centre of pressure (COP) to shift the COM away from the limits of the BOS through the application of vertical ground reaction forces to the standing surface (Winter 1995). The nervous system must also account for the self-initiated postural perturbations that occur during object manipulation, such as loading the laundry into the washing machine. Here, the nervous system must make anticipatory postural adjustments (APAs) prior to or at the onset of postural disturbances to maintain postural equilibrium (Cordo and Nashner 1982; Winter et al. 1990). Furthermore, the nervous system must control motion across multiple free-moving body segments to move accurately while maintaining balance. For example, turning the cap on the laundry detergent and pouring it into the machine requires coordinating several upper-limb joints as well as the trunk and legs to ensure task success. These multi-joint movements require compensation for the dynamic coupling between different body segments, where motion at one joint can cause accelerations at all other joints in the system through interaction torques (Ketcham et al. 2004; Nott et al. 2010; Yu et al. 2011; Zajac 1993). Movements of the shoulder and elbow, for instance, require coordinated muscle co-contractions to control for the effects of dynamic coupling and maintain movement accuracy (Gribble and Ostry 1999; Gribble et al. 2003). Consequently, standing-based movement requires extensive sensorimotor control to ensure safe and successful task performance.

Walking is one of the most common forms of human movement, as it allows us to navigate our surroundings. While this is a challenging task during the developmental stages, people eventually learn to walk over diverse terrain with relative ease. This is impressive because the nature of bipedal walking is such that the nervous system must intermittently control movement of the entire body with only one foot in contact with the ground (Winter, 1995). During each stride, stability is challenged as the forward momentum of the HAT segment causes the body's COM to move beyond the small BOS provided by the planted foot (Patla 2003). As a result, the transition between the single and double support phases of walking is described as a continuous state of controlled falling and recovery, where foot placement of the swinging limb serves to catch the large inertial load of the HAT segment to regain stability after each stride (Perry 1992). People are able to simplify the control required of walking by harnessing the passive dynamics associated with gravity-dependent movement, where motion can be generated without continuous control through active force production (McGeer 1990). Taking advantage of such passive dynamics is one method of keeping the energetics costs of walking low—a primary objective of the nervous system (Abram et al. 2019; Donelan et al. 2001; Selinger et al. 2015; Zarrugh et al. 1974). However, cost minimization is not the only concern during walking, as people must also be accurate in their foot placement to maintain balance and avoid falling over. While passive-dynamic control can provide some degree of step-to-step stability in the sagittal plane, more active control is required for lateral stabilization during foot placement (Bauby and Kuo 2000; Donelan et al. 2004; Kuo 1999; O'Connor and Kuo 2009; Wong et al. 2010). As everyday walking is rarely restricted to planar motions, maintaining stability in more challenging walking situations typically comes with a greater metabolic cost (Donelan et al. 2004). Downhill walking, for example, imposes a greater energetic cost for a more stable gait pattern (Hunter et al. 2010). Despite this additional penalty, however, people still prefer to sacrifice economy for stability in this situation. Thus, the neural control of walking is complicated by both the need to control motion of the entire body, as well as the trade-off between minimizing the risk of falling and the energetic costs associated with more active control strategies.

Though the challenges to standing and walking balance control may differ slightly, both require the nervous system to engage proactive and reactive strategies to prevent falling. During proactive balance control, the nervous system uses past experiences to respond to anticipated perturbations (Patla 2003). Prior knowledge of an upcoming slippery surface, for instance, results in anticipatory postural adjustments, such as reducing lower limb loading and stepping with a flatter foot, that allow a person to walk safely across the surface (Cham and Redfern 2002; Heiden et al. 2006; Marigold and Patla 2002). In contrast, reactive balance control strategies rely on sensory feedback (e.g., vision or proprioception) to rapidly respond to unexpected postural perturbations (Patla

2003). For example, people use reactive balance recovery strategies using the ankle and hip musculature to resist unexpected platform translations (Horak and Nashner 1986). Similarly, people demonstrate reactive balance control during perturbed walking (Eng et al. 1997; Liu et al. 2018), when tripping over obstacles (Schillings et al. 2000; Shirota et al. 2014), and while recovering from a slip (Cham and Redfern 2001; Marigold and Patla 2002; Marigold et al. 2003; Oates et al. 2010). During a slip, for example, people typically employ a rapid arm elevation strategy that serves to shift the COM forward to prevent falling backwards (Marigold and Patla 2002; Marigold et al. 2003; Oates et al. 2010). The inability to appropriately respond to postural perturbations, be it through proactive or reactive strategies, leads to an increased fall risk. This is evident in both older adult and stroke patient populations who demonstrate impaired balance recovery (Buurke et al. 2020; Joshi et al. 2018; Mackey and Robinovitch 2006; Marigold and Eng 2006). Taken together, daily movement is plagued by inherent stability challenges that demand continuous and timely sensorimotor control to achieve and maintain movement accuracy.

1.2.1. Implications of postural threat on sensorimotor learning

Real-world movement errors have real-world consequences. In some cases, the consequences of our actions are severe. As a result, the level of risk associated with a given task can shape how we move. Consider, for example, walking down a flight of stairs. As this is a frequent occurrence, you may view this as a simple task and even feel comfortable skipping every second step. Now imagine the stairs are covered in snow. Given the greater risk of slipping and the possibility of injuring yourself, you might choose to reconsider your two-stair descent strategy and opt for a more cautious approach. This notion is supported by studies demonstrating that the fear of falling can significantly impact postural control and gait. For example, studies that modify the perceived consequences of instability by raising the height of a standing surface show that people adopt more conservative postural control strategies to reduce the body's COM displacement (Adkin and Carpenter 2018; Brown and Frank 1997; Carpenter et al. 2001). Furthermore, the fear of falling elicits changes to gait parameters such as reduced gait speed, shorter stride lengths, and greater gait variability in older adults (Chamberlin et al. 2005; Delbaere et al. 2009; Maki 1997). Such safety-driven strategies are also observed when vision is altered (e.g., blurred vision or reduced lighting) during stair or curb negotiation, such that people tend to slow down, increase toe-clearance height, prolong the double-support phase, and/or reduce COM displacement (Alexander et al. 2014; Buckley et al. 2005; Heasley et al. 2004; 2005). These findings suggest that the nervous system prioritizes balance control in response to the perceived threat of falling during movement.

Taken together, balance control is a prerequisite for most everyday movements to ensure task success and reduce the risk of falling. As a result, decisions about how we move are made under constant consideration of postural threat and the potential injurious consequences of losing balance. Nevertheless, research exploring adaptation focusses predominantly on isolated movements that are devoid of any real-life consequences for losing balance. Thus, for this thesis, we probed how balance constraints impact sensorimotor learning.

1.3. Overall goal and specific aims of this thesis

The ability to recalibrate movement in response to sensorimotor changes is essential for successful motor performance over a lifetime. Research exploring sensorimotor learning highlights the versatility of our nervous system and demonstrates that learning conditions can be leveraged for improved motor performance and recovery following neurological disease and injury. However, most experimental paradigms assess adaptation during constrained tasks that fail to capture the complexity of natural movement and the possible role that balance plays in sensorimotor learning. Given that challenges to postural stability, and indeed the need to control balance, is a central component of voluntary movement during most everyday tasks, it is surprising that this aspect of motor control is often overlooked in experimental paradigms. ***Thus, the overall goal of this thesis is to determine how the necessity to maintain balance during unconstrained, whole-body tasks affects sensorimotor adaptation, generalization, and retention of newly learned movement patterns.*** The results of this thesis provide a novel perspective on how learning during unconstrained, naturalistic behaviours that necessitate balance control might be beneficial for motor performance. Furthermore, these findings may inform the development of rehabilitation interventions designed to facilitate sensorimotor learning in clinical populations that suffer from neurological impairments as a result of injury, disease, and/or aging. The following outlines the specific aims of my thesis:

Aim 1 (Chapter 2): Determine how challenging balance during sensorimotor adaptation affects generalization. Research exploring adaption during isolated upper-limb movements demonstrates that the extent of generalization in these tasks varies widely and it is often quite limited. Yet, everyday experience indicates that people can generalize between a variety of motor behaviours. One possible explanation for this discrepancy is that most experimental paradigms fail to capture the complexity of real-life movements that often challenge our balance. We propose that the balance challenges associated with such naturalistic movements increase the value to the nervous system of using a more comprehensive and accurate internal model for motor control. We use the term “more comprehensive” to describe an internal model that represents more degrees of freedom that derive from the body’s anatomy, such as additional body segments, muscles, and neurons. Because a more comprehensive model is less tailored to a specific task, it might be more generalizable. Thus, in this first study, we test the hypothesis that challenging balance during adaptation increases generalization of a newly learned internal model.

Aim 2 (Chapter 3): Determine how challenging balance affects sensorimotor savings. Safe and successful motor performance over a lifetime relies, in part, on the memory of past motor experiences. As maintaining balance is a primary objective of the nervous system, we might expect the nervous system to prioritize remembering information that minimizes threats to postural stability to avoid harm and ensure safe motor performance in the future. Thus, we propose that adaptation during balance-challenged tasks that require greater control to prevent falling increases the value assigned to maintaining a learned internal model. As it may serve to benefit future performance, we propose that a greater-valued model is a more retainable model. Therefore, in this study, we test the hypothesis that challenging balance during adaptation increases sensorimotor savings, reflected by faster relearning one week later.

Aim 3 (Chapter 4): Determine how the consequence of movement error affects sensorimotor learning. Real-life movement errors can have severe consequences and result in injury. As most experimental paradigms are devoid of significant penalties imposed for movement errors, it is unclear how the consequence of being inaccurate affects how we learn new motor behaviours. In this final study, we test the hypothesis that a stability consequence experienced during movement errors increases the value of movement accuracy and enhances sensorimotor learning, reflected by greater generalization and motor memory consolidation.

Chapter 2.

Challenging balance during sensorimotor adaptation increases generalization

> *"So be sure when you step, Step with care and great tact. And remember that life's A Great Balancing Act."*
>
> *(Dr. Seuss)*

2.1. Abstract

From reaching to walking, real-life experience suggests that people can generalize between motor behaviors. One possible explanation for this generalization is that real-life behaviors often challenge our balance. We propose that the exacerbated body motions associated with balance-challenged, whole-body movements increases the value to the nervous system for using a comprehensive internal model to control the task. Because it is less customized to a specific task, a more comprehensive model is also a more generalizable model. Here we tested the hypothesis that challenging balance during adaptation would increase generalization of a newly learned internal model. We encouraged participants to learn a new internal model using prism lenses that created a new visuomotor mapping. Four groups of participants adapted to prisms while performing either a standing-based reaching or precision walking task, with or without a manipulation that challenged balance. To assess generalization after the adaptation phase, participants performed a single trial of each of the other group's tasks without prisms. We found that both the reaching and walking balance-challenged groups showed significantly greater generalization to the equivalent, non-adapted task than the balance-unchallenged groups. Additionally, we found some evidence that all groups generalized across tasks, for example, from walking to reaching, and vice versa, regardless of balance manipulation. Overall, our results demonstrate that challenging balance increases the degree to which a newly learned internal model generalizes to untrained movements.

2.2. Introduction

Humans are able to make an assortment of coordinated movements. This versatility is achieved to a large extent by adapting acquired motor skills to specific sensorimotor conditions or task demands. It is thought that our nervous system uses internal models of the body’s dynamics to help estimate the body’s state, and to determine appropriate motor commands for a given task (Shadmehr et al. 2010; Wolpert et al. 2011), though model-free mechanisms may also be relevant (see, for example, Huang et al. 2011). The ability to transfer, or generalize, learned behaviors to novel contexts is critical for successful performance of everyday movements. This is also of practical importance following physical rehabilitation, as it enables patients to generalize what is learned in a clinical setting to the real world.

Research exploring generalization has focused predominantly on adaptation during isolated upper limb movements. The extent of generalization in these tasks varies widely, but it is often quite limited (Balitsky Thompson and Henriques 2010; Carroll et al. 2014; Ghahramani et al. 1996; Krakauer et al. 2000; Morton et al. 2001; Wang 2008; Wang and Sainburg 2004). There is evidence to suggest that practicing a broader range of movements during force field adaptation (Berniker et al. 2014) or sampling more of the visuomotor workspace during training (Krakauer et al. 2000) is advantageous for performance during generalization. However, the benefits of broad experience are not always apparent (Mattar and Ostry 2007, 2010). Interlimb generalization is also often asymmetric, with some studies reporting that adaptation with the non-dominant arm generalizes to the dominant arm but not vice versa (Wang and Sainburg 2003, 2004), while others have found the opposite (Balitsky Thompson and Henriques 2010). These patterns can depend on the location of the workspace and handedness (Wang and Sainburg 2006a,b).

Unlike many experimental paradigms, most everyday motor tasks make use of multiple body segments and limbs. For instance, both hands are typically used to open a jar, walking requires the coordination of both legs, and reaching to grasp a doorknob requires coordination of multiple upper limb joints as well as the trunk and legs. It seems reasonable that the nervous system requires a more comprehensive internal model to coordinate the entire body compared to the movements of a single finger or limb. We use the term “more comprehensive” to describe an internal model that represents more of the body's degrees of freedom, be they arise from additional body segments, joints, muscles, neurons, or other aspects of the body's biomechanics and physiology. Without a more comprehensive model, the nervous system would not account for the dynamic coupling between body segments, where motion of one segment results in acceleration of another (Nott et al. 2010; Yu et al. 2011; Zajac 1993).

How might whole-body movements, where a more comprehensive model is important, affect generalization? Although research addressing this question is limited, symmetrical generalization between the two legs does occur when learning a leg tracking task while walking (Krishnan et al. 2017). In addition, we have shown that prism adaptation while walking and stepping on targets or over obstacles generalizes between the two tasks, albeit not completely (Alexander et al. 2013). Furthermore, the adaptation to split-belt treadmill walking generalizes to over-ground walking to some degree (Choi and Bastian 2007; Torres-Oviedo and Bastian 2012), though there is limited generalization of this adaptation between walking and running (Ogawa et al. 2012). Interestingly, Morton and Bastian (2004) showed that prism adaptation of walking generalized to standing-based reaching but not vice versa. Other research using different reaching and walking tasks, however, found the opposite (Michel et al. 2008): prism adaptation during reaching generalized to walking, but walking did not generalize to reaching. Taken together, simply using more of the body during adaptation does not appear to maximize generalization, suggesting that other factors are involved.

Balance is fundamental to virtually all meaningful motor tasks. For instance, both reaching to grab a box of cereal from a shelf or walking across different terrain relies on appropriate foot placement and extensive muscle coordination to control the body. The seated, isolated upper-limb tasks typically studied in the lab fail to account for the balance required in real-life movements and the possible role that balance plays in sensorimotor learning. Even in many lab-based walking paradigms (e.g., Roemmich and Bastian 2015), balance is not challenged to the same extent as in real-world environments. Challenges to balance increase the body's sensitivity to movement disturbances, including disturbances that arise from discrepancies between the nervous system's internal model of the body's dynamics and the body's actual dynamics. For instance, under stable conditions, some unintended motion may be ignored and not represented in the nervous system's internal model of the body, since the effects of this motion are trivial. When balance is challenged, however, the same motion might destabilize the body to a greater extent and therefore needs to be modelled to prevent a fall. We argue that the necessity to control exacerbated body motions associated with balance-challenged, whole-body movements increases the value to the nervous system for using an accurate and comprehensive internal model. A more comprehensive model is also a more generalizable model—it is less customized to a specific task. Therefore, we tested the hypothesis that challenging balance during adaptation enhances generalization.

To test our hypothesis, we had different groups of participants adapt to a novel visuomotor mapping induced by prism lenses while performing a standing-based reaching or walking task, with and without a manipulation that challenged balance. The prisms caused a mismatch between what the participants saw and how they moved, making their current internal model obsolete. The nervous system had to adapt its model to perform the task successfully. Previous work from our lab demonstrated model-based learning in prism adaptation during a precision walking task similar to that used in this study (Maeda et al. 2017a). We then probed generalization of this new model by having participants perform a different, non-adapted task/condition. As a primary test of our hypothesis, we probed generalization between balance-unchallenged and balance-challenged reaching and between balance-unchallenged and balance-challenged walking. Given the conflicting results of past research (Michel et al. 2008; Morton and Bastian 2004; Savin and Morton 2008), and as a secondary test of our hypothesis, we also probed generalization across the standing-based reaching and walking tasks.

2.3. Materials and methods

2.3.1. Participants

Forty-eight participants (mean age ± SD: age = 22.9 ± 3.7; 25 males, 23 females; right-limb dominant, as defined by the limb used to either kick or throw a ball), with no known musculoskeletal, neurological, or visual disease participated in this study. Four participants wore corrective lenses (glasses or contact lenses) during the experiments. The Office of Research Ethics at Simon Fraser University approved the study and each participant provided informed, written consent prior to participating.

2.3.2. Experimental tasks and data collection

We randomly assigned participants to one of four adaptation groups (n = 12 each). Each group learned a novel visuomotor mapping induced by prism lenses (Fig. 2.1A), while performing either a precision reaching or walking task. These tasks were performed while balance was challenged (balance-challenged) or without an additional balance manipulation (balance-unchallenged). This created the following groups: balance-unchallenged reaching, balance-challenged reaching, balance-unchallenged walking, and balance-challenged walking. We assessed how the balance manipulation affected a) the generalization of the learned visuomotor mapping across the different balance conditions for the same task (e.g., generalization from the balance-unchallenged to the balance-challenged walking tasks), and b) the generalizability of learning across different tasks (e.g., from reaching balance-unchallenged to walking balance-unchallenged). To assess generalization, participants performed a single trial of each of the other groups' tasks without prisms, as well as a non-limb-based, seated reaching task using head movements. Figure 2.1C illustrates the experimental tasks performed during the testing session.

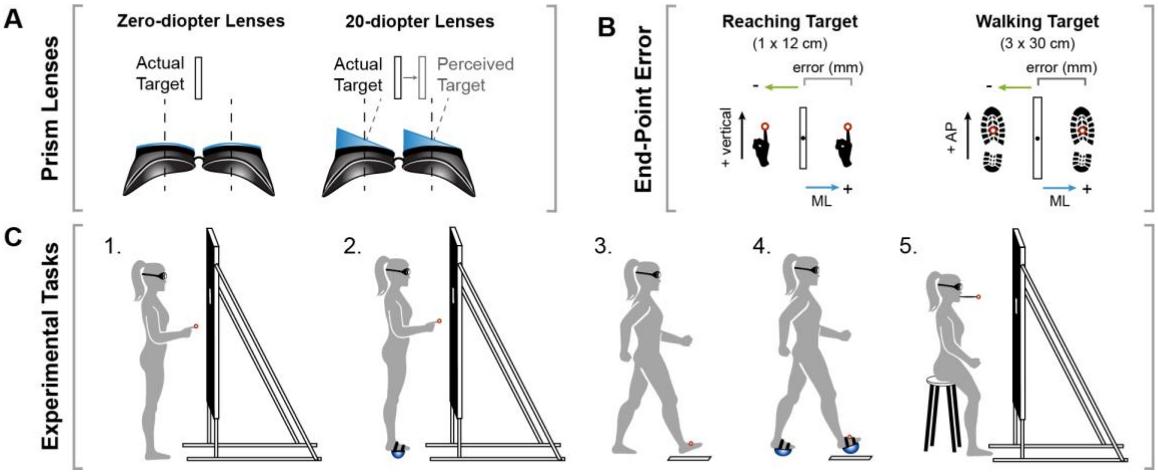

Figure 2.1 Experimental tasks
A) A simulated view of the target through the goggles coupled with zero-diopter (non-visual-field-shifting) lenses and 20-diopter prism lenses that shift the perceived location of the target 11.4° to the right. ***B)*** An illustration showing positive (+) and negative (-) medial-lateral (ML) end-point error, defined as the distance between a position marker on the limb and the center of the target line. AP = anterior-posterior direction in laboratory space. C) An illustration of each experimental task performed during the testing session. This includes (from left to right): reaching balance-unchallenged, reaching balance-challenged, walking balance-unchallenged, walking balance-challenged, and the non-limb based, seated reaching tasks.

For the standing-based reaching tasks, participants stood at approximately 90% of their arm's length away from a screen (279 x 218 cm) and reached to the medial-lateral (ML) center of a back-projected target (width: 1 cm; vertical length: 12 cm) with the index finger of their right hand (Fig. 2.1B). As we were primarily concerned with end-point error in the ML dimension, we used a longer target to reduce the accuracy demand in the vertical dimension. Participants wore comfortable walking shoes and performed this task while having their balance challenged or without any additional balance manipulation. For the balance-unchallenged condition, participants performed the task with their feet approximately shoulder-width apart (Fig. 2.1C1). For the balance-challenged condition, participants performed the task with inflatable rubber hemispheres (radii: 8.5 cm) attached to the soles of their shoes to reduce the control afforded by shifting the center of pressure under the base of support (Fig. 2.1C2). We instructed participants to stand with their feet as close together as possible without the rubber hemispheres touching each other. Participants placed the index finger of their reaching hand on their chin before the start of each trial. An experimenter helped stabilize the participants before the start of each trial; thereafter, the participant performed the reach without any assistance. A safety harness system attached to the participants at all times prevented falling to the ground in the event of a loss of balance; however, no participant engaged the system during the course of the experiment.

For the precision walking tasks, participants walked and stepped with their right foot onto the ML center of a projected target (3 x 36 cm) without stopping (Fig. 2.1B). As we were primarily concerned with end-point error in the ML dimension, we used a longer target to reduce the accuracy demand in the anterior-posterior (AP) dimension and to prevent participants from using shuffle steps near the target area. Participants took a minimum of two steps before and after the step to the target. The two preceding steps allowed participants to determine their walking trajectory and align themselves in preparation for the step to the target, which we positioned in the center of the walkway for all trials. Participants performed this task while balance was challenged and without any additional balance manipulation. For the balance-unchallenged condition, participants performed the task while wearing normal walking shoes (Fig. 2.1C3). For the balance-challenged condition, participants performed the task with the same inflatable rubber hemispheres (as described above) attached to the soles of their shoes (Fig. 2.1C4). An experimenter helped stabilize the participants before the start of each trial. Thereafter, the participant performed the task without assistance. We randomized the participant's AP starting location (between 1.5 - 2.5 m) in all trials to avoid learning specific walking sequences or timing and to increase the demand for visual feedback during the task.

For the reaching tasks, an LCD projector (Epson EX7200) back-projected the target onto a screen (279 x 218 cm). We aligned the top of the target to the participant's chin. For the walking tasks, a different LCD projector (Epson PowerLight 5535U; brightness of 5500 lumens) displayed the target on a black uniform mat covering the walking path (~ 6 m long). We configured the target's size and position in MATLAB (The MathWorks, Natick, MA) with the Psychophysics Toolbox, version 3 (Brainard 1997; Kleiner et al. 2007). To diminish the effect of environmental references and increase target visibility, participants performed the tasks under reduced light conditions (~0.9 lux).

We also designed a non-limb-based, seated reaching task to serve as a universal comparison for generalization across adaptation groups. For this task, participants sat on a backless stool at approximately 90% of their arm's length away from a screen (279 x 218 cm) and reached with their head to the ML center of a back-projected target (1 x 12 cm) using a pointing-instrument (tongue depressor, 1.75 x 15.24 cm) placed in their mouth (Fig. 2.1C5). We aligned the top of the target to the participant's chin. The participants used head movements to reach to targets, while in a seated position, to reduce favoring the limbs involved in either reaching or walking task and to minimize the need to control whole-body balance.

For all tasks, we instructed participants to be as accurate as possible when reaching, stepping, or head-pointing to the target. We also instructed participants to perform the tasks at a quick and constant pace. These guidelines minimized online corrections of the finger or leg/foot trajectory to more closely match previous experiments in which the movements are ballistic and emphasize the use of sensory feedback prior to movement. Participants received visual feedback through the lenses during each task; however, we instructed the participants to have their eyes open only when they were performing the task to prevent adaptation between trials. To begin a trial, participants opened their eyes once cued by an audible tone and immediately started moving to the target. An experimenter demonstrated each task prior to the testing.

An Optotrak Certus motion capture camera (Northern Digital, Waterloo, ON, Canada), positioned perpendicular to the walkway, recorded (at 120 Hz) infrared emitting position markers placed on the participant’s mid-back (in line with the sternum), index finger of the right hand, and bilaterally on the heel, mid-foot (second-third metatarsal head), and the toe (third metatarsal). Additionally, we attached a position marker to the end of the tongue depressor used during the non-limb-based, seated reaching task. An electromyography (EMG) system (MA300; Motion Lab Systems, Baton Rouge, LA), synchronized via the Optotrak data acquisition unit, recorded leg muscle activity at a sampling frequency of 2,040 Hz. Prior to electrode placement, we cleaned the skin locations with alcohol. We recorded surface EMG from electrodes placed bilaterally over the belly of the tibialis anterior, medial gastrocnemius, vastus lateralis, and biceps femoris muscles.

2.3.3. Experimental protocol

All participants performed baseline, adaptation, generalization, re-adaptation, and post-adaptation phases. During each phase, participants wore goggles coupled with either 20-diopter prism lenses or zero-diopter (non-visual-field-shifting) lenses (Fig. 2.2A). The 20-diopter prism lenses displaced the perceived location of the target ~11.4° to the right (Fig. 2.1A). This altered the relationship between visual inputs and motor commands and caused errors in the goal-directed limb movements. The goggles blocked a portion of the peripheral visual field, such that the participants had to look through the lenses during the tasks. Figure 2.2 illustrates an example of the experimental protocol and the predicted end-point error responses for each phase of testing.

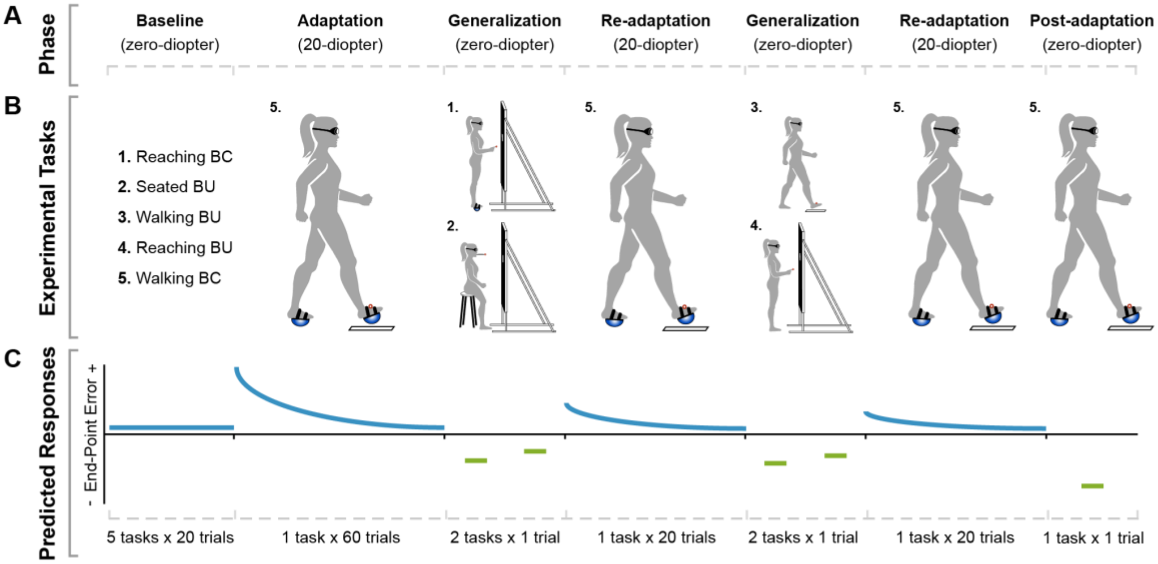

Figure 2.2 Experimental protocol

A) All participants performed baseline, adaptation, generalization, re-adaptation, and post-adaptation phases. Depending on the phase, participants wore goggles paired with either zero-diopter or 20-diopter lenses. ***B)*** An example using the balance-challenged walking group of the experimental tasks performed throughout the testing session. Participants performed a total of five precision reaching and walking tasks, while balance was challenged (balance-challenged, BC) or without an additional balance manipulation (balance-unchallenged, BU). Participants performed the baseline trials for the adaptation task last, prior to the adaptation phase. We randomized the order of the remaining baseline conditions and matched this order for the generalization tasks interspersed within the adaptation phase. ***C)*** An illustration of the predicted end-point error profiles for each phase of testing. See text for details.

Participants performed 20 baseline trials for their respective adaptation tasks, as well as 20 baseline trials for each generalization task (100 trials in total) while wearing zero-diopter lenses. Participants performed the baseline trials for the adaptation task last, prior to the adaptation phase. We randomized the order of the remaining baseline conditions and matched this order for the generalization tasks interspersed within the adaptation phase. During the adaptation phase, participants learned the novel visuomotor mapping induced by the 20-diopter prism lenses while performing 60 trials of their assigned adaptation task.

Each participant performed a total of four generalization trials, which we split into two phases with two generalization tasks each. Participants performed a single generalization trial of each of the other group's adaptation tasks, as well as a non-limb-based, seated reaching task using head movements. For example, the balanced-challenged walking group performed the balance-unchallenged walking task, both the balance-challenged and unchallenged reaching tasks, and the non-limb-based, seated reaching task (see Fig. 2.2B). Participants performed the generalization tasks with the zero-diopter lenses to determine if the learned mapping was applied to the different, non-adapted task. To mitigate any de-adaptation that occurred during the generalization trials, participants performed 20 re-adaptation trials after each generalization phase while wearing the 20-diopter prism lenses (i.e., re-adaptation phases). Finally, participants performed one trial of their respective adaptation tasks after the second re-adaptation phase with the zero-diopter lenses to confirm whether the novel mapping is stored (i.e., post-adaptation trial).

2.3.4. Data and statistical analysis

We analyzed data using custom-written MATLAB programs. We used kinematic data (filtered using a 4th-order, 6 Hz low-pass Butterworth algorithm) to calculate movement speed, velocity, and acceleration profiles of the position markers, and to determine the end-point position of the finger, foot, and pointing-instrument (Maeda et al. 2017b). We used EMG data (full-wave rectified, and low-pass filtered at 50 Hz with a 4th-order Butterworth algorithm) to calculate muscle activity during the reaching and walking tasks.

