VARIABILITY OF PRACTICE AND ITS APPLICATION TO

LOCOMOTOR ADAPTATION

by

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DISSERTATION ABSTRACT

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Asymmetric gait, or a difference in functioning between legs during human locomotion, is a health concern that can lead to secondary complications such as chronic musculoskeletal injury or a more sedentary lifestyle. Restoration of gait symmetry requires a gait adaptation, or a change in the way that an individual walks. Further knowledge of how to best promote a gait adaptation could lead to the creation of future rehabilitative protocols geared towards restoration of symmetric gait. To address this, a variable practice paradigm was implemented in able-bodied individuals walking asymmetrically on a split-belt treadmill. Individuals were assigned into one of three practice groups (from least variable to most: serial, random blocked, random) and walked on the treadmill for 720 strides of motor skill acquisition according to their given paradigm. They were asked to return 24 hours later and were given one of two tests for motor learning: retention or transfer. Three-dimensional kinematic and kinetic data were collected throughout the protocol and used to analyze walking performance between the three practice groups. Results indicated that random blocked practice resulted in the best retention and transfer of mediolateral balance control variability, while serial practice had the highest variability on the transfer test. It was further demonstrated that this paradigm resulted in a unique mechanical strategy implemented by each practice group that further

describes the role of variable practice in gait adaptation: random practice during acquisition, random blocked during retention, and serial during transfer. A principal component analysis showed that variable practice results in the adoption of specific coordinative structuring of joint and segmental kinematics. These structures were different across practice groups during the acquisition and retention phases. While it was generally hypothesized that random practice, which induces the highest amount of error during acquisition, would result in the best retention and transfer of the adapted gait pattern, this practice group did not perform as well as expected on the measured outcomes. Random blocked practice, on the other hand, may provide the optimal level of variability to best facilitate a gait adaptation.

This dissertation includes previously published and unpublished co-authored material.

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TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

CHAPTER I

INTRODUCTION

Background and Significance

Individuals with musculoskeletal injuries such as unilateral lower-limb

amputation, or neurologic injuries such as hemiparetic stroke often ambulate with an

asymmetric gait. This form of locomotion is characterized by a difference in mechanical

walking parameters between the two limbs. For example, people with unilateral trans-

tibial amputation exhibit changes in lower-limb joint kinetics compared to able-bodied

walkers, including a greater distribution of body weight on the unaffected limb (Bamberg

et al. 2010; Powers et al. 1998). Researchers have also noted changes in lower-limb

kinematics, such as a more extended hip and knee during stance (Bateni and Olney 2002;

Sanderson and Martin 1997). These biomechanical adaptations often result in an altered

spatiotemporal gait strategy, where a slower preferred walking velocity, reduced stride

length, and shorter amount of time spent on the affected limb during stance are

observable (Powers et al. 1998; Sanderson and Martin 1997).

One potential problem with walking with adaptations such as these is that it

requires individuals to expend more metabolic energy compared to those who walk with

a symmetric gait (Herr and Grabowski 2011; Hsu et al. 2006; Platts et al. 2006).

Additional physical complications can arise as well, including osteoarthritis and chronic

low-back pain (Devan et al. 2012). The combination of these two factors can lead to an

overall avoidance of walking whenever possible, and these individuals may not receive

the recommended amount of physical activity needed to maintain health and quality of

life (Legro et al. 2001). For example, the increased likelihood of a sedentary lifestyle

1

leads to a greater risk in amputee populations of cardiovascular disease compared to able-bodied individuals (Naschitz and Lenger 2008), and additional social and mental challenges (Deans et al. 2008). Hence, asymmetric gait is a public health concern that can have a large detrimental impact on an individual's quality of life.

To address this concern, researchers have developed a number of new devices and rehabilitative protocols to at least partially restore gait symmetry in populations with gait deficiencies. In those with lower-limb amputation, powered ankle-foot prostheses have been developed to mimic an intact ankle-foot complex by delivering power in place of lost ankle musculature. This restoration of power reduces the metabolic cost of walking in those with unilateral trans-tibial amputation to that of a healthy gait (Herr and Grabowski 2011). For those with stroke, many therapeutic techniques such as orthoses (Mayr et al. 2007), functional electrical stimulation (Kesar et al. 2011), and rhythmic auditory stimulation (Thaut et al. 2007) have all been shown to be effective in restoring gait symmetry to varying degrees. These devices and protocols continue to be refined, making for a promising future in the world of gait rehabilitation, yet they are still largely new and experimental in nature.