We calculated reaching time and gait speed using the position markers placed on the index finger and the mid-back infrared marker, respectively. We determined finger and pointing-instrument placement on each reaching target as the time at which the position marker’s AP velocity and acceleration profiles stabilized to near zero. We determined foot placement on the target as the moment of heel-strike of the foot, derived using the vertical velocity of the mid-foot marker on the right foot (Maeda et al. 2017b). The ML distance between the respective position markers and the center of the target at these time points defined the ML end-point error and served to quantify adaptation and generalization. A positive value represents errors in the direction of the prism shift (right), and a negative value represents errors in the direction opposite to the prism shift (Fig. 2.1B).

When balance is challenged, we expect to see greater trunk motion, variability in performance, and increased muscle activity. Therefore, to test whether balance was indeed more challenged in the balance-challenged conditions, we calculated measures of trunk motion (reflected by trunk acceleration RMS), performance variability (reflected by end-point error variability), and motor cost (reflected by muscle activity) during the last

10 baseline trials for the standing-based reaching and walking tasks. We quantified trunk motion as the mean AP and ML acceleration RMS of the marker on the mid-back (in line with the sternum) during specific time intervals, depending on the task. Specifically, for the reaching tasks, we calculated trunk motion during the reach to the target, defined as the period between when the AP velocity of the finger or pointing-instrument marker exceeded five standard deviations of the mean (calculated over the first 0.4 seconds, or 50 frames of motion capture data, prior to reach initiation) and then stabilized back to zero. For the walking tasks, we calculated trunk motion during one full step cycle, defined as the period from heel strike of the non-dominant leg before the target to heel strike of the non-dominant leg after the target. We quantified performance variability as the standard deviation of the ML end-point error of the relevant position markers for each task. Finally, we calculated a metric for total muscle activation (TMA) for each task to quantify motor cost (Domínguez-Zamora and Marigold 2019). We reasoned that decreased stability due to the balance challenge requires greater leg muscle activation to control the whole body. We separated the EMG data into the reaching and stepping time intervals mentioned above. We first calculated the muscle activation (MA) for each individual muscle:

$$MA = \left(\frac{EMG_{Area}}{EMG_{Area\ SRT}}\right) \tag{2.1}$$

where EMG_{Area} is the area under the muscle profile during each time interval and $EMG_{AreaSRT}$ is the area under the ensemble averaged profile, calculated using the trapezoid method, of the non-limb-based, seated reaching task. We reasoned that the seated reaching task would elicit the least amount of lower-limb muscle activity and serve as a suitable (common) baseline to compare motor cost across standing-based reaching and walking tasks. To account for differences in muscle volume, we used normalized volume fraction values (see Supplementary Table 1 in Handsfield et al. 2014) to calculate a common weighting factor for each muscle (*i*) for all participants, such that the sum of the weight factors equated to 1:

$$Weight\ Factor_i' = \frac{Muscle\ Volume_i}{\sum_{i=1}^{8} Muscle\ Volume_i} \tag{2.2}$$

Finally, we calculated the TMA using a weighted arithmetic mean:

$$TMA = \sum_{i=1}^{8} Weight\ Factor_i' \times MA_i \tag{2.3}$$

where *i* is each muscle that is analyzed. We used this method to account for differences in muscle volume and their relative contribution to muscle activity, where high volume muscles contribute more than low volume muscles. To determine differences in trunk motion, performance variability, and motor cost, we used separate two-sample t tests to determine the differences in balance measures for the reaching and walking groups.

To determine if the learned visuomotor mapping generalized to the non-adapted tasks, we performed separate one-tailed, paired t tests to compare the mean end-point error of the last 10 baselines trials of the task to the end-point error of the generalization trial for each non-adapted task. We used a one-tailed test since errors in the direction opposite to the learned prism shift (i.e., a negative aftereffect) indicate generalization. To quantify the magnitude of generalization, we calculated a Generalization Index:

$$Generalization\ Index = \frac{(G_{i1} - B_{l1})}{(P_{i2} - B_{l2})} * 100 \tag{2.4}$$

where *i* is the initial trial of the particular phase; *l* is the mean of the last ten trials of the particular phase; B, G, and P refer to the baseline, generalization, and post-adaptation phases; 1 is the task for which transfer is being tested; and 2 is the adaptation task (Savin and Morton 2008). This measure calculates the percentage of learning (normalized by baseline performance) that is transferred to the non-adapted tasks, where 100% represents complete generalization. We used separate independent (two-tailed) t tests to compare the magnitude of generalization between the different balance conditions for the reaching and walking tasks.

We used JMP 14 software (SAS Institute Inc., Cary, NC) with an alpha level of 0.05 for all statistical analyses. For ANOVA's, we used Tukey's post hoc tests when we found significant main effects of Phase.

2.4. Results

Four groups of participants adapted to a novel visuomotor mapping induced by prism lenses while performing either a precision reaching or walking task, with or without an additional balance manipulation. We assessed how challenging balance during the standing-based reaching and walking tasks affected the generalization of learned sensorimotor mappings across different balance conditions for the same task (e.g., generalization from the balance-unchallenged to the balance-challenged walking tasks, and vice versa). We also tested the generalizability of learning across different tasks (e.g., from reaching balance-unchallenged to walking balance-unchallenged).

2.4.1. Our manipulation successfully challenges balance

To confirm that maintaining balance is more challenging in the balance-challenged conditions, we calculated measures of trunk motion, task performance variability, and motor cost during the last 10 trials of the baseline phases for the standing-based reaching and walking tasks. The results are illustrated in Figure 2.3. Separate two-sample t tests showed that the balance-challenged conditions had significantly greater trunk motion in the AP (reaching: t_{46}= 3.8, p = 0.0003; walking: t_{46}= 5.3, p = 3.429e-6) and ML dimensions (reaching: t_{46}= 2.3, p = 0.028; walking: t_{46}= 5.1, p = 5.727e-6). Similarly, we found significantly greater performance variability (reaching: t_{46}= 2.8, p = 0.007; walking: t_{46}= 5.1, p = 7.399e-6) in the balance-challenged conditions. Lastly, the balance-challenged groups showed increased motor cost compared to the balance-unchallenged groups for both tasks (reaching: t_{46}= 5.8, p = 5.612e-7; walking: t_{46}= 3.2, p = 0.003). This is also evident in Figures 2.4 and 2.5. Thus, the rubber hemispheres worn under the feet successfully challenged balance during both standing and walking.

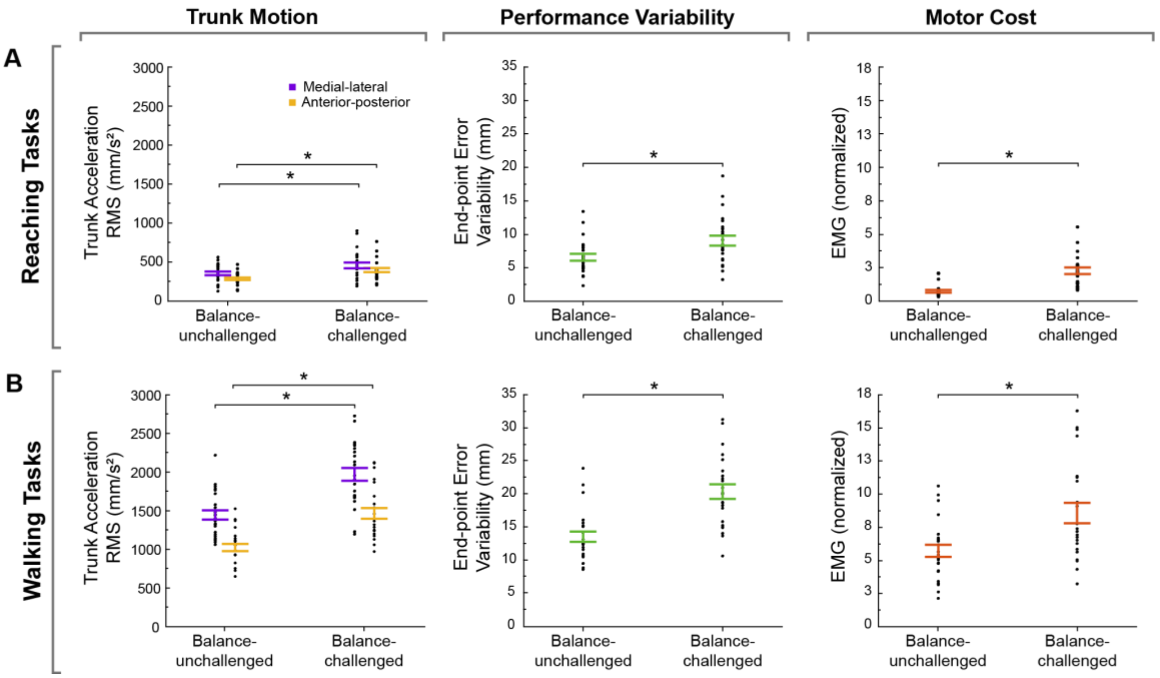

Figure 2.3 Balance measures

The effects of our balance manipulation on trunk motion (reflected by trunk acceleration RMS), performance variability (reflected by limb end-point error variability), and motor cost (reflected by muscle activity), during the last 10 baseline trials for the ***A)*** standing-based reaching tasks and ***B)*** walking tasks. Data are represented as mean ± SE. *Indicates that values are significantly different from each other ($p < 0.05$).

2.4.2. Challenging balance does not impair the ability to adapt to the prisms

Participants in all groups performed each task without making online corrections. We verified the absence of sudden changes in marker trajectory by analyzing the displacement and velocity profiles of the markers placed on the finger, mid-foot, and pointing instrument (Maeda et al. 2017b). For the standing-based reaching tasks, we did not detect significant differences in the average reaching times during the adaptation phase (t_{22}= 0.2, p = 0.847) between the balance-unchallenged (0.49 ± 0.1 s) and the balance-challenged (0.48 ± 0.1 s) groups. Similarly, we did not detect a significant difference in average gait speed between walking groups during adaptation (balance-unchallenged: 1.33 ± 0.13 m/s; balance-challenged: 1.22 ± 0.19 m/s; t_{22}= 1.6, p = 0.133). Furthermore, we found no significant differences in reaching times ($F_{3,44}$= 0.02, p = 0.996) and gait speeds ($F_{3,44}$= 0.8, p = 0.155) between baseline and adaptation phases or balance condition.

Figure 2.4 illustrates the finger trajectory as well as leg muscle activity during a late baseline trial and the first adaptation phase trial during the standing-based reaching task. Representative participants from the reaching balance-unchallenged and reaching balance-challenged groups are shown. Figure 2.5 illustrates the foot trajectory as well as leg muscle activity during a late baseline trial and the first adaptation phase trial during the precision walking task. Representative participants from the walking balance-unchallenged and walking balance-challenged groups are shown.

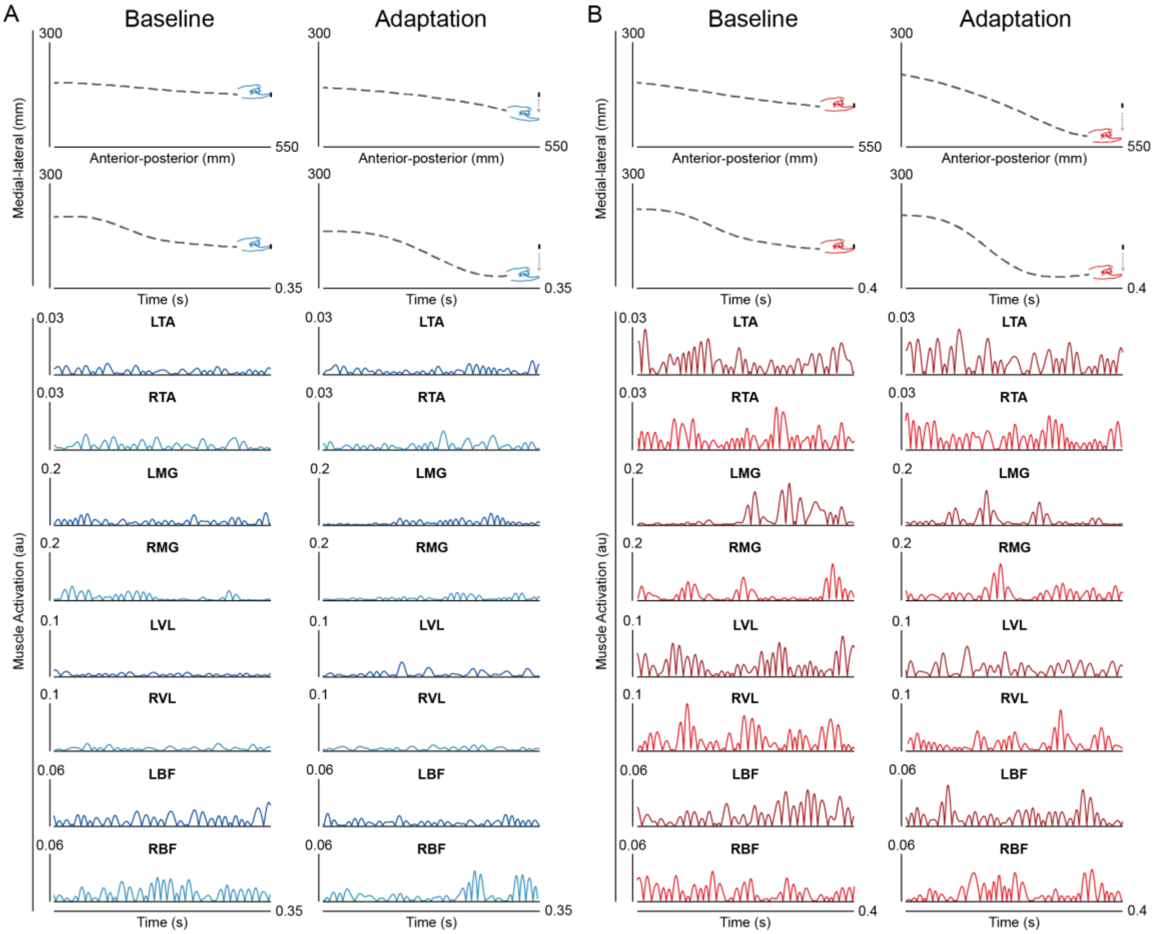

Figure 2.4 Participant behavior during reaching

An illustration of finger trajectory (dashed line) and end-point placement relative to the target (black rectangle), as well as leg muscle activity during a late baseline trial and the first adaptation trial for the standing-based reaching tasks. Representative participant data from the ***A)*** balance-unchallenged and ***B)*** balance-challenged reaching groups are shown. Dashed arrows indicate medial-lateral end-point error during the adaptation trials. Bilateral muscle activity recorded from the tibialis anterior (TA), medial gastrocnemius (MG), vastus lateralis (VL), and biceps femoris (BF) muscles, where L and R denote the left and right leg, respectively.

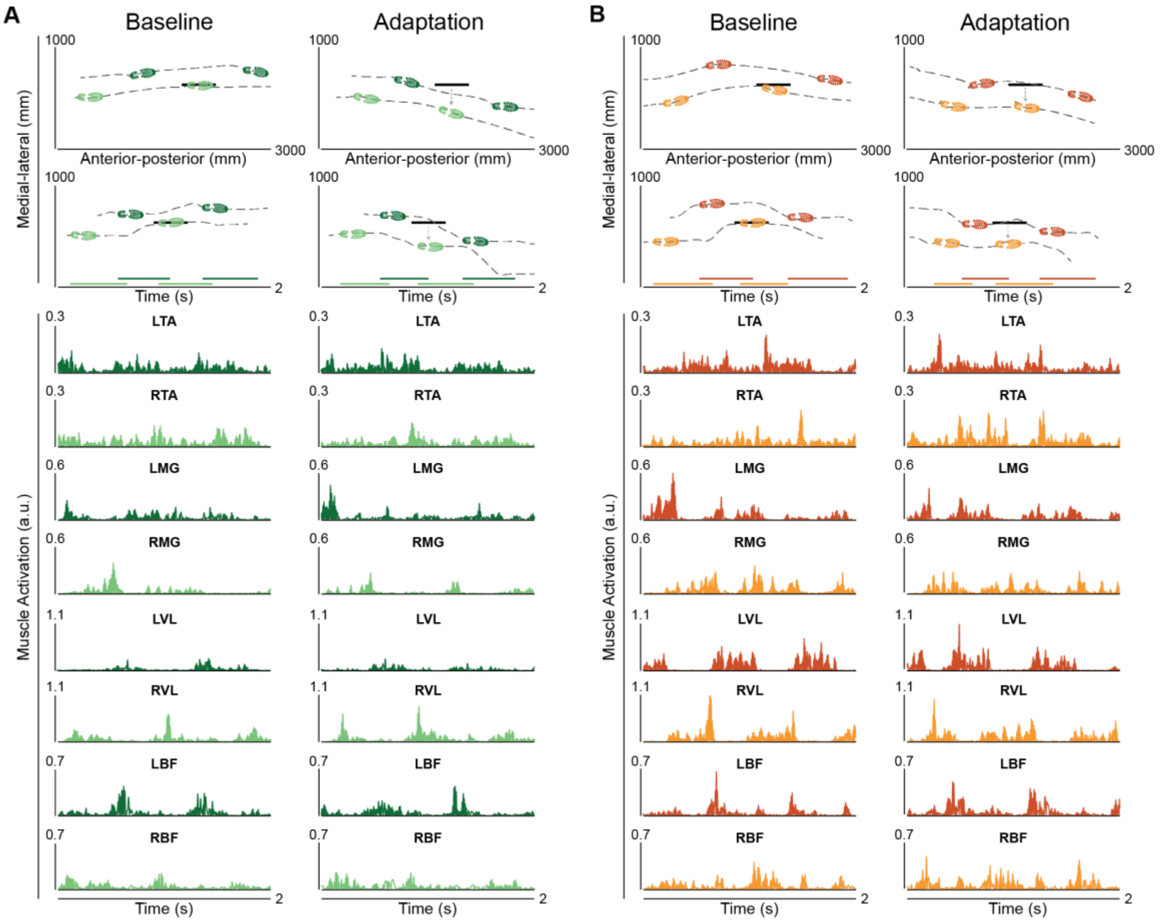

Figure 2.5 Participant behavior during walking.

An illustration of foot trajectories (dashed lines) and foot placement relative to the target (black bar), as well as leg muscle activity during a late baseline trial and the first adaptation trial for the precision walking tasks. Representative participant data from the ***A)*** balance-unchallenged and ***B)*** balance-challenged walking groups are shown. Data are presented over two strides (two steps prior to the step to the target and one step after the target) and depict the moment of heel strike (denoted by the shoeprints) and stance phase for each leg (horizontal lines). Dashed arrows indicate the medial-lateral foot-placement error during the adaptation trials. Bilateral muscle activity recorded from the tibialis anterior (TA), medial gastrocnemius (MG), vastus lateralis (VL), and biceps femoris (BF) muscles, where L and R denote the left and right leg, respectively.

Upon initial exposure to the 20-diopter (rightward-shifting) prism lenses, participants showed a large, rightward deviation in limb placement to the target for the reaching (balance-unchallenged: 53.5 ± 18.2 mm, balance-challenged: 49.9 ± 18.1 mm) and walking (balance-unchallenged: 283.6 ± 36.2 mm, balance-challenged: 263.5 ± 44.6 mm) tasks. The end-point error gradually returned to near-baseline levels as the participants adapted to the prisms. We found no significant differences in the mean end-point error of the last five trials between each adaptation phase for the reaching (balance-unchallenged: $F_{2,33}$= 0.07, p = 0.935, balance-challenged: $F_{2,33}$= 0.4, p = 0.682) and walking (balance-unchallenged: $F_{2,33}$= 0.2, p = 0.795, balance-challenged: $F_{2,33}$= 0.03, p = 0.968) groups. Following the adaptation phases, removal of the prism lenses resulted in a large end-point error to the left of the target (i.e., a negative aftereffect). Finally, we did not detect significant differences in the end-point error for the post-adaptation trials between balance conditions for the reaching (t_{22}= 0.4, p = 0.725) or walking (t_{22}= 0.3, p = 0.779) tasks. Taken together, our balance manipulation did not impair adaptation to the novel, prism-induced visuomotor mapping.

2.4.3. Challenging balance increases within-task generalization

To determine if the learned visuomotor mappings generalized within the same reaching task (e.g., from reaching balance-unchallenged to reaching balance-challenged), participants performed a single trial of the non-adapted reaching task with the zero-diopter lenses after adaptation. To assess generalization, we compared the mean end-point error of the last 10 baselines trials to the end-point error of the generalization trial for the non-adapted task. Errors in the direction opposite to the learned prism shift (i.e., a negative value) indicate generalization. We found that the balance-unchallenged reaching group generalized to the (non-adapted) balance-challenged reaching task (t_{11}= 5.4, p = 0.0001) and the balance-challenged reaching group (t_{11}= 7.8, p = 4.19e-6) generalized to the (non-adapted) balance-unchallenged reaching task (Fig. 2.6A). To assess the effect of challenging balance on generalization, we compared the magnitude of generalization across balance conditions for each reaching task using our Generalization Index. This measure calculates the percentage of learning that is generalized to the non-adapted tasks, where 100% represents complete generalization. We found that while the balance-unchallenged group generalized approximately 47% to the balance-challenged task, the balance-challenged group generalized approximately 83% to the balance-unchallenged task. According to the Generalization Index, the balance-challenged reaching group showed significantly greater percent generalization (t_{22}= 3.9, p = 0.0008) compared to the balance-unchallenged reaching group (Fig. 2.6B).

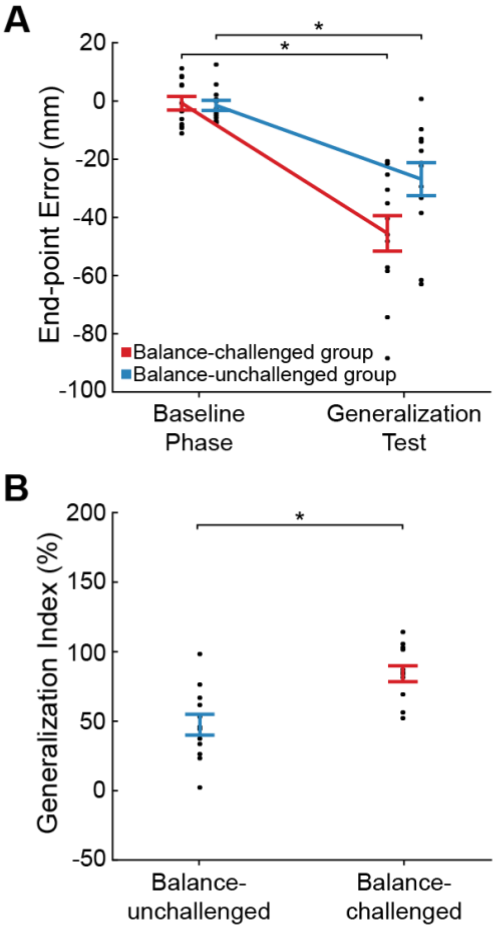

Figure 2.6 Generalization within reaching tasks
The effects of challenging balance on ***A)*** generalization to the non-adapted reaching task. Here, we compared the mean end-point error of the last 10 baselines trials to the end-point error of the generalization trial for the non-adapted task. The balance-unchallenged reaching group (blue) generalized to the non-adapted, balance-challenged reaching task. Similarly, the balance-challenged reaching group (red) generalized to the non-adapted, balance-unchallenged reaching task***. B)*** The magnitude of generalization for the two reaching groups, calculated using the Generalization Index. Data are represented as mean ± SE. *Indicates that values are significantly different from each other ($p < 0.05$).

The above pattern of generalization also held true for walking in that both the balance-unchallenged group (t_{11}= 3.1, p = 0.005) and balance-challenged group (t_{11}= 7.9, p = 3.52e-6) generalized to the non-adapted walking task (Fig. 2.7A). According to the Generalization Index, the balance-unchallenged group generalized approximately 54% to the balance-challenged task, while the balance-challenged group generalized approximately 102% to the balance-unchallenged task. Similar to the reaching groups, the balance-challenged walking group showed significantly greater percent generalization (t_{22}= 2.6, p = 0.018) (Fig. 2.7B). Thus, challenging balance enhanced generalization for both the reaching and walking groups.

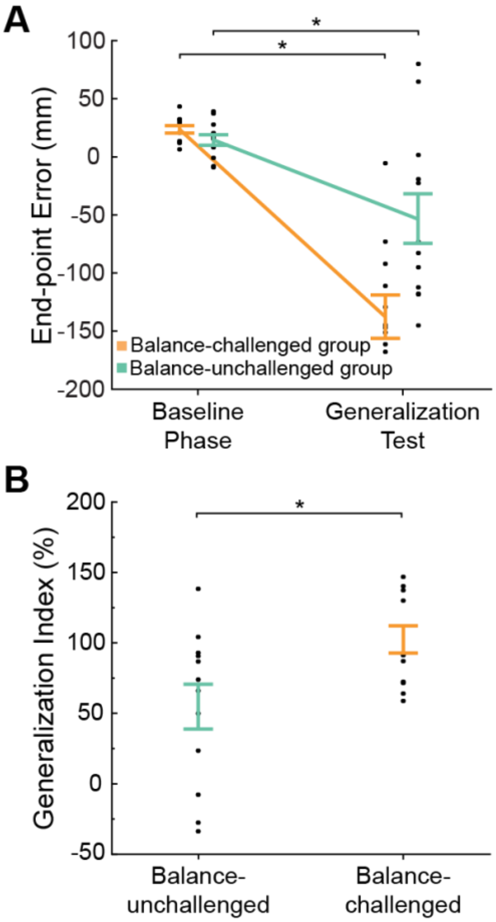

Figure 2.7 Generalization within walking tasks
The effects of challenging balance on ***A)*** generalization to the non-adapted walking task. Here, we compared the mean end-point error of the last 10 baselines trials to the end-point error of the generalization trial for the non-adapted task. The balance-unchallenged walking group (green) generalized to the non-adapted, balance-challenged walking task. Similarly, the balance-challenged walking group (yellow) generalized to the non-adapted, balance-unchallenged walking task. ***B)*** The magnitude of generalization for the two walking groups, calculated using the Generalization Index. Data are represented as mean ± SE. *Indicates that values are significantly different from each other ($p < 0.05$).

2.4.4. The effects of challenging balance on across-task generalization

As a secondary test of our hypothesis, we tested whether learning also generalizes across tasks (e.g., from reaching balance-unchallenged to walking balance-unchallenged). To answer this question, for each of our four groups, we compared end-point error between the baseline and generalization phases of their non-adapted tasks. The results are summarized in Table 2.1 and illustrated in Figure 2.8. First, we determined whether this was the case for the balance-unchallenged reaching group. Interestingly, this group was the only one to show significant generalization to the non-limb-based, seated reaching task (t_{11}= 3.2, p = 0.004). However, the balance-unchallenged reaching group did not generalize to the balance-unchallenged (t_{11}= -0.4, p = 0.638) or balance-challenged (t_{11}= -0.3, p = 0.632) walking tasks. Second, we determined whether the balance-challenged reaching group generalized across tasks. Although this group generalized to the balance-unchallenged walking task (t_{11}= 3.7, p = 0.002), it did not show significant generalization to the seated reaching (t_{11}= 0.5, p = 0.302) or balance-challenged walking (t_{11}= 0.7, p = 0.254) tasks. Third, we determined whether the balance-unchallenged walking group generalized across tasks. This group generalized to the balance-challenged reaching task (t_{11}= 2.3; p = 0.020), but not to the seated (t_{11}= 1.7, p = 0.063) or balance-unchallenged (t_{11}= -0.2, p = 0.575) reaching tasks. Finally, we determined whether the balance-challenged walking group generalized across tasks. This group generalized to the balance-challenged reaching task (t_{11}= 2.4, p = 0.018). However, we found no significant generalization to the seated reaching task (t_{11}= 1.6, p = 0.072) or the balance-unchallenged reaching task (t_{11}= -1.1, p = 0.846). In summary, there is mixed evidence that suggests challenging balance increased generalization across the reaching and walking tasks.

Table 2.1. Across-task generalization

	Reaching Groups							
	Balance-unchallenged				Balance-challenged			
	Baseline (mm)	Generalization (mm)	GI (%)	P	Baseline (mm)	Generalization (mm)	GI (%)	P
Generalization Task:								
Seated, Non-limb Reaching	13.6 ± 1.6	4.5 ± 2.5	17.9 ± 7.1	**0.004**	5.9 ± 2.9	4.0 ± 3.0	6.1 ± 9.4	0.302
Walking Balance-unchallenged	11.6 ± 2.4	13.9 ± 6.9	-8.3 ± 15.5	0.638	8.1 ± 4.8	-4.9 ± 7.2	24.4 ± 7.6	**0.002**
Walking Balance-challenged	15.5 ± 4.2	17.0 ± 6.9	-10.9 ± 15.4	0.632	6.2 ± 5.9	2.1 ± 4.9	10.4 ± 10.3	0.254

	Walking Groups							
	Balance-unchallenged				Balance-challenged			
	Baseline (mm)	Generalization (mm)	GI (%)	P	Baseline (mm)	Generalization (mm)	GI (%)	P
Generalization Task:								
Seated, Non-limb Reaching	10.6 ± 1.8	3.0 ± 4.6	3.4 ± 2.6	0.063	12.6 ± 1.5	8.2 ± 2.8	5.4 ± 1.7	0.072
Reaching Balance-unchallenged	-4.1 ± 1.6	-3.4 ± 3.4	-0.2 ± 3.2	0.575	-2.8 ± 2.2	-0.3 ± 3.7	-4.2 ± 3.6	0.846
Reaching Balance-challenged	-4.8 ± 1.2	-14.8 ± 5.1	8.7 ± 4.2	**0.020**	-3.9 ± 1.8	-12.7 ± 4.1	8.9 ± 3.5	**0.018**

Bold text denotes significant generalization ($p < 0.05$). GI = Generalization Index; P = P value; mm = millimeters; % = percentage.

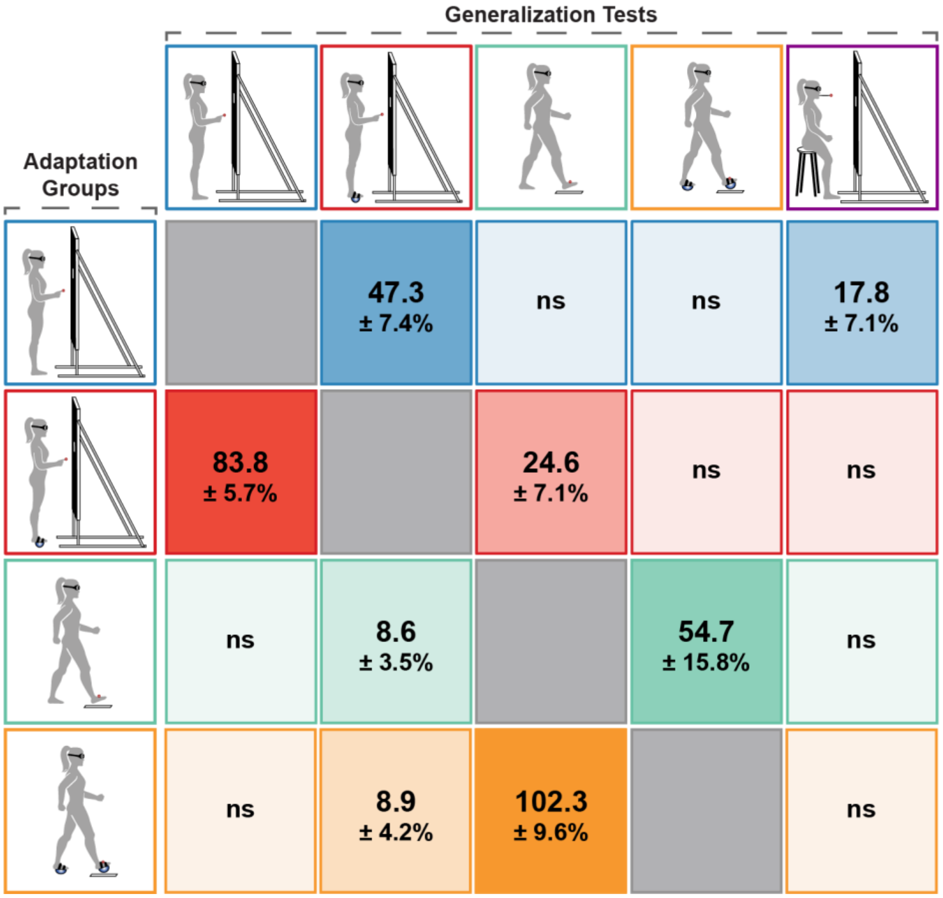

Figure 2.8 Generalization summary
A summary diagram of the significant within- and across-task generalization. The percent values represent the magnitude of generalization, calculated using the Generalization Index (mean ± SD).

2.5. Discussion

The ability to generalize movement to novel contexts is an important component of learning and contributes to an array of skilled everyday motor behaviors. Here, we tested the hypothesis that challenging balance during adaptation would increase generalization. We found that challenging balance resulted in greater generalization for both the reaching and walking tasks. These results suggest that the effects of challenging balance are not specific to the task, but instead, apply to motor learning more broadly. Thus, it appears that challenging balance leads to a more generalizable model. Although we demonstrate strong evidence for this concept, the explanation for these findings is less clear. We discuss possible reasons below.

2.5.1. Challenging balance may increase the value assigned to the learned internal model

Challenging balance doubled the amount of generalization for both the reaching and walking tasks. One hypothesis for this enhanced generalization is that learning under balance-challenged conditions increases the value (or importance) assigned to the updated internal model. This change in assignment may result from the necessity to control exacerbated motion of the body induced by the rubber hemispheres to maintain balance or occur because of the perceived threat of falling and causing injury.

When balance is challenged, the effects that the motion of one body segment or limb has on the motion of another become more pronounced due to the interconnected nature of our musculoskeletal system. Consequently, the nervous system requires better control over the body to maintain an upright position and to ensure successful task performance. This may increase the computational demand on the sensorimotor system, as well as the mechanical and metabolic demand on the musculoskeletal system. Ultimately, decisions about movement control involve weighing the benefits of potential rewards (or penalties) associated with the task against the effort required to act (Gallivan et al. 2018). These decisions require an estimate of the value associated with allocating control to a given task (i.e., the expected value of control) to determine if it is worth pursuing (Rangel et al. 2008; Shenhav et al. 2013). The goal of our tasks was to hit a target with either the finger or the foot. In each case, the inability to minimize unwanted motion of the body would jeopardize the likelihood of success. Thus, there is increased value in controlling balance.

Although we did not directly measure fear or anxiety, the increased risk of falling and injury during the balance-challenged tasks may have altered these emotions and thus also contributed to the generalization patterns observed for these groups. Perceived threat and fear of falling can significantly affect balance and gait (Adkin et al. 2002; Adkin and Carpenter 2018). There is also evidence suggesting that colliding with an obstacle during prism adaptation may facilitate subsequent generalization (Alexander et al. 2013). Similarly, Green et al. (2010) argue that arousal level, which reflects perceived risk and task difficulty, affects locomotor aftereffects experienced during walking on a stationary sled that was previously moving (also known as the “broken escalator phenomenon”). These studies suggest that perceived threat can modulate generalization.

In the present study, the perceived threat associated with the risk of falling during the balance-challenged tasks may have modified the value assigned to the model and altered the strategy used during generalization. From a safety perspective, it's more important to get the right strategy when balance is challenged then it is to get the wrong strategy when balance is not challenged. Thus, it's better to broadly generalize the learned balance-challenged strategy and not take the risk of selecting the wrong strategy. This is, to some extent, related to statistical decision theory in that our participants might have chosen to adopt a more conservative "just in case" approach to minimize the probability of being penalized for selecting the incorrect strategy (Trommershäuser et al. 2003). In these circumstances, participants are able to leverage their knowledge about a perturbation to consciously modify their motor performance. This notion is supported by recent research demonstrating that generalization is maximized around the intended location of an explicitly accessible motor plan (Day et al. 2016; McDougle et al. 2017). Furthermore, there is evidence to suggest that explicit components of learning generalize broadly across the workspace (Heuer and Hegele 2008, 2011).

Another possible contributing factor for the enhanced within-task generalization observed in our balance-challenged groups is that our balance manipulation might alter the assignment of errors experienced during adaptation. Previous research shows that solving the credit assignment problem is essential for sensorimotor recalibration and that changes in the assignment of errors can modulate generalization (Berniker and Kording 2008; Fercho and Baugh 2014; Kluzik et al. 2008; Torres-Oviedo and Bastian 2012; Wilke et al. 2013). For example, previous research has concluded that errors within the natural range of movement variability are typically assigned to the person (i.e., produced by the body) and generalize beyond training, whereas unusual or abrupt errors are frequently attributed to an external source (i.e., produced by the environment) and are largely context dependent (Torres-Oviedo and Bastian 2012). By this logic, however, our balance-challenged groups should have demonstrated less generalization because they experience exaggerated movements during adaptation that should, in theory, be attributed to an external source (i.e., the rubber hemispheres). In contrast, we demonstrate that our balance-challenged groups exhibit significantly greater generalization compared to their balance-unchallenged counterparts. One possible explanation for our seemingly contradictory findings may relate to the nature of our balance manipulation. During our balance-challenged tasks, the direction and magnitude of the perturbation may be directly associated with the participant’s own movement, since the rubber hemispheres are attached to their feet. As a result, this manipulation may shift the assignment of errors experienced during adaptation from the environment to the person, and they may attribute performance errors to their inability to produce accurate movements. Coupled with the increased necessity for greater control, this potential change in credit assignment toward errors in motor execution may favor context-independent adaptation and strengthen generalization across motor behaviors.

Prisms induce a visuo-proprioceptive mismatch, and as such, adaptation entails some combination of remapping these sensory signals with motor signals responsible for re-establishing movement accuracy (Hay and Pick 1966; Petitet et al. 2018; Redding and Wallace 1988). What role, if any, does sensory information play in the improved generalization of our balance-challenged groups? Although we did not design our experiment to address this question, we can still speculate as to a possible answer. Our balance manipulation led to greater upper-body motion and limb movement variability relative to the balance-unchallenged condition. Increased upper-body motion would result in greater optic flow as well as greater activation in vestibular organs. The exaggerated body motion, in conjunction with the increased limb movement variability, would also alter proprioceptive feedback during the adaptation. One future testable hypothesis is that heightened activity in visual, vestibular, and proprioceptive pathways facilitates the formation of a more comprehensive internal model, which in turn enhances generalization.

The greater necessity for control, combined with the greater risk of falling, may increase recruitment of certain brain areas. Indeed, neuroimaging studies show that coordinated movement involves a distributed network of brain activity that may be increased during more complex tasks (Debaere et al. 2001; Hülsdünker et al. 2015, 2016; Swinnen 2002). For example, overall activity in the supplementary motor area, cingulate motor cortex, premotor cortex, primary motor cortex, somatosensory cortex, and cerebellum during tasks that require across-limb coordination exceeds that observed during isolated limb movements (Debaere et al. 2001). Furthermore, challenging balance during standing results in greater electroencephalography spectral power within certain frequencies across many different cortical regions (Hülsdünker et al. 2015, 2016). In conjunction, perceived threat may contribute to broader behavioral generalization through the recruitment of brain areas that mediate negative reinforcers and respond to aversive stimuli, such as the ventral striatum and the amygdala (Armony et al. 1997; Bromberg-

Martin et al. 2010; Jensen et al. 2003; Taub and Mintz 2010; Tom et al. 2007). These changes in brain activity may reflect (or serve to reinforce) the value placed on the updated internal model. The anterior cingulate cortex is thought to contribute to the estimated value of control by integrating information about the expected payoff and cost related to allocating control to a given task (Shenhav et al. 2013). Interestingly, this region is one of several that show greater theta band spectral power with a loss of balance during walking (Sipp et al. 2013). One potential future direction of our work is to determine how changes in brain activity during our tasks relates to the observed generalization patterns.

Taken together, the necessity to control exacerbated body motions and the perceived threat associated with the balance-challenged conditions may each contribute—to varying degrees—to generalization. Each of these contributions may accomplish this by altering the learning process and increasing the value assigned to the internal model formed during adaptation. As such, we propose that this greater valued model increases generalization.

2.5.2. Challenging balance modulates across-task generalization

The reaching and walking groups showed bi-directional, within-task generalization. For example, the balance-challenged reaching group generalized to the balance-unchallenged reaching task, and vice versa. These results are unsurprising and support the substantial amount of evidence demonstrating generalization among tasks that share similar movement characteristics (Carroll et al. 2014; Gandolfo et al. 1996; Ghahramani et al. 1996; Thoroughman and Shadmehr 2000; Morton et al. 2001; Mattar and Ostry 2010). Is there evidence that challenging balance affects generalization across different tasks (e.g., from reaching to walking, and vice versa)?

To compare the magnitude of generalization across tasks, we normalized the generalization trials to the participants' performance during baseline and used the post-adaptation trial as an indication of how much each participant learned during adaptation (Savin and Morton 2008). One possible issue with this method is that the post-adaptation trial was performed at the end of our protocol, after several adaptation phases, and therefore may not be a true reflection of adaptation. We based our protocol decision on a practical compromise to accommodate multiple across-task generalization trials (randomized) and based our generalization index decision to account for individual differences in learning. There are alternative ways to quantify generalization using the initial and final adaptation error to reflect learning (Carroll et al. 2014; Morton et al. 2001). As an additional test, we quantified generalization using these methods. Although our results are consistent, the percentage values were substantially higher (between 140 - 210%) when using the adaptation trials to quantify learning. Furthermore, the magnitude of the post-adaptation trials in the present study are comparable to the results from previous studies from our lab (Maeda et al. 2017a). Given that our results do not depend on the whether we use the post-adaptation or adaptation trials as an indicator of learning, we argue that our choice of generalization index is both suitable and appropriate.

We show that challenging balance modulates generalization across reaching and walking tasks. For example, we found that the balance-challenged reaching group generalized to the balance-unchallenged walking task, whereas the balance-unchallenged reaching group did not generalize to either walking task (Table 2.1; Fig. 2.8). Both of the walking groups also showed small, but significant, generalization (~8%) to the reaching balance-challenged task. However, we found no difference between the two balance conditions. We reason that the lack of a significant contribution of the upper limbs during the walking tasks may have limited further generalization to the reaching tasks. In contrast, reaching to the target while balance was challenged required rigorous control of the lower limb and trunk muscles to counter this perturbation, maintain balance, and complete the task successfully. Thus, the balance-challenged reaching task arguably requires the greatest interdependent control of the upper and lower limbs for task success, the benefits of which are reflected in the noteworthy generalization (~24%) to the walking balance-unchallenged task. We did not find significant generalization between the balance-unchallenged reaching and walking tasks, which contradicts the findings of Morton and Bastian (2004). These conflicting results may relate to the differences between the walking tasks being evaluated. For example, our study assessed adaptation during a precision walking task using end-point error while the other study measured the extent of lateral deviation along the walking path. Finally, we show that only the balance-unchallenged reaching group generalized to the non-limb-based, seated reaching task. These findings support the results from Seidler et al. (2001) that showed arm adaptation generalizes to a head pointing task. However, the reasons for the lack of significant generalization observed from the other groups is unclear. It is possible that our non-limb-based task was sub-optimal for the purpose of comparing generalization across groups. Overall, given the pattern and limited extent of generalization across our reaching and walking tasks, it is clear that there are still other non-balance-related factors contributing to the transfer of learning.

2.5.3. Conclusion

Taken together, our results demonstrate that challenging balance enhances the degree to which visuomotor mappings generalize to untrained movements. We propose that challenging balance increases the value assigned to the internal model formed during learning, whether this be from a greater need to control motion at different body segments or greater perceived threat, thus making it more generalizable. Overall, our study demonstrates the significance of studying motor learning during unconstrained, natural behaviors.

2.6. Chapter contributions

Conceptualization, Amanda Bakkum (A.B.), J. Maxwell Donelan (J.M.D), and Daniel S. Marigold (D.S.M); Methodology, A.B., J.M.D, and D.S.M; Investigation, A.B.; Formal Analysis, A.B.; Writing – Original Draft, A.B. and D.S.M; Writing – Reviewing & Editing, A.B., J.M.D, and D.S.M.

Chapter 3.

Savings in sensorimotor learning during balance-challenged walking but not reaching

> *“Memory is the mother of all wisdom.”*
>
> *(Aeschylus)*

3.1. Abstract

Safe and successful motor performance relies on the ability to adapt to physiological and environmental change and retain what is learned. An open question is what factors maximize this retention? One overlooked factor is the degree to which balance is challenged during learning. We propose that the greater need for control and/or perceived threat of falling or injury associated with balance-challenging tasks increases the value assigned to the learned internal model. And we propose that a greater-valued model is a more retainable model, as it serves to benefit future motor performance. Thus, we tested the hypothesis that challenging balance increases motor memory retention. Four groups of participants adapted to a novel visuomotor mapping induced by prism lenses while performing a reaching or walking task, with and without an additional balance challenge. We found that challenging balance did not disrupt visuomotor adaptation during reaching or walking. We then probed retention by having participants repeat the adaptation protocol one week later. For reaching, we found that the balance-challenged group recalled the mapping, though neither group demonstrated faster relearning (i.e., savings) upon re-exposure to the prisms. In contrast, both walking groups demonstrated significant motor memory retention, reflected by initial recall and savings. Additionally, we found that challenging balance significantly enhanced savings during walking. Taken together, our results demonstrate the robustness of motor memories formed during walking and highlight the potential influence of balance control on sensorimotor learning.

3.2. Introduction

Sensorimotor adaptation serves to maintain movement accuracy in response to altered body states, environmental conditions, or task demands. For example, the effects of aging and injury can disrupt the normal relationship (or mapping) between sensory input and motor output, causing errors in movement that are thought to drive adaptation (Mazzoni and Krakauer 2006; Tseng et al. 2007; Wallman and Fuchs 1998). An interesting observation following sensorimotor adaptation is the phenomenon known as savings, whereby people demonstrate faster adaptation (or relearning) when they re-encounter a familiar perturbation (Brashers-Krug et al. 1996; Krakauer et al. 2005). These performance savings are often considered an indicator of motor memory retention and demonstrate the potential benefit of past experience on subsequent learning. As our bodies and the environment change over time, the ability to adapt to these changes and retain what is learned becomes important for successful motor performance in everyday life. This is also clinically relevant, as it can facilitate rehabilitation by enabling patients to capitalize on previous training.

Research in both reaching and walking demonstrates that motor memories formed during sensorimotor adaptation are retained for extended periods of time (Brashers-Krug et al. 1996; Day et al. 2018; Haith et al. 2015; Huberdeau et al. 2015; Hussain and Morton 2014; Klassen et al. 2005; Krakauer et al. 2005; Leech et al. 2018; Leech and Roemmich 2018; Maeda et al. 2017b; 2018; Malone et al. 2011; Mawase et al. 2014; Roemmich and Bastian 2015). However, the extent to which motor memories are retained and savings occurs is often dictated by the initial training conditions, such as the size of the perturbation (Leech et al. 2018; Malone et al. 2011; Morehead et al. 2015) and exposure duration (Alhussein et al. 2019; Day et al. 2018; Landi et al. 2011; Nguyen et al. 2019; Roemmich and Bastian 2015; Yamamoto et al. 2006). Interestingly, previous studies demonstrate that motor memories formed during overground walking are stored for at least one week and even up to one year without additional training and despite exposure to a competing mapping in the first testing session (Maeda et al. 2017b, 2018). This suggests that motor memories formed during walking are, at least to some extent, resistant to interference.

From making your morning coffee to running to catch a bus, most everyday movements require the individual to control balance to achieve some predetermined goal. However, this aspect of daily motor behavior is often overlooked in experimental paradigms, particularly in studies that assess sensorimotor adaptation during seated, reaching tasks where maintaining balance is not a major concern. Consequently, most adaptation research does not account for the possible role that balance plays in sensorimotor learning. In a recent study from our lab, we explored the notion that balance-challenges associated with unconstrained, real-life movements may increase the value to the nervous system for using a more accurate and comprehensive internal model for motor control (Bakkum et al. 2020). We reasoned that when balance is challenged, the effects of dynamic coupling between body segments, where motion of one segment results in acceleration of another, become more pronounced because of the interconnected nature of our musculoskeletal system (Nott et al. 2010; Yu et al. 2011; Zajac 1993). Consequently, the nervous system requires a more comprehensive internal model for better control over the body to ensure safe and successful task performance. As it is less tailored to a specific task, a more comprehensive model may be a more generalizable model. Indeed, we found that challenging balance during sensorimotor adaptation significantly increased generalization in both reaching and walking tasks (Bakkum et al. 2020), suggesting that the effects of challenging balance may apply broadly to sensorimotor learning.

How might a high-value internal model affect retention of motor memories? By definition, for something to have value it must be useful or important, which implies there is potential for some prospective gain or benefit. It seems reasonable that our memory systems are tuned to remember certain kinds of information better than others, particularly if we are able to capitalize on that information for a future advantage. For instance, it is more important to remember information about potential threats or rewards as opposed to arbitrary occurrences. From a motor control perspective, this may pertain to drawing from past experiences to help safely navigate new environments or recalling information that may increase the likelihood of future task success. This concept is referred to as adaptive memory, and it is based on the premise that our memory systems evolved to process and retain survival-related information (Nairne et al. 2007; Nairne et al. 2008; Nairne and Pandeirada 2016). Following this reasoning, one might expect that people would exhibit enhanced retention for motor memories formed under threatening conditions. While research on this topic is limited, there is evidence to suggest that perceived threat can modulate motor memory retention. For instance, studies show that older adults are able to rapidly learn to resist falls from repeated-slip exposure and that these motor memories are retained for months after a single training session (Bhatt et al. 2006; Bhatt et al. 2012; Pai et al. 2014). We argue that, be it from the greater need for control over moving body segments or from a greater perceived threat, challenging balance increases the subjective value assigned to maintaining the internal model updated during learning. Thus, a greater-valued model is a more retainable model.

Here, we tested the hypothesis that challenging balance during adaptation enhances motor memory retention, reflected by greater recall and faster relearning (i.e., savings). To test this hypothesis, we encouraged four groups of participants to adapt to a novel visuomotor mapping induced by prism lenses while performing a standing-based reaching or walking task, with or without an additional balance manipulation. To regain movement accuracy and perform the task successfully, the nervous system had to update its internal model (Maeda et al. 2017a). We assessed the effects of challenging balance during adaptation to both standing-based reaching and walking to determine whether these effects, if any, were specific to the task or applied to sensorimotor learning more generally. We then probed savings of the new internal model by having participants repeat the adaptation protocol one week later.

3.3. Materials and methods

3.3.1. Participants

This study included a total of forty-eight young adults (mean age ± SD, 22.9 ± 3.7 years; 25 males, 23 females; right-limb dominant, as defined by the limb used to either kick or throw a ball), with no known visual (four participants wore corrective lenses or glasses), neurological, or musculoskeletal disease. These participants were part of a previous study which focused on the effects of challenging balance on generalization (Bakkum et al. 2020). Following the initial training session, the participants returned to the lab one-week later to probe motor memory retention. As such, this study focusses on the effects of challenging balance on retention of motor memories formed during reaching and walking tasks. The Office of Research Ethics at Simon Fraser University approved the study protocol and all participants provided informed, written consent prior to their participation.

3.3.2. Experimental tasks and data collection

All participants adapted to a novel visuomotor mapping induced by prism lenses (Fig. 3.1A), while performing either a precision reaching or walking task. Participants performed these tasks without an additional balance manipulation (balance-unchallenged; Fig. 3.1C) or while balance was challenged (balance-challenged; Fig. 3.1D). We randomly assigned participants to one of four adaptation groups (n = 12 each), namely: balance-unchallenged reaching, balance-challenged reaching, balance-unchallenged walking, and balance-challenged walking. We assessed how the balance manipulation affected adaptation to a novel visuomotor mapping and relearning (or savings) of the learned mapping one week later.

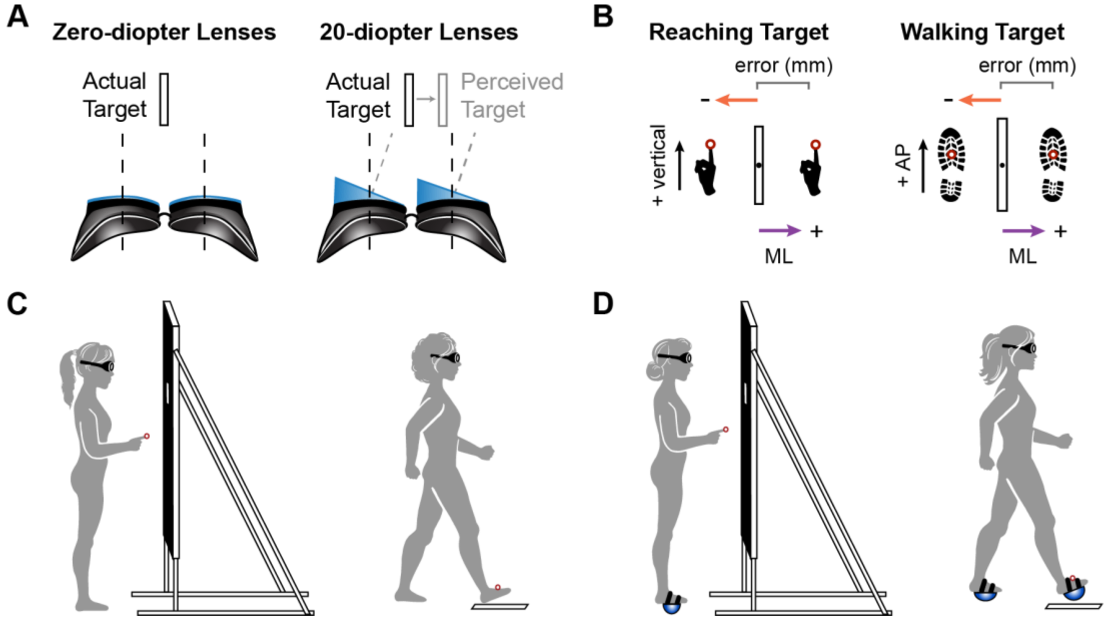

Figure 3.1 Experimental tasks
A) A simulated view of the target through the goggles coupled with zero-diopter (non-visual-field-shifting) lenses and 20-diopter prism lenses that shift the perceived location of the target 11.4° to the right. ***B)*** An illustration showing positive (+) and negative (-) medial-lateral (ML) end-point error, defined as the distance between a position marker on the limb and the center of the target line. AP, anterior-posterior direction in laboratory space. ***C)*** An illustration of the balance-unchallenged reaching and walking task. ***D)*** An illustration of the balance-challenged reaching and walking tasks.

For the precision reaching tasks, participants stood in front of a screen positioned at a distance of approximately 90% of their arm's length. Each participant placed the index finger of their reaching hand on their chin before the start of each trial. Once cued by an audible tone, participants reached using their index finger to the medial-lateral (ML) center of a target (width: 1 cm; vertical length: 12 cm; Fig. 3.1B). Because the prism goggles shift visual perception in the ML direction, we only evaluated ML end-point error, and we used a longer target to reduce the demand for accuracy in the vertical dimension. We used a projector (Epson EX7200) to back-project the target onto a screen (279 x 218 cm) and aligned the top of the target to the height of the participant's chin for each balance condition. We configured the reaching target's size and position in MATLAB (The MathWorks, Natick, MA) with the Psychophysics Toolbox, version 3 (Brainard 1997; Kleiner et al. 2007). Participants wore comfortable walking shoes and performed the task without an additional balance manipulation or while balance was challenged. For the balance-unchallenged condition, participants performed the task while standing with their feet approximately shoulder-width apart (Fig. 3.1C). For the balance-challenged condition, participants performed the task with inflatable rubber hemispheres (radii: 8.5 cm) attached to the soles of their shoes (Fig. 3.1D). These rubber hemispheres reduce the control afforded by shifting the center of pressure under the base of support and significantly increase the root mean square of trunk acceleration, end-point-error variability, and lower-limb muscle activity (Bakkum et al. 2020). We instructed the participants to stand with their feet as close together as possible without the rubber hemispheres touching each other. During the balance-challenged tasks, an experimenter helped stabilize the participants between each trial. Thereafter, the participant performed the reach without any assistance.

For the precision walking tasks, participants stood at the beginning of a walkway (~6 m long) and waited for an audible tone to signal the start of each trial. At the sound of the tone, participants walked and stepped with their right foot onto the ML center of a projected target (3 x 36 cm) without stopping (Fig. 3.1B). We used an LCD projector (Epson PowerLight 5535U; brightness of 5500 lumens) to display the stepping target on a black uniform mat covering the walking path. Participants performed this task without an additional balance manipulation or while balance was challenged. For the balance-unchallenged condition, participants performed the task while wearing comfortable walking shoes (Fig. 3.1C). For the balance-challenged condition, participants performed the task with the same inflatable rubber hemispheres attached to the soles of their shoes as in the reaching task (Fig. 3.1D). An experimenter helped stabilize the participants between each balance-challenged trial. However, the participant performed the walking task without assistance. Participants took a minimum of two steps before and after the step to the target. The two preceding steps allowed participants to determine their walking trajectory and align themselves in preparation for the step to the target, which we positioned in the center of the walkway for all trials. We randomized the participant’s anterior-posterior (AP) starting location (between 1.5 - 2.5 m) for each trial to increase the demand for visual feedback during the task and to prevent participants from learning a specific walking sequence.

To track body motion during the reaching and walking tasks, we used an Optotrak Certus motion capture camera (Northern Digital, Waterloo, ON, Canada) that recorded (at 120 Hz) infrared emitting position markers placed on the participant’s mid-back (in line with the sternum), index finger of the right hand, and bilaterally on the heel, mid-foot (second-third metatarsal head), and the toe (third metatarsal). For all tasks, we instructed participants to be as accurate as possible when reaching or stepping to the target. We also instructed participants to perform the tasks at a quick and constant pace to minimize online corrections of the finger or leg/foot trajectory to more closely match previous experiments in which the movements are ballistic. These guidelines also encourage the use of sensory feedback prior to the reach or step to the target. To minimize adaptation between trials, participants had their eyes open only when they were performing the task and received visual feedback of their performance through the lenses. To increase target visibility and reduce the influence of environmental references, participants performed both tasks under reduced light conditions (~0.9 lux). An experimenter demonstrated each task prior to testing. Additionally, participants were attached to a safety harness system suspended from the ceiling at all times which prevented falling to the ground in the event of a loss of balance. The harness did not provide any body weight support, and no participant engaged the system during the course of the experiment.

3.3.3. Experimental protocol

We measured adaptation and savings over two testing sessions, separated by one week. Figure 3.2 illustrates an example of the experimental protocol for both testing sessions and the predicted end-point error responses for each phase of testing. During the first testing session, participants performed five baseline phases (20 trials each); one for each reaching and walking task, as well as a seated, non-limb-based reaching task. This latter task is described in Bakkum et al. (2020) and is not relevant to this study. Participants performed the baseline phases while wearing zero-diopter (i.e., non-visual-field-shifting) lenses. The baseline trials for the adaptation task were performed last, just prior to the adaptation phase. We randomized the remaining baseline conditions for each participant. During the adaptation phase, participants learned a novel visuomotor mapping induced by 20-diopter prism lenses while performing 60 trials of their assigned adaptation task (e.g., balance-challenged walking). The 20-diopter prism lenses altered the relationship between visual inputs and motor commands by shifting the perceived location of the target to the right (~11.4°; Fig. 3.1A). The goggles blocked a portion of the peripheral visual field, such that the participants had no choice but to look through the lenses during the tasks. Each participant performed a total of four generalization trials, which we split into two phases with two generalization tasks each. Participants performed a single generalization trial of each of the other group's adaptation tasks, as well as a seated, non-limb-based reaching task. This study focuses on the adaptation phases across the two testing sessions. Details regarding generalization are found elsewhere (Bakkum et al. 2020). To mitigate any de-adaptation that occurred during the generalization trials, participants performed 20 readaptation trials after each generalization phase while wearing the 20-diopter prism lenses (i.e., readaptation phases). Finally, participants performed a single trial of their respective adaptation tasks after the second readaptation phase with the zero-diopter lenses to confirm whether the novel mapping is stored (i.e., postadaptation trial). One week later (Fig. 3.2), participants returned to the lab and performed 20 baseline trials of their respective adaptation tasks with the zero-diopter lenses. Participants then performed 60 trials of their adaptation task while wearing the 20-diopter lenses, followed by one postadaptation trial with the zero-diopter lenses.

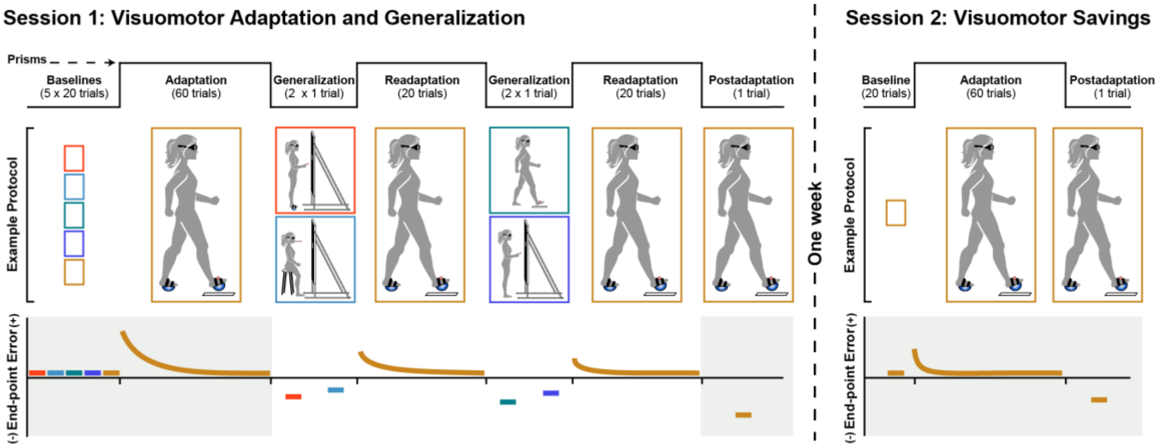

Figure 3.2 Experimental protocol

An example using the balance-challenged walking group of the experimental tasks performed throughout the testing session, as well as the predicted end-point error profiles for each phase of testing. During the first testing session, all participants performed baseline, adaptation, generalization, readaptation, and postadaptation phases. Depending on the phase, participants wore goggles paired with either zero-diopter or 20-diopter lenses. To assess visuomotor savings, participants repeated the adaptation protocol one week later. This study focuses on the baseline, adaptation, and postadaptation phases across the two testing sessions, as denoted by the shaded boxes. See text for details.

3.3.4. Data and statistical analysis

We analyzed data using custom-written MATLAB programs. We filtered kinematic data using a fourth-order, low-pass Butterworth algorithm with a cut-off frequency of 6 Hz. We calculated reaching time and gait speed over 2 meters using the position markers placed on the index finger and the mid-back, respectively. To confirm the lack of online corrections, we verified the absence of sudden trajectory changes by analyzing the displacement and velocity profiles of the finger and mid-foot markers.

All participants performed their respective tasks at a quick and constant pace throughout the experiment, as instructed. We did not detect significant differences in the average reaching times during the adaptation phase (t_{22} = 0.2, p = 0.847) between the balance-unchallenged (0.49 ± 0.1 s) and the balance-challenged (0.48 ± 0.1 s) reaching groups. For the walking groups, we found no significant difference in the average gait speeds across groups during the adaptation phase trials (balance-unchallenged: 1.33 ± 0.13 m/s; balance-challenged: 1.22 ± 0.19 m/s; t_{22} = 1.6, p = 0.133). We also found no significant difference in the reaching times ($F_{3,44}$ = 0.02, p = 0.996) and gait speeds ($F_{3,44}$ = 0.8, p = 0.155) between the baseline and adaptation phases or balance condition. Finally, we found no significant differences in reaching times ($F_{1,22}$ = 0.1, p = 0.705) or gait speeds ($F_{1,22} = 0.7$, $p = 0.429$) between balance conditions during the adaptation phases across testing sessions.

We determined finger-placement on the reaching target as the time at which the position marker's AP velocity and acceleration profiles stabilized to near zero. We determined foot-placement on the target as the moment of heel-strike of the foot, derived using the vertical velocity of the mid-foot marker on the right foot (Maeda et al. 2017b). The ML distance between the respective position markers and the center of the target at these time points defined the ML end-point error. A positive value represents errors in the direction of the prism shift (right), and a negative value represents errors in the left direction, opposite to the prism shift (Fig. 3.1B).

We used JMP software Version 15 (SAS Institute Inc., Cary, NC) with an alpha level of 0.05 for all statistical analyses. To determine the effects of challenging balance on adaptation, we compared end-point error during the baseline phase (average of the last ten trials), first adaptation trial, late adaptation (average of the last ten trials), and postadaptation trials during the first testing session using separate two-way (Group x Phase) mixed-model ANOVAs for the reaching and walking tasks, where we included participant as a random effect. We used Tukey post hoc tests for significant main effects and interactions. When checking for the assumptions of an ANOVA, we found a potential outlier for the balance-challenged walking group (studentized residual > 4.0). Excluding this data point did not change the results, suggesting it was non-influential. Thus, we included this data point in the final statistical model.

To assess relearning one week later, we calculated the change in end-point error during the first adaptation trial (representing the initial recall of the mapping) and early adaptation (i.e., mean of adaptation trials 2 to 8) across testing sessions. Error reduction during trials 2 to 8 captures the large, rapid reduction in error early in the adaptation phase (Maeda et al. 2017b; Malone et al. 2011; Roemmich and Bastian 2015). We also calculated the change in the rate of adaptation across testing sessions, where a greater positive change reflects faster adaptation during the second testing session and therefore, greater savings. We determined the rate of adaptation by fitting an exponential model to the end-point-error data during the 60 adaptation trials.

We define the rate of adaptation as the time constant, which represents the number of trials taken to reach ~ 63.2% of adaptation (Martin et al. 1996a). We used the following equation:

$$y = a - b \times e^{-x/c} \tag{3.1}$$

where *a* is residual error after steady state (i.e., the asymptote), *b* is the magnitude of the adaptation required from the first trial to reach *a*, *c* (the decay constant) represents the rate of adaptation, and *x* is the trial number. To determine if the adaptation groups retained the new visuomotor mapping, we performed separate one-sample t tests or Wilcoxon signed rank tests (hypothesized value = 0), depending on data normality, on the change in first adaptation trial error, early adaptation error, and rate of adaptation measures. We also performed separate one-sample t tests or Wilcoxon signed rank tests (hypothesized value = 0), depending on data normality, on the change in postadaptation trial error for each group. To determine if challenging balance resulted in better relearning, we used separate two-sample t tests or Wilcoxon rank sum tests, depending on data normality, to compare between the balance-unchallenged and balance-challenged reaching and walking groups for each of our measures.

3.4. Results

Four groups of participants adapted to a novel visuomotor mapping induced by prism lenses while performing either a precision reaching or walking task, with or without an additional balance manipulation. We determined how challenging balance affected the ability to adapt and retain the novel visuomotor mapping.

3.4.1. Challenging balance does not affect the ability to adapt to a new visuomotor mapping

All participants adapted to the novel visuomotor mapping. Upon initial exposure to the 20-diopter (rightward-shifting) prism lenses, participants showed a large, rightward deviation in limb end-point placement relative to the target for the reaching and walking tasks. The end-point error gradually returned to near-baseline levels as the participants adapted to the prisms. These results are illustrated in Figures 3.3 and 3.4 for reaching and walking, respectively.

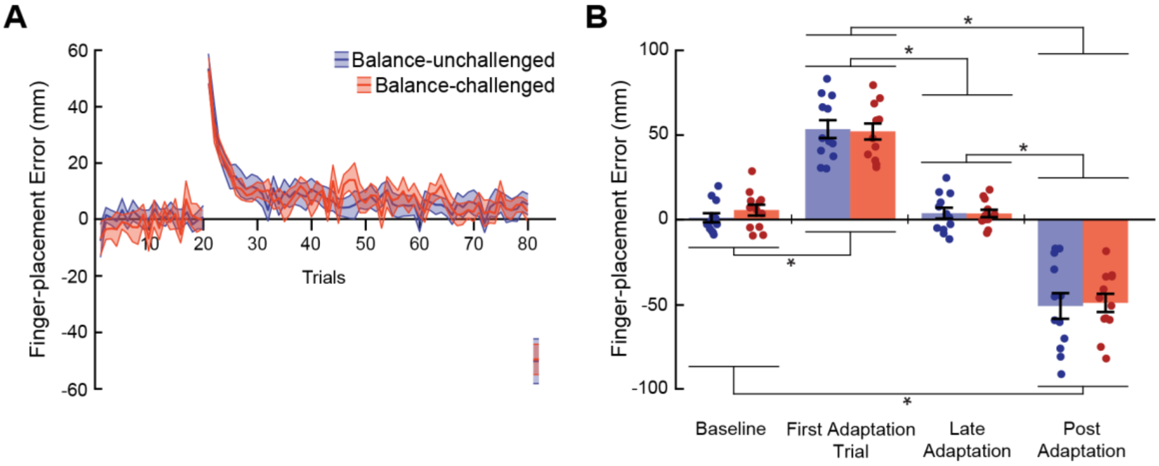

Figure 3.3 Visuomotor adaptation in reaching during session 1

A) Group mean ± SE finger-placement error across all trials for baseline, adaptation, and postadaptation phases during the first testing session for the balance-unchallenged (blue) and balance-challenged (red) reaching groups. ***B)*** Group mean ± SE finger-placement error for the baseline phase (average of the last ten trials), first adaptation trial, late adaptation (average of the last ten trials), and postadaptation trials for the first testing session for the balance-unchallenged (blue) and balance-challenged (red) reaching groups. Individual participant values are superimposed. * Indicate that values are significantly different from each other based on post hoc tests ($p < 0.05$).

To determine the effects of challenging balance on adaptation, we compared end-point error over several phases during the first testing session. For the reaching groups, end-point error differed depending on the phase (Fig. 3.3B; $F_{3,66} = 186.31$, $p = 3.76\text{e-}32$). Post hoc tests revealed significantly greater end-point error during the first adaptation trial compared to the other phases. Furthermore, the end-point error during the postadaptation trials differed significantly from each other phase. We found no significant differences between the balance-unchallenged and balance-challenged reaching groups across the different phases. Similarly, end-point error differed depending on the phase for the walking groups (Fig. 3.4B; $F_{3,66} = 676.90$, $p = 1.75\text{e-}49$). Post hoc tests showed a significant difference between the first adaptation trials and each other phase. Similarly, postadaptation end-point error differed significantly from the other phases. We did not detect any significance differences between the balance conditions for the walking tasks across the testing phases. Taken together, these results suggest that our balance manipulation did not affect the ability to adapt to the novel, prism-induced visuomotor mapping.

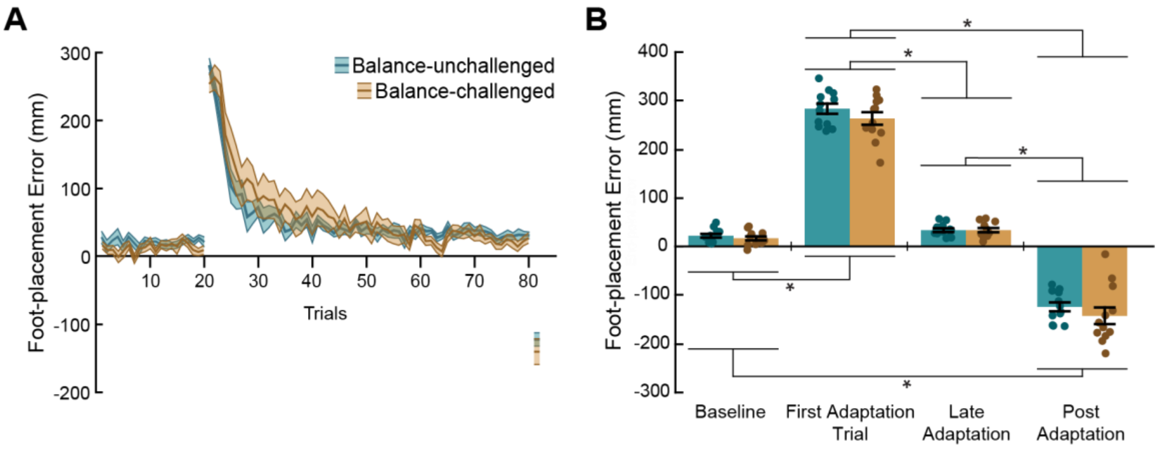

Figure 3.4 Visuomotor adaptation in walking during session 1
A) Group mean ± SE foot-placement error across all trials for baseline, adaptation, and postadaptation phases during the first testing session for the balance-unchallenged (teal) and balance-challenged (gold) walking groups. ***B)*** Group mean ± SE foot-placement error for the baseline phase (average of the last ten trials), first adaptation trial, late adaptation (average of the last ten trials), and postadaptation trials for the first testing session for the balance-unchallenged (teal) and balance-challenged (gold) walking groups. Individual participant values are superimposed. * Indicate that values are significantly different from each other based on post hoc tests ($p < 0.05$).

3.4.2. Challenging balance enhanced savings in walking but not reaching

To determine the effects of challenging balance on visuomotor savings, all participants repeated the adaptation protocol one week later. Figure 3.5A illustrates group mean end-point error across trials for both testing sessions for the reaching groups. To assess initial recall of the mapping, we calculated the change in first adaptation trial error between testing sessions. Here, a greater positive change indicates greater recall of the learned mapping one week later. For the balance-unchallenged reaching group, we did not detect a significant change in the first adaptation trial error between testing sessions ($t_{11} = 1.42$, $p = 0.185$), suggesting they did not recall the learned mapping after one week (Fig. 3.5B). However, the balance-challenged reaching group significantly decreased their first adaptation trial error across testing sessions ($t_{11} = 2.50$, $p = 0.030$), demonstrating initial recall of the mapping.

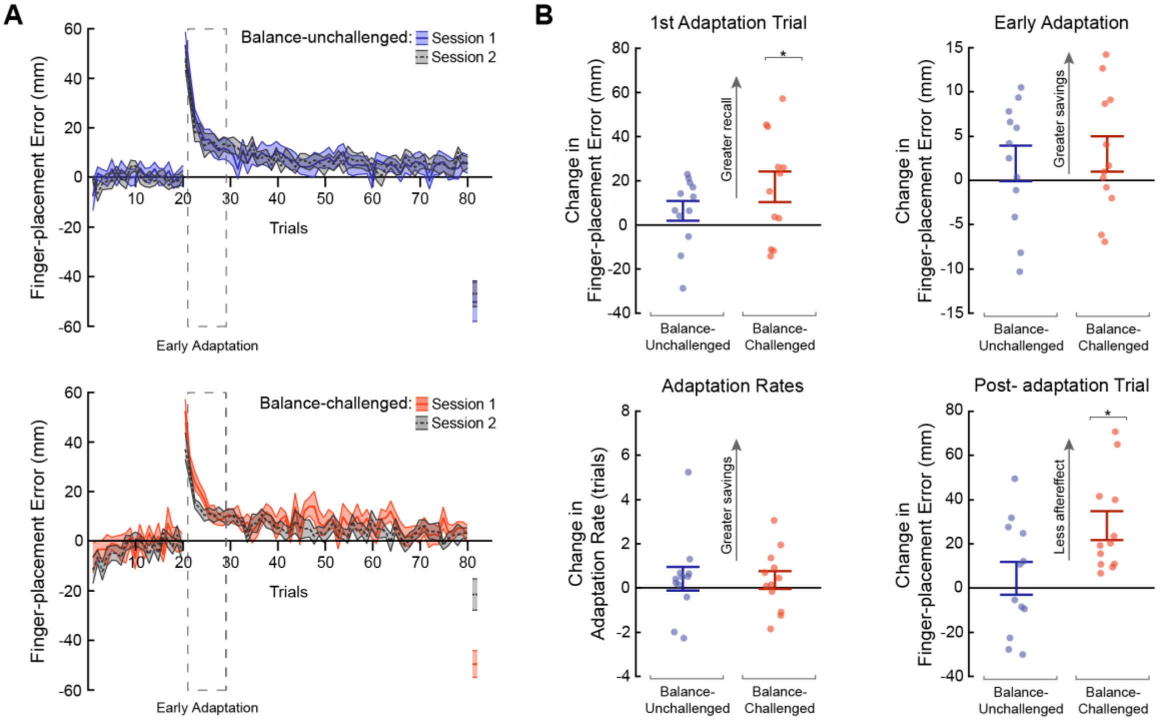

Figure 3.5 Challenging balance and visuomotor savings in reaching.
A) Group mean ± SE finger-placement error for all trials in the baseline, adaptation, and postadaptation phases across testing sessions for the balance-unchallenged (top) and balance-challenged (bottom) reaching groups. ***B)*** The change in first adaptation trial error, early adaptation trial error, rate of adaptation, and postadaptation trial error across testing sessions for the balance-unchallenged (blue) and balance-challenged (red) reaching groups. Group mean ± SE and individual values are shown for each measure. Testing sessions occurred one week apart. * Indicate that the within-group change across testing sessions is significantly different from zero ($p < 0.05$).

To quantify savings, we calculated the change in early adaptation error (i.e., mean of adaptation trials 2 to 8) and rate of adaptation across testing sessions. A faster reduction in error (i.e., faster relearning of the mapping, or savings) indicates that the learned mapping was retained. In this case, a greater positive change in early adaptation error and rate of adaptation reflects greater savings. We found no evidence of savings for either reaching group (Figure 3.5B). Specifically, the balance-unchallenged reaching group showed no significant change in early adaptation error ($t_{11} = 0.94$, $p = 0.369$) or rate of adaptation (session 1: 3.3 ± 3.1 trials; session 2: 2.8 ± 2.4 trials; Wilcoxon: $S = 14.50$, $p = 0.274$) across testing sessions. Similarly, we did not detect any significant change in early adaptation error ($t_{11} = 1.41$, $p = 0.186$) or rate of adaptation (session 1: 2.3 ± 1.1 trials; session 2: 1.9 ± 1.2 trials; $t_{11} = 0.90$, $p = 0.386$) for the balance-challenged reaching group. Interestingly, we found that the balance-challenged reaching group showed a significant decrease in the end-point error during postadaptation across testing sessions (Wilcoxon:

S = 39.00, p = 0.0005), but we did not detect a significant difference for the balance-unchallenged reaching group (t_{11} = 0.57, p = 0.583).

To determine the effects of challenging balance on motor memory retention, we compared our measures of recall and savings between reaching groups. We did not detect significant differences for the change in first adaptation trial error (t_{22} = 1.33, p = 0.197), early adaptation error (t_{22} = 0.35, p = 0.731), or rate of adaptation (Wilcoxon: Z = 0.116, p = 0.908) between the balance-unchallenged and balance-challenged groups. We also did not detect a significant difference in the change in postadaptation error between groups (Wilcoxon: Z = 1.76, p = 0.078). Overall, challenging balance did not appear to affect visuomotor savings during reaching.

Figures 3.6A illustrates group mean end-point error across trials in both testing sessions for the walking groups. Unlike the results for reaching, we found evidence of initial recall and savings for both walking groups. Specifically, the balance-unchallenged walking group showed a significant decrease in end-point error during the first adaptation trial (t_{11} = 2.53, p = 0.028) and early adaptation (t_{11} = 6.49, p = 4.51e-5), which are represented by positive changes (Fig. 3.6B). The balance-unchallenged walking group also showed an increase in the rate of adaptation across testing sessions (session 1: 4.0 ± 2.3 trials; session 2: 2.3 ± 0.9 trials; t_{11} = 3.27, p = 0.008). Similarly, the balance-challenged walking group demonstrated recall and savings one week later, as indicated by a significant reduction in first adaptation trial error (t_{11} = 2.33, p = 0.040) and early adaptation error (t_{11} = 4.66, p = 0.0007) across sessions. The balance-challenged walking group also showed an increase in the rate of adaptation (session 1: 5.7 ± 3.3 trials; session 2: 1.4 ± 0.7 trials; t_{11} = -4.9 p = 0.0004), indicating faster relearning one week later. Similar to the reaching groups, we found that the balance-challenged walking group reduced their error for the postadaptation trial (t_{11} = 4.05, p = 0.002) across testing sessions, but we did not detect a significant difference for the balance-unchallenged walking group (t_{11} = 1.84, p = 0.093).

To determine the effects of challenging balance on motor memory retention during walking, we compared our measures of recall and savings between the walking groups. We found no significant difference for the change in first adaptation trial error (t_{22} = 0.13, p = 0.895), indicating similar recall of the mapping. However, we found that the balance-challenged walking group showed a significantly greater positive change in early adaptation error ($t_{22} = 2.32$, $p = 0.030$) and rate of adaptation ($t_{22} = 2.46$, $p = 0.022$) compared to the balance-unchallenged walking group, indicating greater savings. Additionally, the balance-challenged walking group showed a reduction in postadaptation trial error (or less aftereffect) across testing sessions compared to the balance-unchallenged group ($t_{22} = 3.11$, $p = 0.005$). Taken together, both walking groups showed evidence of faster relearning assessed one week later. Furthermore, challenging balance enhanced savings in our walking task.

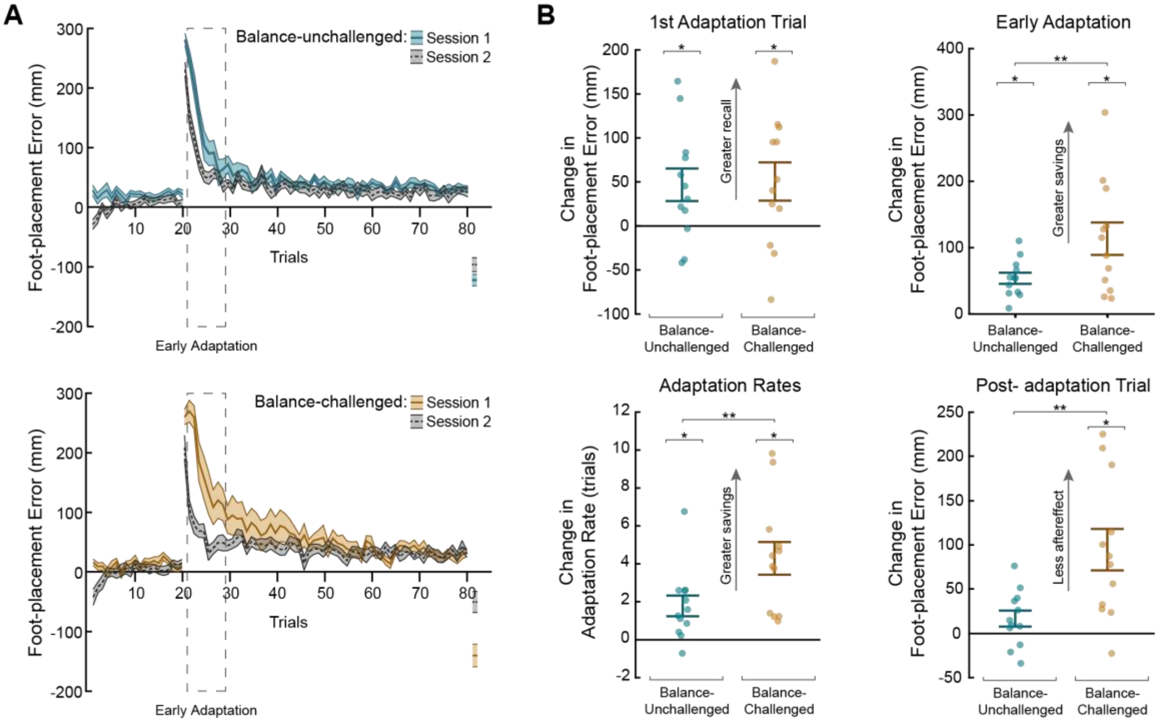

Figure 3.6 Challenging balance and visuomotor savings in walking

A) Group mean ± SE foot-placement error for all trials in the baseline, adaptation, and postadaptation phases across testing sessions for the balance-unchallenged (top) and balance-challenged (bottom) walking groups. ***B)*** The change in first adaptation trial error, early adaptation trial error, rate of adaptation, and postadaptation trial error across testing sessions for the balance-unchallenged (teal) and balance-challenged (gold) walking groups. Group mean ± SE and individual values are shown for each measure. Testing sessions occurred one week apart. * Indicate that the within group change across testing sessions is significantly different from zero ($p < 0.05$). ** Indicate that the magnitude of change across testing sessions is significantly different between the balance-unchallenged and balance-challenged groups ($p < 0.05$).

3.5. Discussion

The ability to adapt to physiological and environmental change and retain what is learned is important for safe and successful motor performance in everyday life. Here, we tested the hypothesis that challenging balance during adaptation would increase motor memory retention, reflected by greater savings assessed one week later. We found that challenging balance did not affect the ability to adapt to the new visuomotor mapping and that only the walking groups demonstrated visuomotor retention. Crucially, we found that challenging balance enhanced savings during walking. Thus, while challenging balance did not dictate whether or not retention occurred, this condition increased savings in tasks where participants retained the new visuomotor mapping. These results highlight the robustness of motor memories associated with walking, as well as the potential influence of balance control on sensorimotor learning.

One hypothesis for our findings is that challenging balance increases the value assigned to maintaining the internal model learned during adaptation. This potential value may arise from two related factors: the necessity for better control over the whole body to ensure safe and successful task performance or from a greater perceived threat of falling typically associated with balance challenges. We discuss the rationale and support for these factors below.

Challenging balance may increase the value of control, as the inability to minimize unwanted body motion would not only affect performance accuracy, but also increase the risk of falling and injury. The decision to move is often dictated by whether or not the potential rewards (or penalties) associated with set goals outweigh the effort required to act (Gallivan et al. 2018). Consequently, these decisions rely on an estimate of the expected value of control associated with the task to determine if it is worth pursuing (Shenhav et al. 2013; Rangel et al. 2008). While value is subjective and difficult to quantify, it may be inferred from the movement decisions that individuals make (Yoon et al. 2020). In our case, the balance-challenged participants were able to reduce their performance errors while also maintaining balance, suggesting that they deemed the greater allocation of control worthwhile. Thus, there is increased value in controlling balance.

Most memories are transient in nature, and we tend to forget information that is unlikely to be useful in the future. In contrast, information that increases the likelihood of future gains may be perceived as more valuable and therefore more readily retained. For instance, we might expect amateur and professional athletes to focus on recalling actions that lead to task success rather than those that worsen performance. This idea is aligned with studies demonstrating that monetary rewards enhance motor memory retention (Abe et al. 2011; Galea et al. 2015). As value increases with the magnitude and probability of reward (Kahnt and Tobler 2017), we might infer that subjective value, monetary or otherwise, can modulate savings. In our study, while both walking groups demonstrated motor memory retention, challenging balance significantly increased savings assessed one week later. These results highlight the significance of balance control on sensorimotor learning and demonstrate that, with respect to a precision walking paradigm, the value of control associated with balance challenges can enhance savings.

As with most balance challenges, there is an element of risk associated with falling and getting injured. While we did not directly assess fear or anxiety associated with our balance-challenged tasks, it is possible that the greater perceived risk of falling contributed to the enhanced retention observed during walking. Imagine having just slipped on ice. When remembering that unpleasant experience, you might choose to modify your gait (Marigold and Patla 2002) or simply avoid a similar area to mitigate the threat of falling in the future. Thus, from a safety perspective, it is important to prioritize information that reduces the risk associated with threatening environments. Correspondingly, studies using Pavlovian fear-conditioning paradigms demonstrate that perceived threat can significantly influence memory retention (see for example, Rogan et al. 1997). This is aligned with the notion that our memory systems are optimized to retain survival-related information (Nairne et al. 2007; Nairne and Pandeirada 2016). While the effects of perceived threat on motor memory retention are less clear, research shows that balance recovery responses from gait trip- or slip- perturbations can be retained for extended periods of time (Bhatt et al. 2006; Bhatt et al. 2012; König et al. 2019; Pai et al. 2014). This suggests that fear of falling can modulate motor memory retention. Thus, coupled with the increased value of control, the greater perceived threat associated with balance-challenges may further increase the value assigned to the model during adaptation and enhance motor memory retention.

An interesting observation in this study was that both the reaching and walking balance-challenged groups significantly decreased their postadaptation trial error after relearning. While the reasons for this are unclear, we speculate that it relates to the increased value associated with maintaining the internal model formed during the balance-challenged tasks. Following adaptation, participants performed a single trial of their respective adaptation tasks without the prism lenses. An error in the opposite direction to the visual shift (i.e., a negative aftereffect) indicates internal model recalibration and storage of the new mapping (Redding and Wallace 1996), with larger aftereffects typically interpreted as greater learning. However, it is unclear what the postadaptation trial error represents after re-exposure to a previously learned mapping. If we assume that it is still a means to quantify learning, does a reduction in error across exposures signify a reduction in learning? We do not believe this to be the case. Rather, we argue that a reduction in postadaptation error reflects a greater capacity to switch between learned mappings (i.e., prisms on versus off). Anecdotally, this is aligned with the observation that, over time, people can adapt to wearing new prescription lenses and are soon able to switch between visuomotor mappings (i.e., glasses on and off) with little to no disruption to performance. This notion is supported by research demonstrating people can learn, retain, and switch between different visuomotor mappings (Martin et al. 1996b; Mcgonigle and Flook 1978; van Dam et al. 2013; Welch et al. 1993). Furthermore, a recent study demonstrated increased savings with smaller aftereffects after each repeated exposure to a learned split-belt treadmill walking pattern (Day et al. 2018). Given that only the balance-challenged groups demonstrate smaller aftereffects after relearning, we speculate that the increased value for control associated with these tasks enhanced the ability to switch between visuomotor mappings to ensure safe and successful task performance.

Another possible contributing factor for the enhanced retention during balance-challenged walking is that the rubber hemispheres may serve as an additional contextual cue driving faster recall of the mapping. Research shows that contextual cues that contain sensory information about movement dynamics (e.g., limb orientation or proprioceptive states) play an important role in the formation and recall of motor memories (Hirashima and Nozaki 2012; Howard et al. 2013; Yeo et al. 2015), though these effects are not always apparent (Gandolfo et al. 1996; Krakauer 2009). Furthermore, recent research suggests that savings can be achieved primarily through the recall of a deliberate strategy (Haith et al. 2015; Morehead et al. 2015). Here, the exacerbated movements associated with the balance-challenged tasks may have strengthened the association between the rubber hemispheres and learned visuomotor mapping, enabling rapid recall of an explicit strategy upon re-exposure to the prisms. In this scenario, we might expect the balance-challenged walking group to demonstrate greater recall of the mapping, reflected by a greater positive change in first adaptation trial error compared to the balance-unchallenged walking group. However, this was not the case, and our findings suggest that both walking groups demonstrate comparable recall. This also appears to be the case for our reaching tasks where neither group retained the mapping. Furthermore, given that participants performed baseline trials prior to relearning to return their performance to pre-adaptive levels, any immediate contextual cues associated with the rubber hemispheres would have been washed out before the readaptation phase. Thus, it seems unlikely that the additional context provided by the rubber hemispheres is responsible for the enhanced savings observed during balance-challenged walking.

In contrast to the walking groups, we found that neither reaching group exhibited savings one week after adaptation. The reasons for this are unclear, however the nature of the reaching task may provide an explanation. For instance, the structure of initial learning, such as perturbation size (Leech et al. 2018; Malone et al. 2011; Morehead et al. 2015) and exposure duration (Alhussein et al. 2019; Day et al. 2018; Nguyen et al. 2019; Roemmich and Bastian 2015) can influence motor memory retention. Here, all participants adapted to a 20-diopter visual shift to the right (~11.4°) (Fig. 3.1A). However, the distance between the eye and the floor (and foot) is larger than the distance between the eye and the target screen (and hand). This means that there is a larger perceived target shift to the right for the walking groups. This may explain the differences in initial end-point error between tasks (~60 mm for reaching compared to ~300 mm for walking; see Figures 3.3A and 3.4A). Thus, the magnitude of the error experienced during adaptation may be less effective at eliciting week-long savings during reaching. Additionally, participants in the walking task groups may have had increased prism exposure during the steps before and after the target which may further facilitate retention. However, we feel that this is unlikely, as participants only interact with the target once per trial regardless of the task and they performed the tasks under reduced light conditions (~ 0.9 lux) and on a black mat to minimize the influence of environmental references. Alternatively, these findings may provide further evidence for the robustness of motor memories associated with walking and observed in previous studies (Day et al. 2018; Maeda et al. 2018; Malone et al. 2011).

How do the effects of challenging balance on generalization compare to those observed for motor memory retention? In our previous study (Bakkum et al. 2020), we found that challenging balance during adaptation increased generalization during reaching and walking, suggesting that the benefits are observed immediately and apply broadly to sensorimotor learning. However, here we show that challenging balance had little effect on motor memory retention during the reaching tasks, likely a result of the fact that retention did not occur to begin with. In contrast, we found that both walking groups retained the new visuomotor mapping one week later, with the balance-challenged group demonstrating increased savings. One possible explanation for the robust motor memories formed during our walking tasks may relate to the greater threat of falling associated with walking while wearing the prism lenses. While both reaching and walking tasks require the participant to be accurate, the consequences of stepping inaccurately and possibly falling during walking are greater than simply missing the reaching target. The threat of falling is further increased with the addition of our balance manipulation, which reduces the control afforded by shifting the foot's center of pressure due to the much smaller base of support. Thus, the greater consequence of failure associated with the walking tasks may serve to reinforce the value placed on maintaining the updated internal model and further contribute to the robust motor memory retention observed for this task.

In summary, we found that challenging balance enhanced savings during walking without penalizing performance during initial adaptation. We propose that challenging balance increases the value of a learned internal model because of a greater need for control and/or greater perceived risk of falling. Because a greater-valued model may serve some future benefit, it is a more retainable model. Overall, our study demonstrates the significance of balance control during sensorimotor learning and the potential performance benefits associated with learning during unconstrained, naturalistic tasks.

3.6. Chapter contributions

Conceptualization, Amanda Bakkum (A.B.), J. Maxwell Donelan (J.M.D), and Daniel S. Marigold (D.S.M); Methodology, A.B., J.M.D, and D.S.M; Investigation, A.B.; Formal Analysis, A.B.; Writing – Original Draft, A.B. and D.S.M; Writing – Reviewing & Editing, A.B., J.M.D, and D.S.M.

Chapter 4.

How the consequence of movement error affects sensorimotor learning

> ‘‘Nothing is worth doing unless the consequences may be serious.”
>
> (*George Bernard Shaw*)

4.1. Abstract

To safely navigate our environment, we must carefully consider the consequences of our actions. As maintaining balance is a primary objective of the nervous system, this requires consideration of any threats to stability and the consequences associated with falling. We propose that the potential injurious consequences of being inaccurate and losing balance may serve to augment the value of movement errors experienced during adaptation and enhance sensorimotor learning. To test this hypothesis, we encouraged two groups of participants to adapt to a novel visuomotor mapping induced by prism lenses while performing a precision walking task that required them to step to the centre of a target positioned along the middle of the walking path. Participants performed this task either with or without experiencing a slip perturbation when making errors in foot placement to the target. We probed how this stability consequence affected generalization and motor memory consolidation. We assessed generalization during an interlimb-transfer test and an obstacle-avoidance task performed without the prism lenses. We found that while both groups demonstrated interlimb-transfer to the un-adapted left leg during the precision walking task, the stability consequence significantly enhanced generalization. Additionally, only the consequence group generalized learning to the obstacle-avoidance task. To assess consolidation, we introduced an opposite direction visuomotor mapping following initial adaptation and evaluated relearning of initial adaptation one week later. We found that the consequence group demonstrated significantly greater motor memory consolidation, reflected by greater recall and faster relearning (i.e., savings). Overall, our results demonstrate that experiencing a physical consequence when making errors enhances sensorimotor learning.

4.2. Introduction

Every action has a consequence. Occasionally, poorly executed movement can give rise to serious consequences. An accidental misstep off a sidewalk, for example, can lead to an injurious fall. While our perception of consequence is largely subjective, a primary concern of the nervous system is to maintain balance to prevent falling over. Even moderate threats to postural stability elicit movement strategies that serve to safeguard balance. When standing on a raised platform, for instance, people demonstrate more conservative postural control strategies to minimise trunk displacement and reduce the risk of falling (Adkin and Carpenter 2018). Such safety-driven movement strategies are also observed during curb or stair negotiation where people tend to slow down and prolong double-support phase in response to reduced ambient light or with visual impairment (Alexander et al. 2014; Buckley et al. 2005; Heasley et al. 2005). Furthermore, research suggests that postural control is scaled in response to increasing levels of postural threat (Adkin et al. 2000; Brown and Frank 1997; Manista and Ahmed 2012). Given that daily movements are plagued by inherent stability challenges, decisions about how we move are made under constant consideration of postural threat and the potential injurious consequences of our actions.

To mitigate the risk of falling, people must maintain movement accuracy despite changing physiological and environmental states. This requires the nervous system to adapt previously learned movements, transfer (or generalize) learning to new contexts, and retain what is learned to facilitate future performance through faster relearning (or savings). Research demonstrates that learning can generalize to new movement directions and/or between limbs (Krakauer et al. 2000; Thoroughman and Shadmehr 2000; Wang and Sainburg 2003) and is retained over time (Brashers-Krug et al. 1996; Krakauer et al. 2005). However, as most of these studies assessed sensorimotor learning during isolated movements (e.g., seated upper-limb tasks), the results cannot be easily extrapolated to naturalistic motor behaviours that typically necessitate balance control. There is evidence to suggest that learning during unconstrained walking tasks results in broad generalization and robust motor memory retention (Alexander et al. 2011; 2013; Maeda et al. 2017b; 2018; Malone et al. 2011; Torres-Oviedo and Bastian 2012). Furthermore, recent research from our lab demonstrates that challenging balance increases the extent of generalization during reaching and walking tasks (Bakkum et al.

2020) and enhances sensorimotor savings during walking (Chapter 3). Taken together, these findings suggest the necessity to maintain balance during naturalistic motor behaviours can modulate sensorimotor learning. We propose that the potential injurious consequences associated with being inaccurate and losing balance may serve to augment the value of movement errors experienced during adaptation. In turn, this may increase the value assigned to an updated internal model. Thus, we tested the hypothesis that a stability consequence associated with movement errors would enhance sensorimotor learning, reflected by increased generalization and motor memory consolidation.

To test this hypothesis, we had two groups of participants adapt to a novel visuomotor mapping induced by prism lenses while performing a precision walking task. The prism lenses altered the normal relationship (or mapping) between visual input and motor output and caused errors in foot placement to a target. Participants performed this task either with or without the possibility of experiencing a slip perturbation when making foot-placement errors. We assessed how this stability consequence affected 1) generalization of the learned visuomotor mapping across different visually guided walking tasks, and 2) consolidation of the learned mapping one week later. Here, we define consolidation as the learned mapping being resistant to interference from an opposite mapping.

4.3. Materials and methods

4.3.1. Participants

Twenty-four participants (mean age ± SD = 26.4 ± 5.0 years; 11 men, 13 women) with no known musculoskeletal, visual (six participants wore corrective lenses or glasses), or neurological disease participated in this study. The Office of Research Ethics at Simon Fraser University approved the study protocol and all participants provided written informed consent prior to their participation.

4.3.2. Experimental tasks and data collection

All participants adapted to a novel visuomotor mapping induced by prism lenses (Fig. 4.1A) while performing a precision walking task (Fig. 4.1B). Participants stood at the beginning of the walkway (~6 m in length) and waited for a go-cue to signal the start of each trial. Once cued, participants took a minimum of two steps before stepping with their right foot onto the medial-lateral (ML) center of a projected target (3 x 36 cm) without stopping. We instructed participants to be as accurate as possible in ML dimension when stepping to the target. We used a long target to reduce the demand for accuracy in the anterior-posterior (AP) dimension and to prevent participants from using shuffle steps as they approached the target. We displayed the target in the center of the walking path using an LCD projector (Epson PowerLight 5535U; brightness of 5500 lumens). Participants performed the task under reduced light conditions (~ 0.9 lux) to minimize the influence of environmental references and increase the visibility of the projected target.

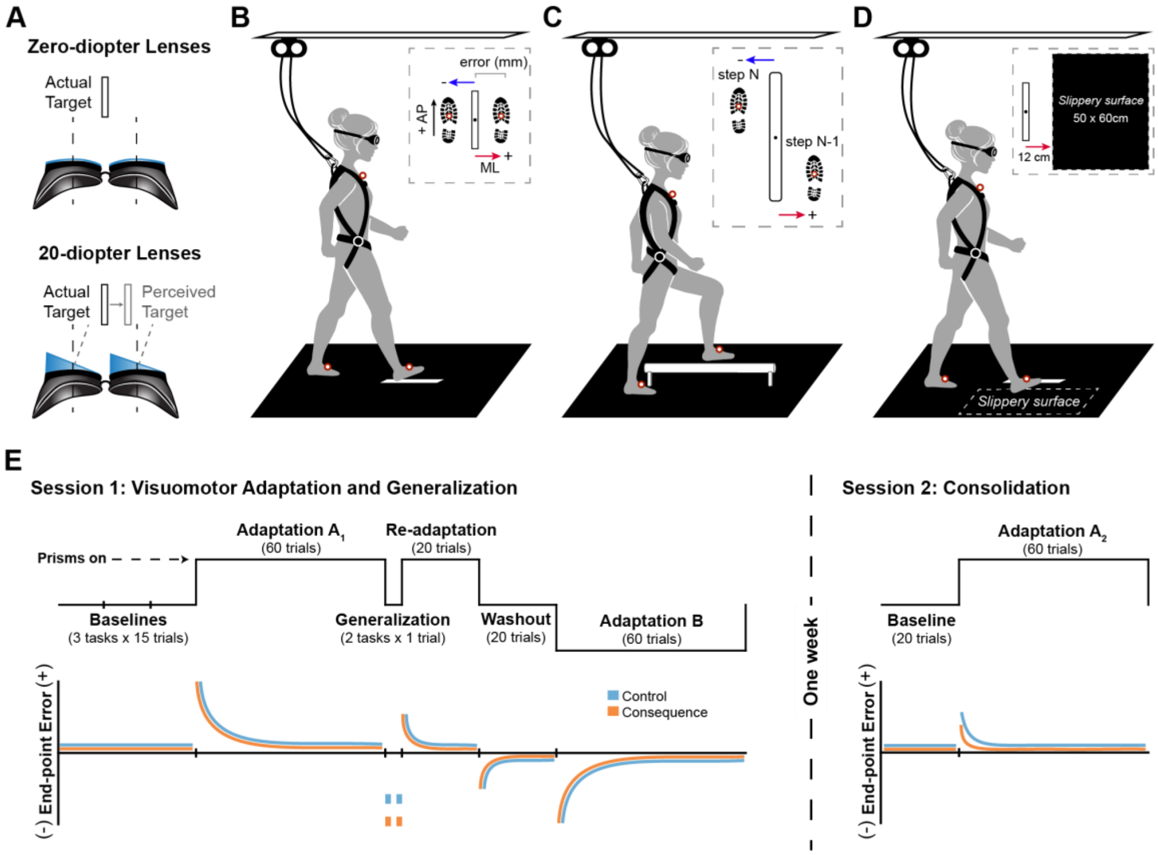

Figure 4.1 Experimental tasks and protocol
A) A simulated view of the stepping target through the goggles coupled with zero-diopter (non-visual-field-shifting) lenses and 20-diopter prism lenses that shift the perceived location of the target 11.4° to the right. ***B)*** An illustration of the precision walking task. Inset: a diagram showing the positive (+) and negative (-) medial-lateral (ML) foot-placement error, defined as the distance between the position marker on the mid-foot and the center of the target. AP, anterior-posterior dimension in laboratory space. ***C)*** An illustration of the obstacle avoidance task. Inset: a diagram showing the positive (+) and negative (-) medial-lateral (ML) deviation from the obstacle, defined as the distance between the center of the obstacle and the position marker on the mid-foot of both the trailing foot (i.e., step N-1: right foot) and leading foot (i.e., step N: left foot). ***D)*** An illustration of the setup for the stability consequence group during the adaptation phase. Inset: a diagram showing the position of the slippery surface with respect to the target. E) An illustration of the

experimental protocol across both testing sessions, as well as the predicted foot-placement error profiles for each phase of testing. During the first testing session, all participants performed baseline, adaptation, generalization, readaptation, and washout phases. Depending on the phase, participants wore goggles paired with either zero-diopter or 20-diopter lenses. To assess consolidation, participants repeated the washout and adaptation phases one week later. See text for details.

We assessed 1) generalization of the learned visuomotor mapping across different visually guided walking tasks, and 2) consolidation of the learned mapping one week later. We assessed generalization during an interlimb-transfer test and an obstacle-avoidance task performed without the prism lenses. During the interlimb-transfer test, participants performed a single trial of the precision walking task using their left foot instead of their right foot to step to the target. For the obstacle-avoidance task, participants walked along the same 6 m long path towards the right side of an obstacle (height = 25 cm; width = 6 cm; length = 80 cm) positioned in the center of the walkway. Once participants were beside the obstacle, they stepped laterally over the middle of it, first with their left leg (i.e., the leading leg), then their right leg (i.e., the trailing leg), before continuing to walk for several more steps (Fig. 4.1C). We instructed participants to avoid colliding with the obstacle. We also probed consolidation, defined as the stabilization of motor memory such that it is resistant to retrograde inference from a competing mapping (Krakauer et al. 2005). Thus, we introduced an opposite direction visuomotor mapping following initial adaptation and revaluated learning one week later to assess consolidation.

We tracked body motion from infrared-emitting position markers placed on the participant’s chest (in line with the sternum) and bilaterally on the mid-foot (second to third metatarsal head) at 120 Hz during each task using an Optotrak Certus motion capture camera (Northern Digital, Waterloo, ON, Canada). To mitigate adaptation between trials, we instructed participants to have their eyes open only when they performed the task. An experimenter guided the participants back to the beginning of the walkway between trials while their eyes were closed. To prevent participants from learning a specific stepping sequence and increase the demand for visual feedback, we randomized the anterior-posterior (AP) starting location (between 1.5 - 2.5 m) for each trial. We also encouraged participants to perform each task at a quick and constant pace to minimize online corrections of leg trajectory during the step to the target. Participants walked with an average speed (±SD) of 1.56 ± 0.16 m/s, and we later verified the absence of these corrections by looking at the kinematic profiles of the midfoot position markers. An experimenter demonstrated all tasks at the beginning of each testing session. Participants wore a safety harness at all times to prevent falling to the ground. No participant engaged the system during the course of this experiment.

4.3.3. Experimental protocol

We measured sensorimotor adaptation, generalization, and consolidation over two testing sessions, separated by one week. Figure 4.1E illustrates the experimental protocol and the predicted foot-placement error responses for each phase of testing. Depending on the phase, participants wore goggles coupled with either zero-diopter (non-visual-field-shifting) or 20-diopter prism lenses (Fig. 4.1A). The goggles block part of the peripheral visual field and participants had no option but to look through the lenses during each task. Participants performed three baseline phases (15 trials each), one for each visually guided walking task, while wearing the zero-diopter (i.e., non-visual-field-shifting) lenses. Participants performed the baseline phase for the adaptation task last, just prior to the adaptation phase. We counterbalanced the order of the two remaining baseline tasks for each participant and matched this order for the generalization tasks.

During the first adaptation phase (Adaptation A_1), participants learned a novel visuomotor mapping induced by the 20-diopter prism lenses while performing 60 trials of the precision walking task using their right foot to step to the target. The 20-diopter lenses shifted the perceived location of the stepping target ~11.4° to the right (i.e., mapping A) (Fig. 4.1A), altering the relationship between visual input and motor output and causing errors in foot placement to the target. Participants adapted to the new visuomotor mapping with (consequence group; n = 12) or without (control group; n = 12) a manipulation that produced an unexpected slip perturbation. For the consequence group, we positioned a low-friction, polypropylene surface (50 x 60 cm) to the right of the target during prism exposure (Fig. 4.1D). We concealed this slippery surface using a solid black, low-friction fabric that covered the entire walking path and did not inform participants about the possibility of a slip. Exposure to the prism lenses induced a rightward deviation in foot placement to the target, which increased the likelihood of participants in the consequence group making contact with the slippery surface. On contact, the shear forces under the participants shoe at heel strike caused the low-friction fabric to slide over the slippery surface (kinetic coefficient of friction $\approx 0.09\ \mu_k$; for reference: ice $\approx 0.02\ \mu_k$) and required a reactive response to prevent falling. We designed this manipulation to simulate slipping during walking and to serve as a stability consequence for movement errors. Participants only experienced the slip perturbation during stepping errors that were large enough that the foot made contact with the slippery surface. To prevent participants from being penalized during stepping errors within the normal range of late prism adaptation, we positioned the slippery surface ~12 cm from the center of the target. A textured polyvinyl chloride (PVC) bottom prevented the slippery surface from sliding along the walkway during contact.

Following adaptation to mapping A, participants performed the interlimb-transfer task and the obstacle-avoidance task (Fig. 4.1C) without the prism lenses to determine if the learned mapping was applied to the non-adapted tasks. Participants then performed 20 readaptation trials while wearing the rightward-shifting 20-diopter lenses to mitigate any deadaptation during the generalization phase. To confirm whether the learned mapping was stored, participants performed 20 washout trials of the adaptation task with the zero-diopter lenses. Finally, we introduced a competing mapping B (~15 minutes after initial adaptation) where participants performed 60 trials of the same adaptation task (i.e., precision walking with the right foot stepping on the target) while wearing the 20-diopter lenses that shifted the visual field in the opposite (i.e., leftward) direction of mapping A. Following the initial testing session, the participants returned to the lab one-week later to probe motor memory consolidation. Participants first performed 20 baseline trials of the adaptation task while wearing the zero-diopter lenses. Thereafter, all participants repeated the 60 adaptation trials with the 20-diopter prism lenses to assess consolidation of mapping A. There was no stability consequence for movement errors during the second testing session.

4.3.4. Data and statistical analysis

We analyzed kinematic data (filtered using a fourth-order, low-pass Butterworth algorithm with a cut-off frequency of 6 Hz) using custom-written MATLAB programs to calculate foot placement during the precision walking and obstacle avoidance tasks. We determined foot placement during each task as the moment of heel strike, derived using the vertical velocity of the mid-foot markers (Maeda et al. 2017b; O’Connor et al. 2007). For the precision walking task, we defined foot-placement error during the step to the target as the ML distance between the position of the mid-foot marker at heel strike and the center of the target. A positive value represents errors in the direction of the prism shift (i.e., to the right of the target) and negative values represent errors in the opposite direction to the prism shift (Fig. 4.1B). For the obstacle avoidance task, we calculated the ML distance between the obstacle and both the trailing foot (i.e., step N-1: right foot) and leading foot (i.e., step N: left foot) at heel strike using the mid-foot marker on each foot (Fig. 4.1C). For step N-1, increasing positive values represent a greater deviation of the right foot from the obstacle, whereas for step N, increasing negative values indicate greater deviation of the left foot from the obstacle.

During any slip perturbations, we expected to see greater forward displacement and velocity of the right foot compared to baseline. Therefore, to test whether our manipulation was effective at eliciting a slip, we calculated two measures to quantify slip severity: slip distance and slip velocity. Figure 4.2 illustrates how the vertical and AP velocity profiles of the right mid-foot marker are used to calculate slip distance and peak slip velocity during the baseline and adaptation phases. We calculated slip distance during the step to the target as the total AP displacement travelled by the right mid-foot marker between heel strike and slip end, the latter of which we defined as the moment AP velocity of the right mid-foot marker profile stabilized to zero. We then calculated peak slip velocity as the maximum AP velocity of the right mid-foot marker within that same time interval (i.e., heel strike to slip end). We defined a slip perturbation trial as a slip distance or slip velocity value of greater than the mean of these slip measures plus two standard deviations for each participant. Since we calculated these slip measures at the moment of heel strike before the foot is firmly planted on the ground, AP displacement and velocity have not yet stabilized to zero. Thus, we are able to compare foot displacement and velocity during the step between groups and across phases such that values greater than baseline represent the slip perturbation. To determine differences in slip severity, we compared slip distance and slip velocity during the baseline phase (mean of the last ten trials) and the first adaptation trial between groups using separate two-way (Group x Phase) mixed model ANOVAs, where we included participant as a random effect.

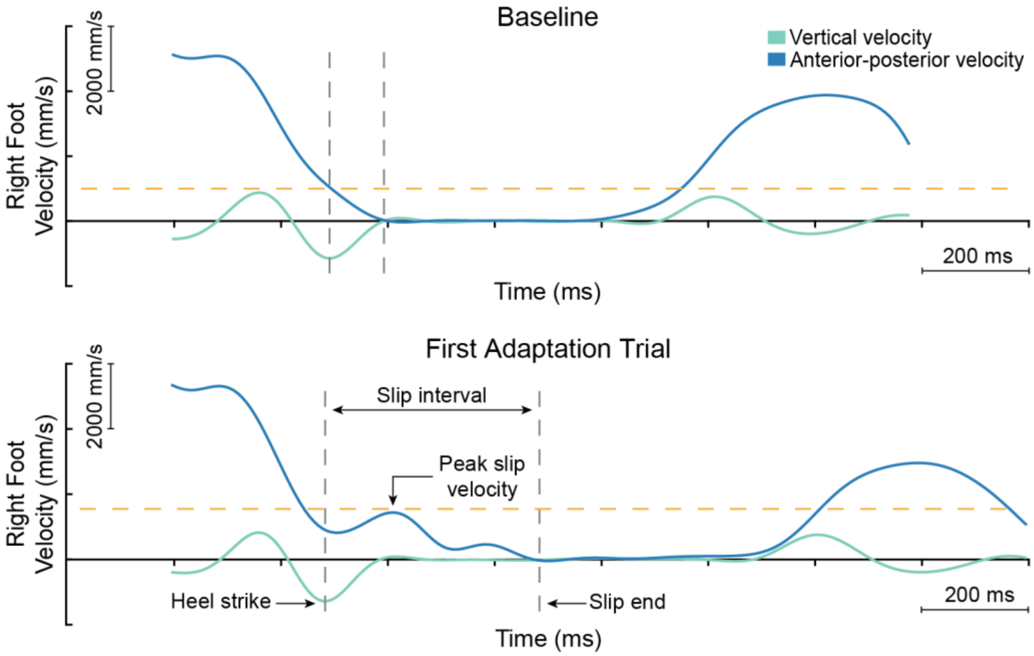

Figure 4.2 Slip severity
An example of the vertical (green) and anterior-posterior (AP) (blue) velocity profiles of the right mid-foot marker during baseline (top) and the first adaptation trial (bottom) for the consequence group. We used two measures to quantify slip severity: slip distance and slip velocity. The total AP distance travelled by the right mid-foot marker between the moment of heel strike and when its AP velocity stabilized to zero (slip end) defined the slip distance. This time interval is illustrated by the vertical grey dashed lines. The maximum AP velocity of the right mid-foot marker between heel strike and slip end defined slip velocity. Peak AP slip velocity is illustrated by the horizontal orange dashed line.

To determine how the stability consequence affected adaptation, we compared foot-placement error during the baseline phase (mean of the last ten trials), first adaptation trial, late adaptation (mean of the last ten trials), and the first washout trial in the first testing session using a two-way (Group x Phase) mixed model ANOVA (with participant as a random effect). When checking for the assumptions of an ANOVA, we found a potential outlier for the control group (studentized residual = 4.5). Excluding this data point did not change the results, suggesting it was non-influential. Thus, we included this data point in the final statistical model. To determine if the learned visuomotor mapping generalized to the non-adapted limb during the precision walking task, we compared foot-placement error during the baseline phase (mean of the last ten trials) and generalization trial using a two-way (Group x Phase) mixed model ANOVA (with participant as a random effect). Foot-placement errors in the direction opposite to the learned prism shift (i.e., a negative value) indicate generalization during the precision walking task.

To determine if the learned visuomotor mapping generalized to the obstacle avoidance task, we compared foot-placement deviation from the obstacle during the baseline phase (mean of the last ten trials) and generalization trial for both the trailing foot (i.e., step N-1: right foot) and leading foot (i.e., step N: left foot). Foot placement relative to the obstacle in the direction opposite to the learned prism shift (i.e., to the left) indicates generalization during the obstacle avoidance task. Thus, for step N-1 (right foot), a smaller value reflects less deviation of the foot from the obstacle (i.e., a leftward shift in foot placement; Fig. 4.1C) and indicates generalization of the learned mapping to the trailing foot. For step N (left foot), a greater negative value reflects greater deviation of the foot from the obstacle (i.e., a leftward shift in foot-placement; Fig. 4.1C) and indicates generalization of the learned mapping to the leading foot. We used separate two-way (Group x Phase) mixed model ANOVAs (with participant as a random effect) to determine if the learned mapping generalized to the obstacle avoidance task.

To assess consolidation, we quantified three measures: the first adaptation trial error, early adaptation error (i.e., mean of adaptation trials 2 – 8), and rate of adaptation. The first adaptation trial error represents the initial recall of the mapping. However, as participants are unaware of the mapping they will encounter (i.e., mapping A or B), they may require some initial context during relearning (i.e., the first adaptation trial) to remember the appropriate one. Therefore, we separate out this trial's error, similar to methods used by others (Krakauer et al. 2005; Maeda et al. 2017b; Malone et al. 2011). Early adaptation error captures the rapid reduction in foot-placement error early in the adaptation phase and does not assume that participants follow a specific pattern (i.e., it is a model-free measure) (Maeda et al., 2017b; Malone et al., 2011; Roemmich & Bastian, 2015). A faster reduction in foot-placement error (i.e., faster relearning of the mapping, or savings) indicates that the learned mapping was consolidated. Model-based rate measures are also used to quantify adaptation and savings (Criscimagna-Hemminger and Shadmehr 2008; Morton and Bastian 2004). Therefore, we also calculated the rate of adaptation by fitting an exponential model to the foot-placement error data during the 60 adaptation trials. We defined adaptation rate as the time constant, which represents the number of trials taken to reach ~ 63.2% of the adaptation (Martin et al. 1996a). We used the following equation:

$$y = a - b \times e^{-x/c} \tag{4.1}$$

where a represents the residual error after asymptote (i.e., steady state), b is the magnitude of the adaptation required to reach a from the first trial, c (the decay constant) represents the rate of adaptation, and x represents the number of trials. We used separate two-way (Group x Session) mixed model ANOVAs (with participant as a random effect) to determine differences in first adaptation trial error, early adaptation error, and adaptation rates between groups.

We used JMP 15 software (SAS Institute Inc., Cary, NC) with an alpha level of 0.05 for all statistical analyses. For ANOVAs, we used Tukey's post hoc tests when we found significant main effects or interactions.

4.4. Results

Two groups of participants learned a novel visuomotor mapping induced by prism lenses while performing a precision walking task. Participants performed this task with or without experiencing a slip perturbation during foot-placement errors to a target. We assessed how this stability consequence affected adaptation, generalization, and consolidation of the learned mapping.

4.4.1. Contact with the slippery surface elicited a slip perturbation

To confirm that participants in the consequence group experienced a slip perturbation when missing the target, we calculated measures of slip distance and slip velocity during the baseline (mean of last ten trials) and adaptation phases for the consequence and control groups. Figure 4.3 illustrates group mean slip distance and slip velocity. We found that every participant in the consequence group (n = 12) experienced a slip during the first adaptation trial, which we define as a slip distance or slip velocity value of greater than the mean plus two standard deviations for each participant. During this first adaptation trial, the consequence group demonstrated a significantly greater slip distance compared to baseline and the control group (Group x Phase interaction: $F_{1,22} = 85.49$, p = 4.927e-9), reflecting greater forward displacement of the right foot after contact with the slippery surface. Similarly, we found that slip velocity was significantly greater for the consequence group during the first adaptation trial compared to their baseline trials and the control group (Group x Phase interaction: $F_{1,22} = 34.85$, p = 6.103e-6). Additionally, all participants in the consequence group slipped during the second adaptation trial.

Thereafter, the number of slips declined, and no participants slipped after adaptation trial six. We found that the number of slips per trial differed slightly depending on the slip measure (i.e., slip distance or slip velocity), though this is likely due to the variability of the slip velocity measure. Overall, contact with the slippery surface during the precision walking task successfully elicited a slip perturbation.

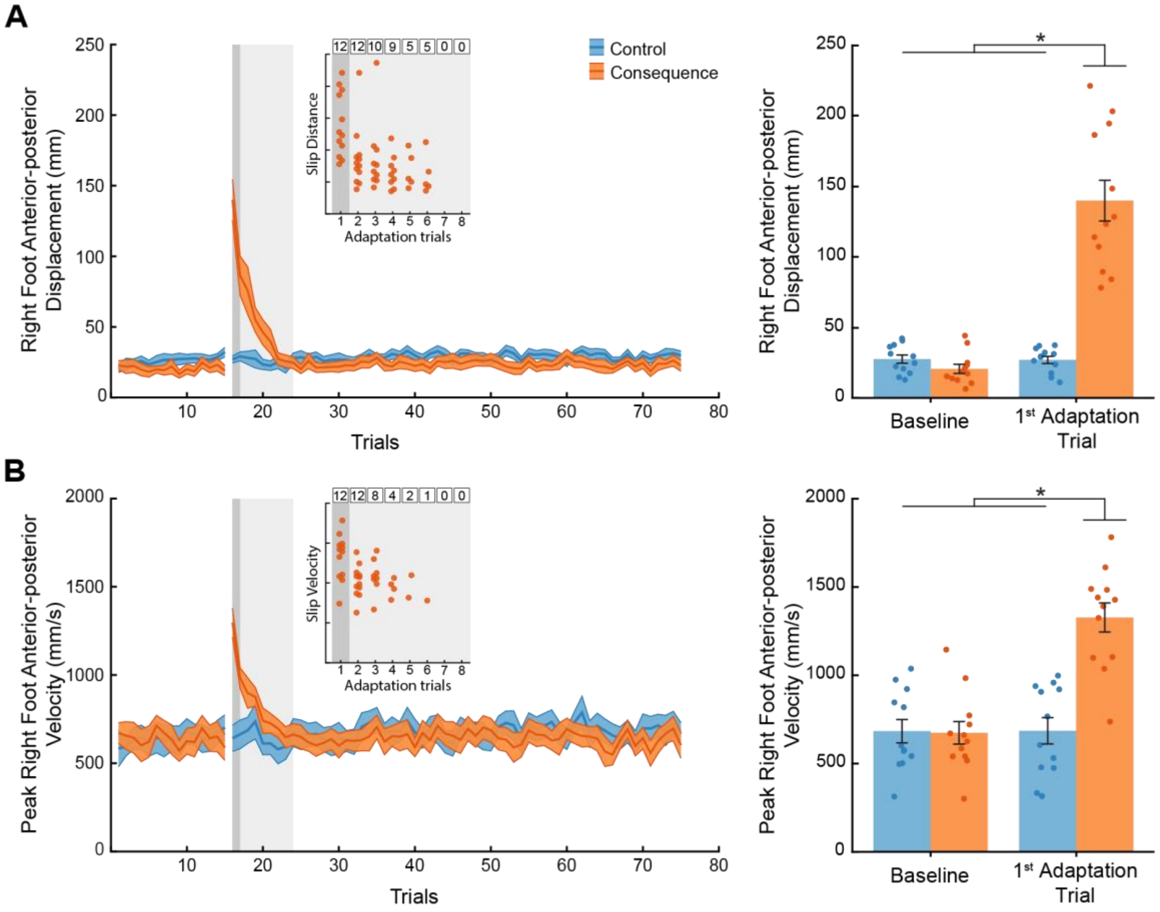

Figure 4.3 Slip measures

A) Left: Group mean ± SE slip distance across all trials for baseline and adaptation phases for the control (blue) and consequence (orange) groups. Right: Group mean ± SE slip distance for the baseline phase (mean of the last ten trials) and the first adaptation trial for the control (blue) and consequence (orange) groups. ***B)*** Left: Group mean ± SE peak slip velocity across all trials for baseline and adaptation phases for the control (blue) and consequence (orange) groups. Right: Group mean ± SE peak slip velocity for the baseline phase (mean of the last ten trials) and the first adaptation trial for the control (blue) and consequence (orange) groups. Individual participant values are superimposed. * Indicate that values are significantly different from each other based on post hoc tests ($p < 0.05$). Insets: individual data points showing significant evidence of a slip perturbation, defined as a slip distance or slip velocity value of greater than the mean plus two standard deviations for each participant. The dark grey shaded box represents the first adaptation trial, and the light grey shaded box represents early adaptation trials. The numbered black boxes represent how many participants slipped during each trial. Every participant in the consequence group slipped during the first two adaptation trials. No participants slipped after adaptation trial six.

4.4.2. The stability consequence did not disrupt initial visuomotor adaptation

Upon initial exposure to the prisms, all participants demonstrated a large, rightward deviation in foot placement relative to the target during the precision walking task. As participants adapted to the new visuomotor mapping, foot-placement error gradually returned to near-baseline levels of performance. Upon removal of the prism lenses, participants demonstrated a large, leftward deviation in foot-placement error (i.e., a negative aftereffect). These results are illustrated in Figure 4.4A.

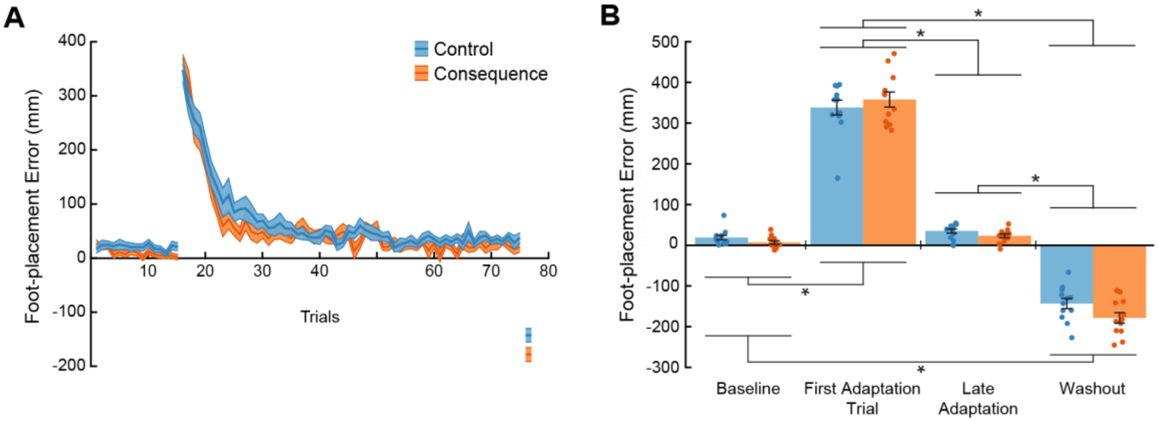

Figure 4.4 Visuomotor adaptation during session 1
A) Group mean ± SE foot-placement error across all trials for baseline and adaptation phases and the first washout trial during the first testing session for the control (blue) and consequence (orange) groups. ***B)*** Group mean ± SE foot-placement error for the baseline phase (mean of the last ten trials), first adaptation trial, late adaptation (mean of the last ten trials), and first washout trial during the first testing session for the control (blue) and consequence (orange) groups. Individual participant values are superimposed. * Indicate that values are significantly different from each other based on post hoc tests ($p < 0.05$).

To determine the effects of a stability consequence on visuomotor adaptation, we compared foot-placement error across the baseline phase (mean of last ten trials), first adaptation trial, early adaptation (i.e., mean of adaptation trials 2-8), and the first washout trial across groups during the first testing session. We found that foot-placement error differed depending on the phase (Fig. 4.4B; $F_{3,66} = 631.01$, $p = 1.65e-48$). Post hoc tests indicated significantly greater foot-placement error during the first adaptation trial compared to the other phases. Furthermore, foot-placement error during the first washout trial differed significantly from the other testing phases. We did not detect significant differences between the control and consequence groups across the testing phases.

Overall, the stability consequence experienced during movement errors did not affect the ability to adapt to the new visuomotor mapping.

4.4.3. A stability consequence associated with movement errors increases generalization

We assessed generalization of the learned mapping across two different visually guided walking tasks: a precision walking task using the non-adapted left leg to step to the target and an obstacle avoidance task. To determine whether the learned visuomotor mapping generalized to the left leg, we compared the mean foot-placement error during the last ten baseline trials to the foot-placement error during the generalization trial of the precision walking task. We found that both the control and consequence groups generalized the learned mapping to the non-adapted left leg (Group x Phase interaction: $F_{1,22} = 12.71$, $p = 0.002$), reflected by foot-placement errors in the direction opposite to the learned prism shift (i.e., a negative value) (Fig. 4.5A). However, the foot-placement error during the generalization trial differed significantly between groups, such that the consequence group demonstrated greater leftward deviation in foot placement from the target, indicating greater generalization to the left leg during precision walking.

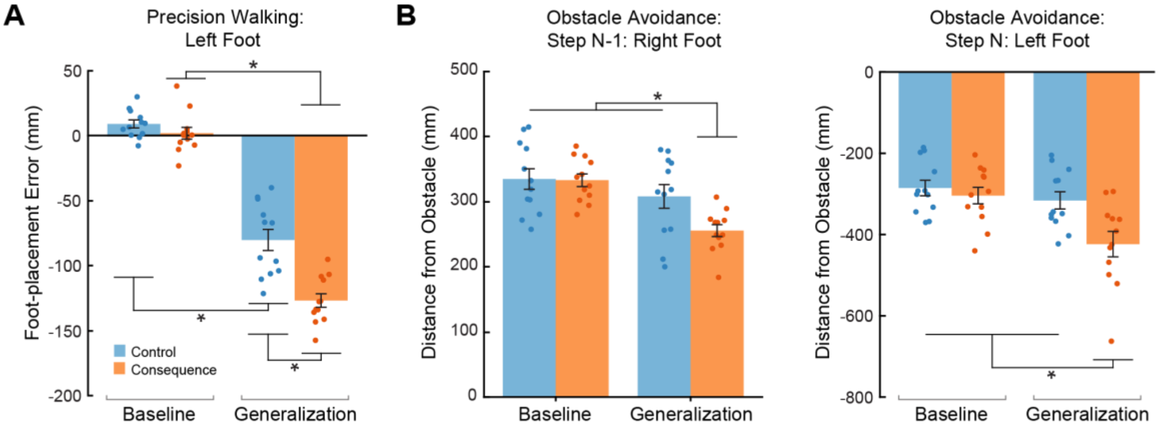

Figure 4.5 Generalization

A) Group mean ± SE foot-placement error for the baseline (mean of the last ten trials) and generalization phases during the precision walking task for the control (blue) and consequence (orange) groups. Foot-placement errors in the direction opposite to the prism shift (i.e., a negative value) indicate generalization. ***B)*** Group mean ± SE foot-placement error for the baseline (mean of the last ten trials) and generalization phases during the obstacle avoidance task for both the trailing foot (i.e., step N-1: right foot) and leading foot (i.e., step N: left foot) for the control (blue) and consequence (orange) groups. A smaller value indicates generalization for step N-1 (right foot), whereas a greater negative value reflects generalization for step N (left foot). Individual participant values are superimposed. * Indicate that values are significantly different from each other based on post hoc tests ($p < 0.05$).

For the obstacle avoidance task, we compared foot-placement deviation from the obstacle during the baseline phase (mean of last ten trials) and the generalization trial for both the trailing foot (i.e., step N-1: right foot) and leading foot (i.e., step N: left foot). For step N-1 (right foot), a smaller value reflects less deviation of the foot from the obstacle and indicates generalization of the learned mapping to the trailing right foot. We found that the consequence group demonstrated a smaller deviation of the right foot from the obstacle (i.e., a leftward shift in foot placement) during step N-1 compared to the control group (Group x Phase interaction: $F_{1,22} = 10.98$, $p = 0.003$) (Fig. 4.5B). For step N (left foot), a greater negative value reflects greater deviation of the foot from the obstacle and indicates generalization of the learned mapping to the leading left foot. We found that the consequence group demonstrated greater deviation of the leading left foot from the obstacle (Group x Phase interaction: $F_{1,22} = 16.18$, $p = 0.0006$). Taken together, a stability consequence associated with movement error increases the degree of generalization across different visually guided walking tasks.

4.4.4. A stability consequence associated with movement errors increases motor memory consolidation

To determine the effects of a stability consequence on motor memory consolidation, both groups of participants repeated the adaptation protocol one week later. We compared three measures across testing sessions: the first adaptation trial error (representing the initial recall of the mapping), early adaptation error (i.e., mean of adaptation trials 2 – 8), and rate of adaptation. Figure 4.6A illustrates group mean foot-placement error during the baseline and adaptation phases during both testing sessions for the control and consequence groups. To assess initial recall of the learned visuomotor mapping, we compared foot-placement error during the first adaptation trial across testing sessions. We found that the consequence group demonstrated greater error reduction in first adaptation trial compared to the control group (Group x Session interaction: $F_{1,22} = 18.18$, $p = 0.0003$), reflecting greater recall of the learned mapping one week later (Fig. 4.6B).

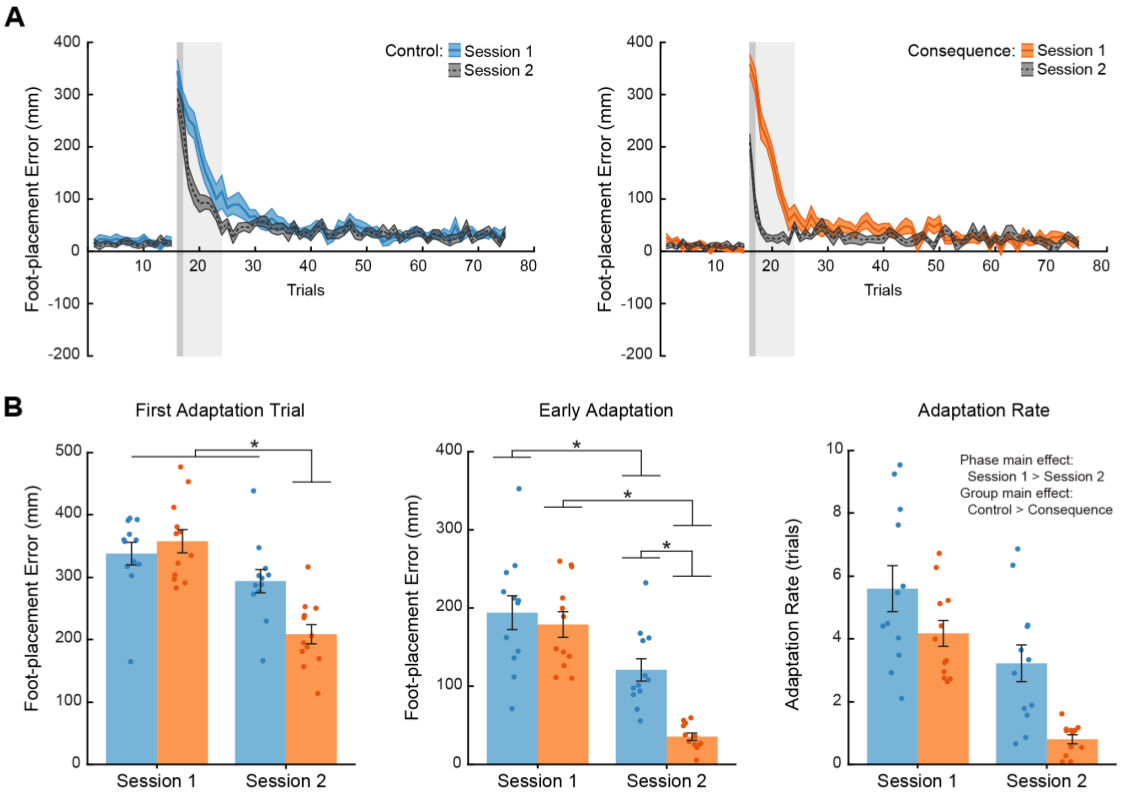

Figure 4.6 Motor memory consolidation
A) Group mean ± SE foot-placement error for all trials in the baseline and adaptation phases across testing sessions for the control (blue) and consequence (orange) groups. ***B)*** Group mean ± SE for the first adaptation trial error (dark grey shaded box), early adaptation error (light grey shaded box), and rate of adaptation across testing sessions for the control (blue) and consequence (orange) groups. One week separated testing sessions. Individual participant values are superimposed. * Indicate that values are significantly different from each other based on post hoc tests ($p < 0.05$).

A faster reduction in foot-placement error (i.e., savings) indicates that the learned mapping was consolidated. To quantify savings of the learned mapping, we compared foot-placement error during early adaptation (i.e., mean of adaptation trials 2 – 8) and the rate of adaptation across testing sessions. We found that both the control and consequence groups showed a significant reduction in foot-placement error during early adaptation (Group x Session interaction: $F_{1,22} = 7.98$, $p = 0.009$). However, the consequence group demonstrated significantly greater error reduction during the second testing session compared to the control group, reflecting greater savings one week later. Finally, we found that both the control and consequence groups demonstrate a faster rate of relearning during the second testing session (Session main effect: $F_{1,22} = 27.58$, $p = 2.86e-5$). In addition, we found that the consequence group demonstrated a faster rate of adaptation across both testing sessions (Group main effect: $F_{1,22} = 15.81$, $p = 0.0006$), though we did not detect a significant Group x Session interaction for this measure ($F_{1,22}$

= 0.82, p = 0.376). Taken together, a stability consequence associated with movement error increases initial recall and savings of a learned mapping one week later, reflective of greater motor memory consolidation.

4.5. Discussion

Learning from the consequences of our actions is imperative for safe and successful motor performance over a lifetime. To determine which behaviours to maintain, people learn to dissociate actions that give rise to desirable outcomes from those that do not. This learning process is likely driven by evolutionary pressures to hardwire specific behaviours that facilitate future performance and promote personal safety (Moore 2004). Following this reasoning, we tested the hypothesis that a stability consequence associated with movement errors would enhance sensorimotor learning. Indeed, we found that participants who experienced the stability consequence during adaptation demonstrated increased interlimb-transfer on a precision walking task and generalization to an obstacle-avoidance task. Furthermore, these participants demonstrated enhanced motor memory consolidation, reflected by greater recall and savings one week later. The differences in generalization and consolidation between groups occurs despite the fact that they initially adapt at the same rate and experience similar foot-placement errors. One possible explanation for our findings is that experiencing a physical consequence when making errors augments the value assigned to maintaining the updated internal model, which increases generalization and consolidation.

People prefer to behave in ways that maximize rewards and minimize penalties. For this reason, we assign greater value to actions that give rise to favourable outcomes compared to those that result in unpleasant consequences. We can then use this subjective value to determine which behaviours are worth pursuing in future. Rewards and punishment serve to strengthen or reinforce the association between actions and their consequences and are therefore, compelling modulators of behaviour (Thorndike 1933; Skinner 1938). For example, people tend to move faster towards stimuli that they associate with increased reward (e.g., money) (Shadmehr et al. 2019). In our study, participants experienced a slip perturbation when making stepping errors to a target during adaptation. Given that maintaining balance is a primary objective during movement, this stability consequence served as a strong deterrent against repeating such errors. As participants adapted to the prisms (i.e., updated their internal model) and became more accurate to the target, they no longer experienced the slip perturbation. Stepping accurately may act as an intrinsic reward. However, the slippery surface remained positioned next to the target and as a result, the threat of slipping persisted throughout adaptation. Thus, there may be greater value assigned to maintaining this updated internal model, as it reduces the likelihood of making contact with the slippery surface. Our findings support this interpretation: experiencing the stability consequence significantly enhanced generalization and motor memory consolidation. Interestingly, the stability consequence did not accelerate initial adaptation. We speculate that the combination of the new visuomotor mapping and the unexpected slip perturbation made it difficult for participants to immediately identify the source of their error to correct for it (Berniker and Kording 2008). This initial credit assignment problem, in combination with a potentially disorientating slip, may have reduced any immediate benefits of the stability consequence. Taken together, our results appear in conflict with previous studies showing that punishment in the form of monetary losses have little impact on motor memory retention (Abe et al. 2011; Galea et al. 2015). However, it is possible that experiencing a physical consequence, as opposed to losing money, is more effective at eliciting long-lasting memories. We designed our stability consequence to simulate slipping during walking and to serve as a functionally meaningful consequence for movement error. Thus, compared to losing money for poor performance, our manipulation may be more ecologically valid in that it is a better representation of the potential consequences associated with movement errors in everyday life.

The fear of falling associated with the slip perturbation may also contribute to our findings by altering participants emotional state during adaptation. Though we did not directly measure fear or anxiety, research shows that fear of falling, or increased postural threat, can significantly impact balance control and gait (Adkin and Carpenter 2018). Furthermore, research in humans and other animals provides compelling evidence for the role of the amygdala in forming and maintaining lasting memories associated with aversive stimuli (McGaugh 2004). Specifically, activation of the amygdala, which is reliably engaged during threat processing (LeDoux 2000), is shown to modulate memory consolidation during emotionally arousing experiences. Emotional arousal during the consolidation period is thought to strengthen a memory through the release of various stress hormones (e.g., epinephrine) and the activation of the basolateral amygdala. This is evident in fear-conditioning paradigms whereby aversive shock stimuli, or the threat of being shocked, induces long-term potentiation in the amygdala and enhances memory formation (Murty et al. 2012; Rogan et al. 1997). In contrast, lesions to the amygdala attenuate the advantageous effects of emotional arousal on memory (Mcgaugh et al. 1996). The amygdala is also implicated in fear generalization: aversive stimuli are broadly generalized to new environments. For example, tones associated with an aversive odor increase the width of auditory tuning curves of amygdala neurons and as a result, allow for better stimulus detection (Resnik and Paz 2015). Overgeneralization of negative experiences is also linked to altered activity in the amygdala in individuals with post-traumatic stress disorders (Ortiz et al. 2019). The modulation of fear responses and memory consolidation during emotionally arousing events may serve to enhance retention of threatening experiences to enable fast and accurate responses when necessary. This notion is aligned with research suggesting that our memory systems are tuned to remember survival-related information that provides some evolutionary advantage (Nairne et al. 2007). Interestingly, neuroimaging results show that reinforcement in the form of monetary losses does not engage the amygdala (Delgado et al. 2011), which may provide an additional explanation for the discrepancies between our findings and monetary-based reinforcement paradigms. Taken together, the slip perturbation may have altered emotions of fear and/or anxiety and enhanced learning through increased recruitment of brain regions engaged in threat processing.

Overall, our results demonstrate that experiencing a threatening physical consequence when making errors enhances sensorimotor learning. These findings provide intriguing implications for the development of rehabilitation interventions aimed at improving performance in individuals with neurological impairment. In particular, our results suggest that patients may benefit from rehabilitation interventions that elicit a physical consequence when making errors. Though research on this topic is scarce, studies show that split-belt treadmills can be used to exaggerate step length asymmetry in stroke patients to achieve after-effects of improved symmetry (Reisman et al. 2007a; 2009; Reisman et al. 2010). In this case, the exaggerated error serves to prompt the nervous system to correct performance. Though our slip perturbation does not necessarily exaggerate movement error, it does increase the severity of the consequences associated with inaccurate movement. As a result, a physical consequence, or the threat of being penalized, when making errors may serve to reinforce learning and facilitate rehabilitation. However, further research is warranted to determine whether and how we can safely and effectively leverage the negative physical consequences of movement error to facilitate rehabilitation.

4.6. Chapter contributions

Conceptualization, Amanda Bakkum (A.B.) and Daniel S. Marigold (D.S.M); Methodology, A.B. and D.S.M; Investigation, A.B.; Formal Analysis, A.B.; Writing – Original Draft, A.B. and D.S.M; Writing – Reviewing & Editing, A.B. and D.S.M.

Chapter 5.

General Discussion and Conclusions

“There is no real ending. It's just the place where you stop the story.”

(Frank Herbert)

5.1. Summary of thesis

Despite the necessity to maintain balance for safe and successful motor performance, experimental paradigms often overlook the effects of balance control on sensorimotor learning. This thesis provides a novel perspective on how learning during naturalistic motor behaviours that necessitate balance control might be beneficial for motor performance. Specifically, I explored how challenges to balance, or the potential consequences of falling, impact sensorimotor adaptation, generalization, and retention of motor memories formed during unconstrained, whole-body tasks.

Humans are able to produce an impressive array of complex and coordinated motor behaviours. This versatility is achieved by adapting previously learned movement patterns and applying what is learned to new situations. However, it is unclear how the necessity to maintain balance while moving influences these aspects of sensorimotor learning. In **Chapter 2**, I tested how challenging balance during sensorimotor adaptation affected generalization of learning. To do this, I encouraged four groups of participants to learn a new internal model using prisms lenses that create a new visuomotor mapping. These lenses altered the normal relationship between visual input and motor output, making their current internal model obsolete. Participants adapted to the prisms while performing either a standing-based reaching or walking task, with or without a manipulation that challenged balance. To assess generalization, participants performed a single trial of each of the other group’s tasks without the prism lenses. I found that challenging balance during both the reaching and walking tasks increases the degree to which a newly learned internal model generalized to the equivalent, non-adapted task. I also found some evidence for across-task generalization for all groups regardless of balance manipulation. In **Chapter 3**, I tested how challenging balance during sensorimotor adaptation effected motor memory retention. To do this, the same four groups of participants returned to the lab one week after initial learning and repeated the adaptation protocol performed during the first testing session. For reaching, I found that the balance-challenged group initially recalled the learned mapping, reflected by a smaller end-point error during the first adaptation trial one-week later. However, neither reaching group demonstrated faster relearning (or savings) during re-exposure to the prisms. In contrast, both walking groups demonstrated significant motor memory retention, reflected by initial recall and savings. Crucially, I found that challenging balance significantly enhanced savings during walking.

After discovering that challenges to balance might serve to enhance generalization and retention of learning, I asked how the potential consequences associated with losing balance might impact sensorimotor learning. In **Chapter 4**, I encouraged two groups of participants to adapt to a new visuomotor mapping while performing a precision walking task. Participants performed this task with or without the possibility of a stability consequence associated with movement errors. I assessed generalization during an interlimb-transfer test and an obstacle-avoidance task performed without the prism lenses. I found that experiencing a physical consequence when making errors led to increased generalization to both visually guided walking tasks. To assess consolidation, I introduced an opposite direction visuomotor mapping following initial adaptation and evaluated relearning one week later. Importantly, I found that participants who experienced the stability consequence associated with movement error demonstrated significantly greater motor memory consolidation, reflected by increased initial recall and sensorimotor savings. Taken together, the results from this thesis suggest that the necessity to maintain balance, or the consequence of falling, may increase the value assigned to maintaining an updated internal model and as a result, enhance sensorimotor learning.

5.2. Thesis limitations

There are limitations to this thesis that may hinder the scope of our conclusions. First, I assessed sensorimotor learning in a relatively small sample size, which may not be representative of the larger population. I determined this sample size based on a combination of the sample sizes used in previous research studies and statistical power analyses performed with statistical software GPower3. I calculated effect sizes based on data from previous studies in our lab (Alexander et al. 2011; Maeda et al. 2017b) for all comparisons of interest (i.e., generalization and retention measures). Based on this data, I determined that a sample size of n=12 per group would yield 80% power with an alpha level of 0.05 for all comparisons. This sample size is consistent with previous adaptation studies that typically recruit between 8 to 12 participants per group (Alexander et al. 2011; Maeda et al. 2017b; McDougle et al. 2015; Torres-Oviedo and Bastian 2012). As a result, it is unlikely that the differences identified in this thesis were detected by chance alone. Thus, it seems reasonable to use these findings to draw inferences about the larger population.

A second possible limitation to this thesis may relate to the real-life validity of the balance manipulation used in **Chapter 2** and **Chapter 3**. As most everyday tasks require balance control, the purpose of this thesis was to determine how the necessity to maintain balance affects sensorimotor learning. However, I acknowledge that standing and walking while wearing rubber inflatable hemispheres is not overly realistic. The decision to use these hemispheres was based on extensive pilot data aimed at identifying a manipulation that increased the need for balance control while also allowing participants to move freely while performing their tasks. I reasoned that the rubber hemispheres produced a similar perturbation for both the reaching and walking tasks—which allowed for across-task comparisons—and did not impair natural movement. For example, they did not restrict the ability to engage typical balance control strategies using the ankle, knee, or hip musculature. Additionally, as the rubber hemispheres are attached to the participants shoes, the direction and magnitude of the perturbation is directly associated with the participant’s own movement. As a result, this balance manipulation may resemble standing or walking across unstable terrain, including terrain with some degree of compliance (e.g., soggy grass, mud, or snow), where participants need to engage proactive and/or reactive balance control strategies to prevent falling. Overall, this manipulation was successful at challenging balance in a manner that, for the most part, requires control strategies that are similar to those experienced in real-world situations.

Another possible limitation to the studies presented in **Chapter 2** and **Chapter 3** is that I did not assess sensorimotor learning during conditions that enhance balance (i.e., conditions that reduce the degree of balance control required to perform the task). While I was able to test my hypothesis that challenging balance would improve sensorimotor learning, it is unclear whether enhancing balance during adaptation impacts learning. The reason I did not include this condition is that I was unable to reduce the need for balance control during the walking task in a manner that would not interfere with adaptation to the prism-induced visual-field-shift. One option was to allow participants to use handrails during adaptation to provide additional support during the walking task. However, these handrails might interfere with adaptation as they restrict leg movement by preventing wider steps, as well as provide environmental cues about the position of the target. Another option would be to secure participants to a bodyweight-support harness system that serves to unload the body and reduce the degree of balance control required to prevent falling. However, this too would restrict the participants movement and affect adaptation. As a result, I only assessed the effects of challenging balance on sensorimotor learning during the reaching and walking tasks. Similarly, in **Chapter 4**, I assess how the consequence of movement error affects sensorimotor learning. The results from this study demonstrate that experiencing a slip perturbation when making errors significantly enhances generalization and consolidation of learning. While these effects are robust, it is unclear whether they are a result of the additional feedback provided for performance errors or whether they are specific to experiencing the stability consequence. Thus, future work is required to determine if these findings can be replicated using other means of reinforcement. I discuss possible options for future projects in section 5.5 below.

5.3. The possible neural basis for our findings

For this thesis, I assessed how the necessity to maintain balance while moving affected sensorimotor learning. In **Chapter 2** and **Chapter 3**, participants who performed the tasks while wearing the inflatable rubber hemispheres attached to their shoes (i.e., the balance-challenged groups) required greater control over their body to maintain balance and ensure task success. In **Chapter 4**, participants required rapid reactive balance recovery during the slip perturbations to prevent a fall. Thus, the greater need for control, combined with the greater threat of falling, associated with these tasks may have increased recruitment of certain brain regions and enhanced sensorimotor learning.

Neuroimaging studies show that coordinated movements are orchestrated by a distributed network of brain activity across cortical and subcortical regions (Debaere et al. 2001). These included regions of the supplementary motor area, cingulate motor cortex, premotor cortex, primary motor cortex, and cerebellum. As tasks become more complex, brain activity across these regions increases. Likewise, research shows that challenging standing balance increases electroencephalography spectral power within certain frequencies across multiple cortical regions (Hülsdünker et al. 2015; Hülsdünker et al. 2016). As standing balance recovery becomes more challenging, perturbation-evoked cortical responses increase (Payne and Ting 2020). Brain activity also increases across several brain regions in response to a loss of balance during walking (Sipp et al. 2013). In particular, challenges to balance (e.g., standing on one leg or walking on a balance beam) increase activation in the anterior cingulate cortex (ACC). This brain region is involved in estimating the value associated with allocating control to a given task (i.e., the expected value of control) to determine if it is worth pursuing (Rangel et al. 2008; Shenhav et al. 2013; Walton et al. 2003). Moreover, the ACC plays a critical role in monitoring performance outcomes and detecting error signals to determine the degree to which internal models must be updated to obtain action goals (Kolling et al. 2016; Van Veen and Carter 2002). Taken together, challenges to balance elicit significant changes in cortical activity, which may contribute to the findings of this thesis.

Sensorimotor adaptation involves a broad network of brain regions. The cerebellum, for example, plays a critical role in sensorimotor learning such that patients with cerebellar damage demonstrate impaired adaptation and reduced generalization (Baizer et al. 1999; Martin et al. 1996a; Morton and Bastian 2004; Tseng et al. 2007). In contrast, stimulation of the cerebellum using anodal transcranial direct current stimulation (tDCS) is shown to accelerate visuomotor adaptation (Galea et al. 2011). Neuroimaging studies show that several other brain regions are also engaged during adaptation and generalization, including regions of the ACC, premotor cortex, primary motor cortex, posterior parietal cortex, prefrontal cortex, as well as the putamen and globus pallidus of the basal ganglia (Danckert et al. 2008; Della-Maggiore et al. 2015; Graydon et al. 2005; Inoue et al. 1997; Krakauer et al. 2004; Seidler et al. 2006; Shadmehr 2004). Thus, challenging balance may have enhanced generalization through increased recruitment of brain areas engaged during adaptation. Likewise, many of these regions are also involved in motor memory retention. For example, research suggests that neural activity shifts from the prefrontal regions of the cortex to the premotor, posterior parietal, and cerebellar cortical structures during motor memory consolidation (Shadmehr and Holcomb 1997). The dorsal premotor cortex—involved in action selection—may also play a role in consolidation of new motor skills in that excitatory repetitive transcranial magnetic stimulation (rTMS) of this region following training enhances retention (Boyd and Linsdell

2009). Additionally, research shows that motor memory consolidation is associated with increased neuronal activity in the cerebellum (Debas et al. 2010). The primary motor cortex is also associated with motor memory retention such that enhancing this region improves savings (Galea et al. 2011; Reis et al. 2009) while disrupting it impairs motor memory (Hadipour-Niktarash et al. 2007). Finally, patients with Parkinson's disease fail to exhibit visuomotor savings 24 hours after adaptation, suggesting the basal ganglia also plays a role in the retention of motor memories (Bédard and Sanes 2011; Leow et al. 2012; Marinelli et al. 2009). Taken together, changes in brain activity that result from balance challenges may reflect, or serve to reinforce, sensorimotor learning and as a result, enhance generalization and motor memory retention.

Finally, as with most challenges to balance, there is a greater threat of falling. This greater perceived threat may have altered participants' emotional states and enhanced sensorimotor learning through increased activation of brains regions that respond to aversive stimuli (Armony et al. 1997; Bromberg-Martin et al. 2010; Jensen et al. 2003; Mineka and Ohman 2002; Taub and Mintz 2010; Tom et al. 2007). Research suggests that emotionally arousing experiences are better remembered due to increased activation of the amygdala and the release of stress hormones that work together to modulate memory consolidation (McGaugh 2004). Correspondingly, research shows that fear-conditioning using aversive shock stimuli can induce long-term potentiation in the amygdala and enhance memory formation (Rogan et al. 1997). Even the threat of being shocked activates the amygdala and facilitates memory retention (Murty et al. 2012). However, the advantageous effects of emotional arousal on retention diminish with lesions to the amygdala (Mcgaugh et al. 1996). Fear generalization, or the generalization of negative experiences, is also related with amygdala function. For example, overgeneralization of fear responses is associated with altered activation in the amygdala of patients with various anxiety disorders (Ortiz et al. 2019). Interestingly, research also provides evidence for the role of the basal ganglia in processing threatening events (Siciliano et al. 2018). For example, aversive stimuli such as electrical shocks are shown to reliably activate the ventral striatum (Sorg and Kalivas 1991). Moreover, activity in the ventral striatum of the basal ganglia increases in anticipation of unpleasant cutaneous electrical stimulation (Jensen et al. 2003). Thus, the threat of falling associated with the balance-challenged tasks (**Chapter 2 and 3**) and the stability consequence (**Chapter 4**) may have increased activation of brains regions engaged in threat processing and further contributed to the enhanced generalization and motor memory retention.

Taken together, the greater need for control and the increased threat of falling associated with our tasks may have increased recruitment of brain regions that facilitate sensorimotor learning. To help disentangle these effects of challenging balance, future studies could investigate how changes in brain activity in our tasks relates to generalization and motor memory retention.

5.4. Implications for neurorehabilitation

Adaptation is important for rehabilitation. It provides some degree of flexibility during movement and can therefore, facilitate recovery after injury or disease. While the focus of this thesis is on sensorimotor learning in young and healthy adults, the results have broad clinical applications. Specifically, this thesis provides a unique perspective on how learning during unconstrained tasks that challenge balance or elicit a physical consequence following movement errors benefits sensorimotor learning. These findings provide intriguing implications for the development of rehabilitation interventions aimed at promoting long-term performance improvements in people with neurological impairments.

The results from **Chapter 2** and **Chapter 3** show that challenging balance can increase generalization and motor memory retention, respectively. Additionally, **Chapter 4** shows that experiencing a slip perturbation when making errors significantly enhances sensorimotor learning. How might these conditions be exploited for rehabilitation purposes? Taken together, these results suggest that individuals with neurological impairment may benefit from rehabilitation interventions that engage the whole body and associate undesirable movements with threatening consequences. Though adaptation research on this topic is limited, studies show that perturbation-based training in stroke patients elicits lasting improvements to reactive balance control (Mansfield et al. 2017; 2018). Stroke patients also demonstrate improved balance performance following push-and-pull perturbation training aimed at destabilizing balance to elicit postural reflexes (Marigold et al. 2005). Likewise, slip-perturbation training in community-dwelling older adults can reduce fall risk (Bhatt et al. 2006; Bhatt et al. 2012; Pai et al. 2014). Research suggests that such perturbation training elicits whole-body responses that engage complex neural circuitry through propriospinal pathways and supraspinal input and as a result, may help facilitate rehabilitation (Marigold and Misiaszek 2009). Propriospinal pathways, for example, connect cervical and lumbar central pattern generators that are thought to be involved in the neural control of walking balance (Misiaszek 2006). Input from supraspinal or cortical centers can then be used to facilitate context-specific responses, such as how to resist a slip perturbation. The additional threat associated with falling may also serve to reinforce learning and enhance memory consolidation through increased recruitment of brain regions that respond to threatening situations, such as the amygdala (McGaugh 2004). Taken together, these findings advocate for the rehabilitation protocols that engage the whole body and associate movement errors with physical consequences. However, further research is warranted to determine how we can safely and effectively leverage these conditions to facilitate rehabilitation.

The findings of this thesis may also have implications for sensorimotor learning in patients with cerebellar damage. The cerebellum plays a critical role in regulating smooth and timely movement and as a result, damage to this region can give rise to a variety of movement disorders (e.g., gait ataxia) (Kandel et al. 2013). Several studies demonstrate that cerebellar damage can impair adaptation (Martin et al. 1996a; Morton and Bastian 2006; Tseng et al. 2007). Furthermore, disrupting the cerebellum using transcranial direct current stimulation (tDCS) can impair motor memory retention (Herzfeld et al. 2014). However, recent research shows that cerebellar patients can learn a reaching task using binary feedback, such as a pleasant tone to signal improvements in reaching trajectory or an unpleasant tone to signal increased errors (Therrien et al. 2016; Therrien et al. 2020). These findings suggest that cerebellar damage does not interfere with reinforcement learning. The results from **Chapter 4** show that experiencing a physical consequence when making errors enhances generalization and motor memory consolidation. While I explored these affects during sensorimotor adaptation, research demonstrates that rewards and punishment are also effective during motor skill learning (Abe et al. 2011; Steel et al. 2016). Furthermore, a recent neuroimaging study demonstrates that functional connectivity between the premotor cortex and the cerebellum increased after training with reward but decreased after training with punishment (Steel et al. 2019). Instead, punishment elicited increased connectivity between the premotor cortex and medial temporal lobe. These findings suggest that reinforcement using punishment may be less reliant on the cerebellum circuitry. Interestingly, research shows that the threat of punishment (e.g., an electrical shock) activates the medial temporal lobe via the amygdala and enhances memory retention (Murty et al. 2012). Taken together, reinforcement through punishment, physical or otherwise, may increase learning and retention in cerebellar patients by recruiting brain regions that respond to threatening stimuli and rely less on the cerebellum. However, further research is warranted to determine if punishment learning can indeed bypass the cerebellar circuitry and whether this is an effective means to promote learning in cerebellar patients.

5.5. Future directions

This thesis demonstrates the potential performance benefits of learning during unconstrained motor behaviours that necessitate balance control. However, it is still unclear whether or how these benefits generalize to other types of learning (e.g., reinforcement learning), different tasks (e.g., split-belt treadmill walking), or to patient populations (i.e., stroke patients). Additionally, the nature of the balance challenging tasks and the slip perturbation makes it difficult to disentangle what factors are driving these findings. Therefore, one pertinent question remains: what is the underlying mechanism responsible for the beneficial effects of challenging balance on sensorimotor learning? While it is likely that the greater need for control, combined with the increased threat of falling, are contributing factors, the results of this thesis cannot directly answer this question.

To start answering this question, it would be useful to assess learning in a way that dissociates the greater need for control from the fear of falling associated with the balance-challenging tasks. For example, the results from **Chapter 2** show that challenging balance during adaptation increases the degree of generalization to untrained movements for reaching and walking tasks. One possible explanation for the results of **Chapter 2** was that, when balance is challenged, the effects of dynamic coupling are more pronounced. As a result, the nervous system requires a more comprehensive and accurate model to control the body. Because a more comprehensive model is less tailored to a specific task, it may be more generalizable. A possible alternative (and perhaps complimentary) explanation for these findings may be that challenging balance shifts adaptation towards goal-level commands, where the main objective is to control the body’s COM to prevent falling. In this case, adaptation of goal-level control, as opposed to more detailed low-level control, may be more generalizable because the ability to maintain balance is critical. One possible future direction of this work is to assess whether and how a greater need to control different body segments affects sensorimotor learning to determine if the results of this thesis are driven exclusively by the need to control balance. To test this idea without challenging balance, several groups of participants could adapt to a new visuomotor mapping while performing tasks that differ in terms of the amount of control required to execute them. For example, tasks could require increasing levels of coordination across multiple degrees of freedom (e.g., different muscles and body segments) which in turn, increases the effects of dynamic coupling during movement. It is also possible to reduce the effects of dynamic coupling using various bracing or casting methods to limit the degrees of freedom involved during movement. This work will provide insight into whether or not a comprehensive model is a more generalizable model and if this concept provides a suitable explanation for the findings in **Chapter 2**.

Another option to disentangle the effects of challenging balance and the slip perturbation is to assess adaptation during tasks that increase postural threat but do not physically manipulate balance. Studies show that standing on a raised platform can evoke fear responses and impact motor behaviour (Adkin and Carpenter 2018). Thus, one option is to have participants adapt to a new mapping while standing or walking on a platform that is raised to different heights that represent increasing levels of postural threat. Another interesting approach would be to use a virtual environment to simulate postural threat during learning. Virtual reality provides a unique medium to study complex motor behaviours without sacrificing experimental control (Levac et al. 2019). Furthermore, research suggests that virtual environments evoke similar behavioural responses to the real world. For example, the threat of being stabbed in the hand in a virtual environment elicits motor cortex activation patterns that would be expected if the real hand was threated and the person tried to avoid harm (González-Franco et al. 2014). Research also shows that virtual environments can facilitate physical rehabilitation (Sveistrup 2004). For example, virtual environments are effective at improving both upper and lower limb function in chronic stroke patients (Lee et al. 2019). Thus, virtual reality technology provides another possible avenue to explore how the results of this thesis can be used to facilitate rehabilitation.

To fully understand the implications of this thesis, it is also important to determine if these findings can be replicated using other means of reinforcement. For example, the results from **Chapter 4** show that experiencing a physical consequence when making errors significantly enhances generalization and motor memory consolidation. As previously mentioned, one limitation of this project is that I only compared performance to a control group. Thus, I cannot exclude the possibility that learning was improved as a result of the additional feedback provided for performance errors. Furthermore, it is unclear if reward-based reinforcement would have been equally effective at enhancing learning, as shown in other studies (Galea et al. 2015). Thus, one possible future project could be to determine if other forms of feedback elicit similar performance improvements compared to the stability consequence group. For example, instead of placing a slippery surface next to the target to penalize stepping errors, there could be a touch-sensitive platform that triggers an unpleasant audible tone on contact to signal error. Alternatively, feedback in the form of monetary rewards and losses can be used to reinforce learning. Another option is to determine if eliciting any physical consequence for movements errors promotes learning during adaptation. Extensive human and animal research provides compelling evidence for the effects of aversive stimuli (e.g., an electric shock) on learning and memory retention (McGaugh 2004). Thus, instead of slipping, performance errors could be penalized using a mild shock stimulation or something similar to induce a physical consequence when making errors. Taken together, these studies will provide insight into what aspects of experiencing the stability consequence when making errors enhance performance and whether or not the robust effects are exclusive to experiencing the slip perturbation when making movement errors.

5.6. Concluding remarks

In conclusion, this thesis provides evidence for the potential performance benefits associated with learning during unconstrained, whole-body tasks and demonstrates the significance of studying sensorimotor learning during naturalistic motor behaviours. These findings provide insight into how the nervous system learns to control movement in real-world settings. Furthermore, the results from this thesis have intriguing implications for the design of rehabilitation interventions aimed at promoting long-lasting performance benefits in people with neurological impairments. Further research is warranted to determine whether and how to safely and effectively leverage these results to facilitate rehabilitation.

References

Abe M, Schambra H, Wassermann EM, Luckenbaugh D, Schweighofer N, Cohen LG. Reward improves long-term retention of a motor memory through induction of offline memory gains. Curr Biol 21: 557-562 (2011).

Abeele S, Bock O. Transfer of sensorimotor adaptation between different movement categories. Exp Brain Res 148: 128-132 (2003).

Abram SJ, Selinger JC, Donelan JM. Energy optimization is a major objective in the real-time control of step width in human walking. J Biomech 91: 85-91 (2019).

Adkin AL, Carpenter MG. New insights on emotional contributions to human postural control. Front Neurol 9: 1-8 (2018).

Adkin AL, Frank JS, Carpenter MG, Peysar GW. Fear of falling modifies anticipatory postural control. Exp Brain Res 143: 160-170 (2002).

Adkin AL, Frank JS, Carpenter MG, Peysar GW. Postural control is scaled to level of postural threat. Gait Posture 12: 87-93 (2000).

Alexander MS et al. Effects of age-related macular degeneration and ambient light on curb negotiation. Optom Vis Sci 91: 975-989 (2014).

Alexander MS, Flodin BWG, Marigold DS. Changes in task parameters during walking prism adaptation influence the subsequent generalization pattern. J Neurophysiol 109: 2495-2504 (2013).

Alexander MS, Flodin BWG, Marigold DS. Prism adaptation and generalization during visually guided locomotor tasks. J Neurophysiol 106: 860-871 (2011).

Alhussein L, Hosseini EA, Nguyen KP, Smith MA, Joiner WM. Dissociating effects of error size, training duration, and amount of adaptation on the ability to retain motor memories. J Neurophysiol 122: 2027-2042 (2019).

Alvarez P, Squire LR. Memory consolidation and the medial temporal lobe: A simple network model. Proc Natl Acad Sci USA 91: 7041-7045 (1994).

Armony JL, Servan-Schreiber D, Romanski LM, Cohen JD, LeDoux JE. Stimulus generalization of fear responses: Effects of auditory cortex lesions in a computational model and in rats. Cereb Cortex 7: 157-165 (1997).

Baizer JS, Kralj-Hans I, Glickstein M. Cerebellar lesions and prism adaptation in macaque monkeys. J Neurophysiol 81: 1960-1965 (1999).

Bakkum A, Donelan JM, Marigold DS. Challenging balance during sensorimotor adaptation increases generalization. J Neurophysiol 123: 1342–1354 (2020).

Bakkum A, Gunn SM, Marigold DS. How aging affects visuomotor adaptation and retention in a precision walking paradigm. *Sci Rep* 1-8 (2021).

Balitsky Thompson AK, Henriques DYP. Visuomotor adaptation and intermanual transfer under different viewing conditions. Exp Brain Res 202: 543-552 (2010).

Bastian AJ. Understanding sensorimotor adaptation and learning for rehabilitation. Curr Opin Neurol 21: 628-633 (2008).

Bauby CE, Kuo AD. Active control of lateral balance in human walking. J Biomech 33: 1433-1440 (2000).

Bédard P, Sanes JN. Basal ganglia-dependent processes in recalling learned visual-motor adaptations. Exp Brain Res 209: 385-393 (2011).

Berniker M, Kording K. Estimating the sources of motor errors for adaptation and generalization. Nat Neurosci 11: 1454-1461 (2008).

Berniker M, Mirzaei H, Kording KP. The effects of training breadth on motor generalization. J Neurophysiol 112: 2791-2798 (2014).

Bernstein N. The coordination and regulation of movements. (Pergamon Press, 1967).

Bhatt T, Wang E, Pai YC. Retention of adaptive control over varying intervals: Prevention of slip-induced backward balance loss during gait. J Neurophysiol 95: 2913–2922 (2006).

Bhatt T, Yang F, Pai YC. Learning to resist gait-slip falls: Long-term retention in community-dwelling older adults. Arch. Phys. Med Rehabil 93: 557–564 (2012).

Bock O, Schneider S, Bloomberg J. Conditions for interference versus facilitation during sequential sensorimotor adaptation. Exp Brain Res 138: 359-365 (2001).

Boyd LA, Linsdell MA. Excitatory repetitive transcranial magnetic stimulation to left dorsal premotor cortex enhances motor consolidation of new skills. BMC Neurosci 10: (2009).

Brainard DH. The psychophysics toolbox. Spat Vis 10: 433-436, 1997.

Brashers-Krug T, Shadmehr R, Bizzi E. Consolidation in human motor memory. Nature 382: 252-255 (1996).

Bromberg-Martin ES, Matsumoto M, Hikosaka O. Dopamine in motivational control: Rewarding, aversive, and alerting. Neuron 68: 815-834 (2010).

Brown LA, Frank JS. Postural compensations to the potential consequences of instability: Kinematics. Gait Posture 6: 89-97 (1997).

Buch ER, Young S, Contreras-Vidal JL. Visuomotor adaptation in normal aging. Learn Mem 10: 55-63 (2003).

Buckley JG, Heasley K, Scally A, Elliott DB. The effects of blurring vision on medio-lateral balance during stepping up or down to a new level in the elderly. Gait Posture 22: 146-153 (2005).

Buurke TJW, Liu C, Park S, den Otter R, Finley JM. Maintaining sagittal plane balance compromises frontal plane balance during reactive stepping in people post-stroke. Clin Biomech 80: 105135 (2020).

Caithness G et al. Failure to consolidate the consolidation theory of learning for sensorimotor adaptation tasks. J Neurosci 24: 8662-8671 (2004).

Carpenter MG, Frank JS, Silcher CP, Peysar GW. The influence of postural threat on the control of upright stance. Exp Brain Res 138: 210-218 (2001).

Carroll TJ, Poh E, De Rugy A. New visuomotor maps are immediately available to the opposite limb. J Neurophysiol 111: 2232-2243 (2014).

Cham R, Redfern MS. Changes in gait when anticipating slippery floors. Gait Posture 15: 159-171 (2002).

Cham R, Redfern MS. Lower extremity corrective reactions to slip events. J Biomech 34: 1439-1445 (2001).

Chamberlin ME, Fulwider BD, Sanders SL, Medeiros JM. Does fear of falling influence spatial and temporal gait parameters in elderly persons beyond changes associated with normal aging? Journals Gerontol - Ser A Biol Sci Med Sci 60: 1163:1167 (2005).

Choi JT, Bastian, AJ. Adaptation reveals independent control networks for human walking. Nat Neurosci 10: 1055-1062 (2007).

Classen J, Liepert J, Wise SP, Hallett M, Cohen LG. Rapid plasticity of human cortical movement representation induced by practice. J Neurophysiol 79: 1117-1123 (1998).

Cordo P, Nashner L. Properties of postural adjustments associated with rapid arm movements. J Neurophysiol 47: 287-302 (1982).

Cothros N, Wong JD, Gribble PL. Are there distinct neural representations of object and limb dynamics? Exp Brain Res 173: 689-697 (2006).

Criscimagna-Hemminger SE, Bastian AJ, Shadmehr R. Size of error affects cerebellar contributions to motor learning. J Neurophysiol 103: 2275-2284 (2010).

Criscimagna-Hemminger SE, Shadmehr R. Consolidation patterns of human motor memory. J Neurosci 28: 9610-9618 (2008).

Danckert J, Ferber S, Goodale MA. Direct effects of prismatic lenses on visuomotor control: An event-related functional MRI study. Eur J Neurosci 28: 1696-1704 (2008).

Day KA, Leech KA, Roemmich RT, Bastian AJ. Accelerating locomotor savings in learning: Compressing four training days to one. J Neurophysiol 119: 2100-2113 (2018).

Day KA, Roemmich RT, Taylor JA, Bastian AJ. Visuomotor learning generalizes around the intended movement. eNeuro 3: 1-12, (2016).

Debaere F, Swinnen SP, Béatse E, Sunaert S, Van Hecke P, Duysens J. Brain areas involved in interlimb coordination: A distributed network. NeuroImage 14: 947-958 (2001).

Debas K et al. Brain plasticity related to the consolidation of motor sequence learning and motor adaptation. Proc Natl Acad Sci USA 107: 17839-17844 (2010).

Delbaere K, Sturnieks DL, Crombez G, Lord SR. Concern about falls elicits changes in gait parameters in conditions of postural threat in older people. Journals Gerontol - Ser A Biol Sci Med Sci 64: 237-242 (2009).

Della-Maggiore V, Landi SM, Villalta JI. Sensorimotor adaptation: Multiple forms of plasticity in motor circuits. Neuroscientist 21: 109-125 (2015).

Dhawale AK, Smith MA, Olveczky BP. The role of variability in motor learning. Annu Rev Neurosci 40: 479-98 (2017).

Diedrichsen J, White O, Newman D, Lally N. Use-dependent and error-based learning of motor behaviors. J Neurosci 30: 5159-5166 (2010).

Domínguez-Zamora FJ Marigold DS. Motor cost affects the decision of when to shift gaze for guiding movement. J Neurophysiol 122: 378-388 (2019).

Donelan JM, Kram R, Kuo AD. Mechanical and metabolic determinants of the preferred step width in human walking. Proc R Soc B Biol Sci 268: 1985-1992 (2001).

Donelan JM, Shipman DW, Kram R, Kuo AD. Mechanical and metabolic requirements for active lateral stabilization in human walking. J Biomech 37: 827-835 (2004).

Doyon J, Penhune V, Ungerleider LG. Distinct contribution of the cortico-striatal and cortico-cerebellar systems to motor skill learning. Neuropsychologia 41: 252-262 (2003).

Dudai Y. The neurobiology of consolidations, or, how stable is the engram? Ann. Rev Psychol 55: 51-86 (2004).

Eng JJ, Winter DA, Patla AE. Intralimb dynamics simplify reactive control strategies during locomotion. J Biomech 30: 581-588 (1997).

Fercho K, Baugh L. It's too quick to blame myself-the effects of fast and slow rates of change on credit assignment during object lifting. Front Hum Neurosci 8: 554 (2014).

Galea JM, Mallia E, Rothwell J, Diedrichsen J. The dissociable effects of punishment and reward on motor learning. Nat Neurosci 18: 597-602 (2015).

Galea JM, Vazquez A, Pasricha N, Orban De Xivry JJ, Celnik P. Dissociating the roles of the cerebellum and motor cortex during adaptive learning: The motor cortex retains what the cerebellum learns. Cereb Cortex 21: 1761-1770 (2011).

Gallivan JP, Chapman CS, Wolpert DM, Flanagan JR. Decision-making in sensorimotor control. Nat Rev Neurosci 19: 519-534 (2018).

Gandolfo F, Mussa-Ivaldi FA, Bizzi E. Motor learning by field approximation. Proc Natl Acad Sci 93: 3843-3846 (1996).

Ghahramani Z, Wolpert DM, Jordan MI. Generalization to local remappings of the visuomotor coordinate transformation. J Neurosci 16: 7085-7096 (1996).

Gibo TL, Criscimagna-Hemminger SE, Okamura AM, Bastian AJ. Cerebellar motor learning: Are environment dynamics more important than error size? J Neurophysiol 110: 322-333 (2013).

Goedert KM, Willingham DB. Patterns of interference in sequence learning and prism adaptation inconsistent with the consolidation hypothesis. Learn Mem 9: 279-292 (2002).

González-Franco M, Peck TC, Rodríguez-Fornells A, Slater M. A threat to a virtual hand elicits motor cortex activation. Exp Brain Res 232: 875-887 (2014).

Graydon FX, Friston KJ, Thomas CG, Brooks VB, Menon RS. Learning-related fMRI activation associated with a rotational visuo-motor transformation. Cogn Brain Res 22: 373-383 (2005).

Green DA, Bunday KL, Bowen J, Carter T, Bronstein AM. What does autonomic arousal tell us about locomotor learning? Neurosi 170: 42-53 (2010).

Gribble PL, Mullin LI, Cothros N, Mattar A. Role of cocontraction in arm movement accuracy. J Neurophysiol 89: 2396-2405 (2003).

Gribble PL, Ostry DJ. Compensation for interaction torques during single- and multijoint limb movement. J Neurophysiol 82: 2310-2326 (1999).

Hadipour-Niktarash A, Lee CK, Desmond JE, Shadmehr R. Impairment of retention but not acquisition of a visuomotor skill through time-dependent disruption of primary motor cortex. J Neurosci 27: 13413-13419 (2007).

Haith AM, Huberdeau DM, Krakauer JW. The influence of movement preparation time on the expression of visuomotor learning and savings. J Neurosci 35: 5109-5117 (2015).

Haith AM, Krakauer JW. Model-based and model-free mechanisms of human motor learning. Adv Exp Med Biol 782: 1-21 (2013).

Handsfield GG, Meyer CH, Hart JM, Abel MF, Blemker SS. Relationships of 35 lower limb 658 muscles to height and body mass quantified using MRI. J Biomech 47: 631-638 (2014).

Hay JC, Pick HL. Visual and proprioceptive adaptation to optical displacement of the visual stimulus. J Exp Psychol 71: 150-158 (1966).

Heasley K, Buckley JG, Scally A, Twigg P, Elliott DB. Falls in older people: Effects of age and blurring vision on the dynamics of stepping. Investig Ophthalmol Vis Sci 46: 3584-3588 (2005).

Heasley K, Buckley JG, Scally A, Twigg P, Elliott DB. Stepping up to a new level: Effects of blurring vision in the elderly. Investig Ophthalmol Vis Sci 45: 2122-2128 (2004).

Heiden TL, Sanderson DJ, Inglis JT, Siegmund GP. Adaptations to normal human gait on potentially slippery surfaces: The effects of awareness and prior slip experience. Gait Posture 24: 237-246 (2006).

Herzfeld DJ et al. Contributions of the cerebellum and the motor cortex to acquisition and retention of motor memories. Neuroimage 98: 147-158 (2014).

Herzfeld DJ, Vaswani PA, Marko MK, Shadmehr R. A memory of errors in sensorimotor learning. Science 345: 1349-1353 (2014).

Heuer H, Hegele M. Adaptation to visuomotor rotations in younger and older adults. Psychol Aging 23: 190-202 (2008).

Heuer H, Hegele M. Generalization of implicit and explicit adjustments to visuomotor rotations across the workspace in younger and older adults. J Neurophysiol 104: 2078-2085 (2011).

Hinder MR, Walk L, Woolley DG, Riek S, Carson RG. The interference effects of non-rotated versus counter-rotated trials in visuomotor adaptation. Exp Brain Res 180: 629-640 (2007).

Hirashima M, Nozaki D. Distinct motor plans form and retrieve distinct motor memories for physically identical movements. Curr Biol 22: 432-436 (2012).

Horak FB, Nashner LM. Central programming of postural movements: Adaptation to altered support-surface configurations. J Neurophysiol 55: 1369-1381 (1986).

Horak FB. Postural orientation and equilibrium: What do we need to know about neural control of balance to prevent falls? Age and Ageing 35: 7-11 (2006).

Howard IS, Ford C, Cangelosi A, Franklin DW. Active lead-in variability affects motor memory formation and slows motor learning. Sci Rep 7: 1-12 (2017).

Howard IS, Wolpert DM, Franklin DW. The effect of contextual cues on the encoding of motor memories. J Neurophysiol 109: 2632-2644 (2013).

Huang VS, Haith A, Mazzoni P, Krakauer JW. Rethinking motor learning and savings in adaptation paradigms: model-free memory for successful actions combines with internal models. Neuron 70: 787-801 (2011).

Huberdeau DM, Haith AM, Krakauer JW. Formation of a long-term memory for visuomotor adaptation following only a few trials of practice. J Neurophysiol 114: 969-977 (2015).

Hülsdünker T, Mierau A, Neeb C, Kleinöder H, Strüder HK. Cortical processes associated with continuous balance control as revealed by EEG spectral power. Neurosci Lett 592: 1-5 (2015).

Hülsdünker T, Mierau A, Strüder HK. Higher balance task demands are associated with an increase in individual alpha peak frequency. Front Hum Neurosci 9:695, 2016.

Hunter LC, Hendrix EC, Dean JC. The cost of walking downhill: Is the preferred gait energetically optimal? J Biomech 43: 1910-1915 (2010).

Hussain SJ, Morton SM. Perturbation schedule does not alter retention of a locomotor adaptation across days. J Neurophysiol 111: 2414-2422 (2014).

Inoue K et al. Activity in the parietal area during visuomotor learning with optical rotation. Neuroreport 8: 3979-3983 (1997).

Izawa J, Criscimagna-Hemminger SE, Shadmehr R. Cerebellar contributions to reach adaptation and learning sensory consequences of action. J Neurosci 32: 4230-4239 (2012).

Izawa J, Shadmehr R. Learning from sensory and reward prediction errors during motor adaptation. PLoS Comput Biol 7: e1002012 (2011).

Jensen J, McIntosh AR, Crawley AP, Mikulis DJ, Remington G, Kapur S. Direct activation of the ventral striatum in anticipation of aversive stimuli. Neuron 40: 1251-1257 (2003).

Joshi M, Patel P, Bhatt T. Reactive balance to unanticipated trip-like perturbations: A treadmill-based study examining effect of aging and stroke on fall risk. Int Biomech 1-13 (2018)

Kagerer FA, Contreras-Vidal JL, Stelmach GE. Adaptation to gradual as compared with sudden visuo-motor distortions. Exp Brain Res 115: 557-561 (1997).

Kahnt T, Tobler PN. Reward, value, and salience. Decision Neuroscience: An Integrative Perspective, 109–120 (Elsevier Inc., 2017).

Kandel ER, Schwart, JH, Jessell, TM, Siegelbaum SA, Hudspeth AJ. Principles of neural science. (New York: McGraw-Hill, 2013).

Ketcham CJ, Dounskaia NV, Stelmach GE. Multijoint movement control: The importance of interactive torques. Prog Brain Res 143: 207-218 (2004).

Kitago T, Krakauer JW. Motor learning principles for neurorehabilitation. Handb Clin Neurol 110: 93-103 (2013).

Klassen J, Tong C, Flanagan JR. Learning and recall of incremental kinematic and dynamic sensorimotor transformations. Exp Brain Res 164: 250–259 (2005).

Kleiner M, Brainard D, Pelli D, Ingling A, Murray R, Broussard C. What's new in Psychtoolbox-3. Perception 36: 1-16 (2007).

Kluzik JA, Diedrichsen J, Shadmehr R, Bastian AJ. Reach adaptation: What determines whether we learn an internal model of the tool or adapt the model of our arm? J Neurophysiol 100: 1455-1464 (2008).

Kolling N et al. Value, search, persistence and model updating in anterior cingulate cortex. Nat Neurosci 19: 1280-1285 (2016).

König M, Epro G, Seeley J, Potthast W, Karamanidis K. Retention and generalizability of balance recovery response adaptations from trip perturbations across the adult life span. J Neurophysiol 122: 1884-1893 (2019).

Krakauer JW et al. Differential cortical and subcortical activations in learning rotations and gains for reaching: A PET study. J Neurophysiol 91: 924-933 (2004).

Krakauer JW, Ghez C, Ghilardi MF. Adaptation to visuomotor transformations: Consolidation, interference, and forgetting. J Neurosci 25: 473-478 (2005).

Krakauer JW, Ghilardi M-FF, Ghez C. Independent learning of internal models for kinematic and dynamic control of reaching. Nat Neurosci 2: 1026-1031 (1999).

Krakauer JW, Hadjiosif AM, Xu J, Wong AL, Haith AM. Motor learning. Compr Physiol 9: 613-663 (2019).

Krakauer JW, Mazzoni P. Human sensorimotor learning: Adaptation, skill, and beyond. Curr Opin Neurobiol 21: 636644 (2011).

Krakauer JW, Pine ZM, Ghilardi MF, Ghez C. Learning of visuomotor transformations for vectorial planning of reaching trajectories. J Neurosci 20: 8916-8924 (2000).

Krakauer JW, Shadmehr R. Consolidation of motor memory. Trends Neurosci 29: 58-64 (2006).

Krakauer JW. Motor learning and consolidation: The case of visuomotor rotation. Learning 629: 405-421 (2009).

Krishnan C, Ranganathan R, Tetarbe M. Interlimb transfer of motor skill learning during walking: No evidence for asymmetric transfer. Gait Posture 56: 24-30 (2017).

Kuo AD. Stabilization of lateral motion in passive dynamic walking. Int J Rob Res 18: 917-930 (1999).

Landi SM, Baguear F, Della-Maggiore V. One week of motor adaptation induces structural changes in primary motor cortex that predict long-term memory one year later. J Neurosci 31: 11808-11813 (2011).

Lee HS, Park YJ, Park SW. The effects of virtual reality training on function in chronic stroke patients: A systematic review and meta-analysis. Biomed Res Int 2019: (2019).

Leech KA, Roemmich RT, Bastian AJ. Creating flexible motor memories in human walking. Sci Rep 8: (2018).

Leech KA, Roemmich RT. Independent voluntary correction and savings in locomotor learning. J Exp Biol 221 (2018).

Lei Y, Johnson MJ, Wang J. Separation of visual and motor workspaces during targeted reaching results in limited generalization of visuomotor adaptation. Neurosci Lett 541: 243-247 (2013).

Leow L-A, de Rugy A, Marinovic W, Riek S, Carroll TJ. Savings for visuomotor adaptation require prior history of error, not prior repetition of successful actions. J Neurophysiol 116: 1603-1614 (2016).

Leow LA, Loftus AM, Hammond GR. Impaired savings despite intact initial learning of motor adaptation in Parkinson’s disease. Exp Brain Res 218: 295-304 (2012).

Lerner G et al. The origins of anterograde interference in visuomotor adaptation. Cereb Cortex 30: 4000-4010 (2020).

Levac DE, Huber ME, Sternad D. Learning and transfer of complex motor skills in virtual reality: A perspective review. J Neuroeng Rehabil 16: 1-15 (2019).

Liu C, De Macedo L. Finley JM. Conservation of reactive stabilization strategies in the presence of step length asymmetries during walking. Front Hum Neurosci 12: 251 (2018).

Mackey DC, Robinovitch SN. Mechanisms underlying age-related differences in ability to recover balance with the ankle strategy. Gait Posture 23: 59-68 (2006).

Maeda RS, McGee SE, Marigold DS. Consolidation of visuomotor adaptation memory with consistent and noisy environments. J Neurophysiol 117: 316-326 (2017b).

Maeda RS, McGee SE, Marigold DS. Long-term retention and reconsolidation of a visuomotor memory. Neurobiol Learn Mem 155: 313-321 (2018).

Maeda RS, O'Connor SM, Donelan JM, Marigold DS. Foot placement relies on state estimation during visually guided walking. J Neurophysiol 117: 480-491 (2017a).

Maki BE. Gait changes in older adults: Predictors of falls or indicators of fear? J Am Geriatr Soc 45: 313-320 (1997).

Malfait N, Gribble PL, Ostry DJ. Generalization of motor learning based on multiple field exposures and local adaptation. J Neurophysiol 93: 3327-3338 (2005).

Malone LA, Vasudevan EVL, Bastian AJ. Motor adaptation training for faster relearning. J Neurosci 31: 15136-15143 (2011).

Manista GC, Ahmed AA. Stability limits modulate whole-body motor learning. J Neurophysiol 107: 1952-1961 (2012).

Mansfield A et al. Does perturbation training prevent falls after discharge from stroke rehabilitation? a prospective cohort study with historical control. J Stroke Cerebrovasc Dis 26: 2174-2180 (2017).

Mansfield A et al. Does perturbation-based balance training prevent falls among individuals with chronic stroke? A randomised controlled trial. BMJ Open 8: 21510 (2018).

Marigold DS et al. Exercise leads to faster postural reflexes, improved balance and mobility, and fewer falls in older persons with chronic stroke. J Am Geriatr Soc 53: 416-423 (2005).

Marigold DS, Bethune AJ, Patla AE. Role of the unperturbed limb and arms in the reactive recovery response to an unexpected slip during locomotion. J Neurophysiol 89: 1727-1737 (2003).

Marigold DS, Eng JJ. Altered timing of postural reflexes contributes to falling in persons with chronic stroke. Exp Brain Res 171: 459-468 (2006).

Marigold DS, Misiaszek JE. Whole-body responses: Neural control and implications for rehabilitation and fall prevention. Neuroscientist 15: 36-46 (2009).

Marigold DS, Patla AE. Strategies for dynamic stability during locomotion on a slippery surface: Effects of prior experience and knowledge. J Neurophysiol 88, 339-353 (2002).

Marinelli L et al. Learning and consolidation of visuo-motor adaptation in Parkinson’s disease. Park Relat Disord 15: 6-11 (2009).

Martin TA, Keating JG, Goodkin HP, Bastian AJ, Thach WT. Throwing while looking through prisms I. Focal olivocerebellar lesions impair adaptation. Brain 119: 1183-1198 (1996a).

Martin TA, Keating JG, Goodkin HP, Bastian AJ, Thach WT. Throwing while looking through prisms II. Specificity and storage of multiple gaze-throw calibrations. Brain 119: 1199-1211 (1996b).

Mattar AAG, Ostry DJ. Generalization of dynamics learning across changes in movement amplitude. J Neurophysiol 104: 426-438 (2010).

Mattar AAG, Ostry DJ. Modifiability of generalization in dynamics learning. J Neurophysiol 98: 3321-3329 (2007).

Mawase F, Shmuelof L, Bar-Haim S, Karniel A. Savings in locomotor adaptation explained by changes in learning parameters following initial adaptation. J Neurophysiol 111: 1444-1454 (2014).

Mazzoni P, Krakauer JW. An implicit plan overrides an explicit strategy during visuomotor adaptation. J Neurosci 26: 3642-3645 (2006).

McDougle SD, Bond KM, Taylor JA. Explicit and implicit processes constitute the fast and slow processes of sensorimotor learning. J Neurosci 35: 9568-9579 (2015).

McDougle SD, Bond KM, Taylor JA. Implications of plan-based generalization in sensorimotor adaptation. J Neurophysiol 118: 383-393 (2017).

Mcgaugh JL, Cahill L, Roozendaal B. Involvement of the amygdala in memory storage: Interaction with other brain systems. Proc Natl Acad Sci USA 93: 13508-13514 (1996).

McGaugh JL. The amygdala modulates the consolidation of memories of emotionally arousing experiences. Annu Rev Neurosci 27: 1-28 (2004).

McGeer T. Passive Dynamic Walking. Int J Rob Res 9: 62-82 (1990).

Mcgonigle BO, Flook J. Long-term retention of single and multistate prismatic adaptation by humans. Nature 272: 364-366 (1978).

McGowan K, Gunn SM, Vorobeychik G, Marigold DS. Short-term motor learning and retention during visually guided walking in persons with multiple sclerosis. Neurorehabil. Neural Repair 31: 648-656 (2017).

Miall RC, Jenkinson N, Kulkarni K. Adaptation to rotated visual feedback: A re-examination of motor interference. Exp Brain Res 154: 201-210 (2004).

Michel C, Vernet P, Courtine G, Ballay Y, Pozzo T. Asymmetrical after-effects of prism adaptation during goal oriented locomotion. Exp Brain Res 185: 259-268 (2008).

Mineka S, Ohman A. Phobias and preparedness: the selective, automatic, and encapsulated nature of fear. Biol Psychiatry 52: 927-37 (2002).

Misiaszek, JE. Neural control of walking balance: IF falling THEN react ELSE continue. Exerc Sport Sci Rev 34: 128-134 (2006).

Moore BR. The evolution of learning. Biol Rev 79: 301-335 (2004).

Morehead JR, Qasim SE, Crossley MJ, Ivry R. Savings upon re-aiming in visuomotor adaptation. J Neurosci 35: 14386-14396 (2015).

Morton SM, Bastian AJ. Cerebellar contributions to locomotor adaptations during splitbelt treadmill walking. J Neurosci 26: 9107-9116 (2006).

Morton SM, Bastian AJ. Prism adaptation during walking generalizes to reaching and requires the cerebellum. J Neurophysiol 92: 2497-2509 (2004).

Morton SM, Lang C. Bastian AJ. Inter- and intra-limb generalization of adaptation during catching. Exp Brain Res 141: 438-445 (2001).

Murty VP, LaBar KS, Adcock RA. Threat of punishment motivates memory encoding via amygdala, not midbrain, interactions with the medial temporal lobe. J Neurosci 32: 8969-8976 (2012).

Mussa-Ivaldi FA. Modular features of motor control and learning. Curr Opin Neurobiol 9: 713-717 (1999).

Nairne JS, Pandeirada JNS, Thompson SR. Adaptive memory: The comparative value of Survival processing. Psychol Sci 19: 176-180 (2008).

Nairne JS, Pandeirada JNS. Adaptive memory: The evolutionary significance of survival processing. Perspect Psychol Sci 11: 496-511 (2016).

Nairne JS, Thompson SR, Pandeirada JNS. Adaptive memory: Survival processing enhances retention. J Exp Psychol Learn Mem Cogn 33: 263-273 (2007).

Nguyen KP et al. The 24-h savings of adaptation to novel movement dynamics initially reflects the recall of previous performance. J Neurophysiol 122: 933-946 (2019).

Nott CR, Zajac FE, Neptune RR, Kautz SA. All joint moments significantly contribute to trunk angular acceleration. J. Biomech. 43: 2648-2652 (2010).

O’Connor CM, Thorpe SK, O’Malley MJ, Vaughan CL. Automatic detection of gait events using kinematic data. Gait Posture 25: 469-474 (2007).

O’Connor SM, Kuo AD. Direction-dependent control of balance during walking and standing. J Neurophysiol 102: 1411-1419 (2009).

Oates AR, Frank JS, Patla AE. Control of dynamic stability during adaptation to gait termination on a slippery surface. Exp Brain Res 201: 47-57 (2010).

Ogawa T, Kawashima N, Ogata T, Nakazawa K. Limited transfer of newly acquired movement patterns across walking and running in humans. PLoS One 7: e46349 (2012).

Ortiz S. et al. Anterior cingulate cortex and ventral hippocampal inputs to the basolateral amygdala selectively control generalized fear. J Neurosci 39: 6526-6539 (2019).

Pai YC, Yang F, Bhatt T, Wang E. Learning from laboratory-induced falling: Long-term motor retention among older adults. Age 36: 1367-1376 (2014).

Patla AE. Strategies for dynamic stability during adaptive human locomotion. IEEE Engineering in Medicine and Biology Magazine 22: 48-52 (2003).

Payne AM, Ting LH. Worse balance is associated with larger perturbation-evoked cortical responses in healthy young adults. Gait Posture 80: 324-330 (2020).

Perry J. Gait Analysis: Normal and pathological function. (Thorofare, NJ: Slack, 1992).

Petitet P, O'Reilly JX, O'Shea J. Towards a neuro-computational account of prism adaptation. Neuropsychologia 115: 188-203 (2018).

Poggio T, Bizzi E. Generalization in vision and motor control. Nature 431: 768-774 (2004).

Rangel A, Camerer C, Montague PR. A framework for studying the neurobiology of value-based decision making. Nat Rev Neurosci 9: 545-556 (2008).

Redding GM, Rossetti Y, Wallace B. Applications of prism adaptation: A tutorial in theory and method. Neurosci Biobehav Rev 29: 431-444 (2005).

Redding GM, Wallace B. Adaptive spatial alignment and strategic perceptual-motor control. J Exp Psychol Hum Percept Perform 22: 379-394 (1996).

Redding GM, Wallace B. Components of prism adaptation in terminal and concurrent exposure: organization of the eye-hand coordination loop. Percept Psychophys 44: 59-68 (1988).

Redding GM, Wallace B. Strategic calibration and spatial alignment: A model from prism adaptation. J Mot Behav 34: 126-138 (2002).

Reis J et al. Noninvasive cortical stimulation enhances motor skill acquisition over multiple days through an effect on consolidation. Proc Natl Acad Sci USA 106: 1590-1595 (2009).

Reisman DS, McLean H, Bastian AJ. Split-belt treadmill training poststroke: A case study. J Neurol Phys Ther 34: 202-207 (2010).

Reisman DS, Wityk R, Silver K, Bastian AJ. Locomotor adaptation on a split-belt treadmill can improve walking symmetry post-stroke. Brain 130: 1861-1872 (2007).

Reisman DS, Wityk R, Silver K, Bastian AJ. Split-belt treadmill adaptation transfers to overground walking in persons poststroke. Neurorehabil Neural Repair 23: 735-744 (2009).

Resnik J, Paz R. Fear generalization in the primate amygdala. Nat Neurosci 18: 188-190 (2015).

Reynolds RF, Bronstein AM. The Moving Platform Aftereffect: Limited Generalization of a Locomotor Adaptation. J Neurophysiol 91: 92-100 (2004).

Richardson AG et al. Disruption of primary motor cortex before learning impairs memory of movement dynamics. J Neurosci 26: 12466-12470 (2006).

Roemmich RT, Bastian AJ. Two ways to save a newly learned motor pattern. J Neurophysiol 113: 3519-3530 (2015).

Rogan MT, Staubli UV, LeDoux JE. Fear conditioning induces associative long-term potentiation in the amygdala. Nature 390: 604-607 (1997).

Sainburg RL, Wang J. Interlimb transfer of visuomotor rotations: Independence of direction and final position information. Exp Brain Res 145: 437-447 (2002).

Savin DN, Morton SM. Asymmetric generalization between the arm and leg following prism-induced visuomotor adaptation. Exp Brain Res 186: 175-182 (2008).

Schechtman E, Laufer O, Paz R. Negative valence widens generalization of learning. J Neurosci 30: 10460-10464 (2010).

Schieber MH. Muscular production of individuated finger movements: The roles of extrinsic finger muscles. J Neurosci 15: 284-297 (1995).

Schillings AM, van Wezel BMH, Mulder T, Duysens J. Muscular responses and movement strategies during stumbling over obstacles. J Neurophysiol 83: 2093-2102 (2000).

Schlerf JE, Xu J, Klemfuss NM, Griffiths TL, Ivry RB. Individuals with cerebellar degeneration show similar adaptation deficits with large and small visuomotor errors. J Neurophysiol 109: 1164-1173 (2013).

Seidler R, Noll D, Chintalapati P. Bilateral basal ganglia activation associated with sensorimotor adaptation. Exp Brain Res 175: 544-555 (2006).

Seidler RD, Bloomberg JJ, Stelmach GE. Patterns of transfer of adaptation among body segments. Behav Brain Res 122: 145-157 (2001).

Seidler RD. Multiple motor learning experiences enhance motor adaptability. J Cogn Neurosci 16: 65-73 (2004).

Selinger JC, O'Connor SM, Wong JD, Donelan JM. Humans can continuously optimize energetic cost during walking. Curr Biol 25: 2452-2456 (2015).

Shadmehr R Moussavi ZM. Spatial generalization from learning dynamics of reaching movements. J Neurosci 20: 7807-15 (2000).

Shadmehr R, Brashers-Krug T. Functional stages in the formation of human long-term motor memory. J Neurosci 17: 409-419 (1997).

Shadmehr R, Holcomb HH. Neural correlates of motor memory consolidation. Science 277: 821-825 (1997).

Shadmehr R, Krakauer JW. A computational neuroanatomy for motor control. Exp Brain Res 185: 359-381 (2008).

Shadmehr R, Mussa-Ivaldi FA. Adaptive representation of dynamics during learning of a motor task. J Neurosci 14: 3208-3224 (1994).

Shadmehr R, Smith MA, Krakauer JW. Error correction, sensory prediction, and adaptation in motor control. Annu Rev Neurosci 33: 89-108 (2010).

Shadmehr R, Wise SP. The computational neurobiology of reaching and pointing. A foundation for motor learning. (Cambridge: The MIT Press, 2005).

Shadmehr R. Generalization as a behavioral window to the neural mechanisms of learning internal models. Hum Mov Sci 23: 543-568 (2004).

Shenhav A, Botvinick MM, Cohen JD. The expected value of control: An integrative theory of anterior cingulate cortex function. Neuron 79: 217-240 (2013).

Shimada H, Obuchi S, Furuna T, Suzuki T. New intervention program for preventing falls among frail elderly people. Am J Phys Med Rehabil 83: 493-499 (2004).

Shirota C, Simon AM, Kuiken TA. Trip recovery strategies following perturbations of variable duration. J Biomech 47: 2679-2684 (2014).

Shmuelof L et al. Overcoming motor 'forgetting' through reinforcement of learned actions. J Neurosci 32: 14617-14621 (2012).

Siciliano CA, Mills F, Tye KM. Double threat in striatal dopamine signaling. Nat Neurosci 21: 1296-1297 (2018).

Sipp AR, Gwin JT, Makeig S, Ferris DP. Loss of balance during balance beam walking elicits a multifocal theta band electrocortical response. J Neurophysiol 110: 2050-2060 (2013).

Skinner B. The behavior of organisms: an experimental analysis. (New York: Appleton-Century., 1938).

Smith MA, Ghazizadeh A, Shadmehr R. Interacting adaptive processes with different timescales underlie short-term motor learning. PLoS Biol 4: e179 (2006).

Sorg BA, Kalivas PW. Effects of cocaine and footshock stress on extracellular dopamine levels in the ventral striatum. Brain Res 559: 29-36 (1991).

Spampinato D, Celnik P. Multiple motor learning processes in humans: defining their neurophysiological bases. Neuroscientist (2020)

Squire LR. Memory and the hippocampuss: A synthesis from findings with rats, monkeys, and humans. Psychol Rev 99: 195-231 (1992).

Steel A, Silson EH, Stagg CJ, Baker CI. Differential impact of reward and punishment on functional connectivity after skill learning. Neuroimage 189: 95-105 (2019).

Steel A, Silson EH, Stagg CJ, Baker CI. The impact of reward and punishment on skill learning depends on task demands. Sci Rep 6: 1-9 (2016).

Sveistrup H. Motor rehabilitation using virtual reality. J Neuroeng Rehabil 1: 1-8 (2004).

Swinnen SP. Intermanual coordination: From behavioural principles to neural-network interactions. Nat Rev Neurosci 9: 348-359 (2002).

Synofzik M, Lindner A, Thier P. The cerebellum updates predictions about the visual consequences of one’s behavior. Curr Biol 18: 814-818 (2008).

Taub AH, Mintz M. Amygdala conditioning modulates sensory input to the cerebellum. Neurobiol Learn Mem 94: 521-529 (2010).

Taylor JA, Ivry RB. Flexible cognitive strategies during motor learning. PLoS Comput Biol 7: e1001096 (2011).

Taylor JA, Krakauer JW, Ivry RB. Explicit and implicit contributions to learning in a sensorimotor adaptation task. J Neurosci 34: 3023-3032 (2014).

Therrien AS, Statton MA, Bastian AJ. Reinforcement signaling can be used to reduce elements of cerebellar reaching ataxia. The Cerebellum 1-12 (2020)

Therrien AS, Wolpert DM, Bastian AJ. Effective reinforcement learning following cerebellar damage requires a balance between exploration and motor noise. Brain 139: 101-114 (2016).

Thorndike E. A proof of the law and effect. Science 77: 173-175 (1933).

Thoroughman KA, Shadmehr R. Learning of action through adaptive combination of motor primitives. Nature 407: 742-747 (2000).

Tom SM, Fox CR, Trepel C, Poldrack RA. The neural basis of loss aversion in decision-making under risk. Science 315: 515-518 (2007).

Torres-Oviedo G, Bastian AJ. Natural error patterns enable transfer of motor learning to novel contexts. J Neurophysiol 107: 346-356 (2012).

Trommershäuser J, Maloney L, Landy M. Statistical decision theory and trade-offs in the control of motor response. Spa Vis 16: 255-275 (2003).

Tseng YW, Diedrichsen J, Krakauer JW, Shadmehr R, Bastian AJ. Sensory prediction errors drive cerebellum-dependent adaptation of reaching. J Neurophysiol 98: 54-62 (2007).

van Beers RJ, Baraduc P, Wolpert DM. Role of uncertainty in sensorimotor control. Philos Trans R Soc B Biol Sci 357: 1137-1145 (2002).

van Dam LCJ, Hawellek DJ, Ernst MO. Switching between visuomotor mappings: Learning absolute mappings or relative shifts. J Vis 13: 1-12 (2013).

Van Veen V, Carter CS. The anterior cingulate as a conflict monitor: FMRI and ERP studies. Physiol Behav 77: 477-482 (2002).

Wallman J, Fuchs AF. Saccadic gain modification: Visual error drives motor adaptation. J Neurophysiol 80: 2405-2416 (1998).

Walton ME, Bannerman DM, Alterescu K, Rushworth MFS. Functional specialization within medial frontal cortex of the anterior cingulate for evaluating effort-related decisions. J Neurosci 23: 6475-6479 (2003).

Wang J, Sainburg RL. Interlimb transfer of visuomotor rotations depends on handedness. Exp Brain Res 175: 223-230 (2006b).

Wang J, Sainburg RL. Adaptation to visuomotor rotations remaps movement vectors, not final positions. J Neurosci 25: 4024-4030 (2005).

Wang J, Sainburg RL. Interlimb transfer of visuomotor rotations depends on handedness. Exp Brain Res 175: 223-230 (2006b)

Wang J, Sainburg RL. Limitations in interlimb transfer of visuomotor rotations. Exp. Brain Res. 155: 1-8 (2004).

Wang J, Sainburg RL. Mechanisms underlying interlimb transfer of visuomotor rotations. Exp Brain Res 149: 520-526 (2003).

Wang J, Sainburg RL. The symmetry of interlimb transfer depends on workspace locations. Exp Brain Res 170: 464-471, 2006a.

Wang J. A dissociation between visual and motor workspace inhibits generalization of visuomotor adaptation across the limbs. Exp Brain Res 187: 483-490 (2008).

Welch RB, Bridgeman B, Anand S, Browman KE. Alternating prism exposure causes dual adaptation and generalization to a novel displacement. Percept Psychophys 54: 195-204 (1993).

Wigmore V, Tong C, Flanagan JR. Visuomotor rotations of varying size and direction compete for a single internal model in motor working memory. Exp Psychol Hum Percept Perform 28: 447-457 (2002).

Wilke C, Synofzik M, Lindner A. Sensorimotor recalibration depends on attribution of sensory prediction errors to internal causes. PLoS One 8: (2013).

Winter D. Human balance and posture control during standing and walking. Gait Posture 3: 193-214 (1995).

Winter DA, Patla AE, Frank JS. Assessment of balance control in humans. Med Prog Technol 16: 31-51 (1990).

Wolpert DM, Diedrichsen J, Flanagan JR. Principles of sensorimotor learning. Nat Rev Neurosci 12: 739-751 (2011).

Wolpert DM, Flanagan JR. Computations underlying sensorimotor learning. Curr Opin Neurobiol 37: 7-11 (2016).

Wolpert DM, Ghahramani Z, Flanagan JR. Perspectives and problems in motor learning. Trends Cogn Sci 5: 487-494 (2001).

Wolpert DM, Ghahramani Z. Computational principles of movement neuroscience. Nat Neurosci 3: 1212-1217 (2000).

Wong, JD, Donelan JM. Principles of energetics and stability in human locomotion. Handb Humanoid Robot 1-18 (2010)

Wu HG, Miyamoto YR, Castro LNG, Ölveczky BP, Smith MA. Temporal structure of motor variability is dynamically regulated and predicts motor learning ability. Nat Neurosci 17: 312-321 (2014).

Yamamoto K, Hoffman DS, Strick PL. Rapid and long-lasting plasticity of input-output mapping. J Neurophysiol 96: 2797–2801 (2006).

Yeo SH, Wolpert DM, Franklin DW. Coordinate representations for interference reduction in motor learning. PLoS One 10: 1-14 (2015).

Yoon T, Jaleel A, Ahmed AA, Shadmehr R. Saccade vigor and the subjective economic value of visual stimuli. J Neurophysiol 123: 2161-2172 (2020).

Yu J, Ackland DC, Pandy MG. Shoulder muscle function depends on elbow joint position: An illustration of dynamic coupling in the upper limb. J Biomech 44: 1859-1868 (2011).

Zajac FE. Muscle coordination of movement: A perspective. J Biomech 26: 109-124 (1993).

Zarrugh MY, Todd FN, Ralston HJ. Optimization of energy expenditure during level walking. Eur. J. Appl. Physiol. Occup Physiol 33: 293-306 (1974).

Zatsiorsky VM, Prilutsky BI. Biomechanics of skeletal muscles. (Human Kinetics, 2012).