When developing or enhancing a gait rehabilitation technique, it is necessary to determine its long-term effects, because evidence suggests that the means in which a novel gait pattern is introduced ultimately impacts how a person adapts to it. One reason for this is that the human central nervous system (CNS) uses a flexible, multi-layered control strategy to coordinate walking parameters in a changing environmental context such as uneven terrain or when a new prosthetic foot is introduced. At the spinal cord, the basic locomotor rhythm is sustained during walking through coordinated firing of central

pattern generators (Andersson and Grillner 1983; Takakusaki 2013). Fine adjustments to

that rhythm are made in higher-order brain centers. For example, in cortical regions the

premotor and supplementary motor areas generate motor programs for walking based on

sensory information integrated in the posterior parietal and vestibular cortices (Massion

1992; Takakusaki 2013). Arguably, the most important control area for gait adaptation is

the cerebellum, which predicts sensory feedback during walking and weighs it against

actual incoming sensory information. If a discrepancy between the two exists, the

cerebellum then corrects for it by updating a forward model that adjusts postural muscle

tone and the basic locomotor rhythm set by spinal central pattern generators (Bastian

2008; Miall and Wolpert 1996; Middleton and Strick 2000). Information about these

discrepancies, also known as sensory prediction errors, is also relayed to the cortical

planning areas for updating of the motor command (Diedrichsen et al. 2010; Miall and

Wolpert 1996). In total, the cerebellum provides individuals with the ability to adapt their

gait pattern according to sensory feedback (Tseng et al. 2007).

It is also possible that the type of error experienced drives how the cerebellum

adapts a gait pattern. Experimentally, researchers have tested this through asymmetric

split-belt treadmill walking (SBW), a task where the two belts of a split-belt treadmill are

driven at different velocities. Early asymmetric SBW research has described these

adjustments as predictive adaptations, as it was noted that when a person is given a novel

walking asymmetry, movement parameters such as interlimb coordination, step length,

and double support time continuously change over time, even when belt velocities do not

(Dietz et al. 1994; Morton and Bastian 2006; Reisman et al. 2005). These observations

are indicative of a feed-forward control mechanism. Since individuals with cerebellar

damage are unable to adapt these parameters over time, it is further evident that the cerebellum is responsible for controlling these predictive adjustments (Morton and Bastian 2006).

Since the early experimental asymmetric SBW studies, additional research has revealed the ability to apply this paradigm in a rehabilitative setting for those with hemiparetic stroke. First, Reisman et al. (2007) noted that individuals with stroke are capable of making predictive gait adjustments such as altering step length and double support time, indicating that only a fully intact cerebellum (and not necessarily damages cortical areas) is necessary to make predictive gait adjustments. Then, this group later demonstrated that when the paretic limb is driven faster than the other during a bout of asymmetric SBW, a transient effect of improved overground spatiotemporal symmetry is observable (Reisman et al. 2010; Reisman et al. 2013). In addition, other groups have reported improvements in post-stroke joint kinetic symmetry (Lauziere et al. 2014). Thus, asymmetric SBW can be used in two different ways. In one way, fundamental questions about gait adaptation can be answered by having able-bodied individuals walk asymmetrically, and noting how gait parameters are adjusted based on the exposure to a novel gait. This process can then be used to create rehabilitation protocols for clinical populations, the second purpose of asymmetric SBW.

In order to fine-tune rehabilitation protocols, more fundamental work needs to be done to further clarify the relationship between sensory prediction errors and locomotor output. In a recent study, Torres-Oviedo and Bastian (2012) found that the size of sensory prediction errors experienced during a bout of asymmetric SBW influences how gait is adapted. In another set of studies, one practice group was given a sudden training

paradigm, where subjects were immediately given a 2:1 asymmetry (where one belt was moving twice as fast as the other) and continued walking at that asymmetry throughout the practice session. Hence, this group experienced one large sensory prediction error. Another group had one treadmill belt gradually accelerated from a 1:1 belt velocity ratio to the 2:1 asymmetry over the course of the practice session, thereby experiencing small sensory prediction errors as the belt acceleration occurred. It was found that the gradual introduction of asymmetry resulted in improved retention and transfer of limb endpoint control (Sawers and Hahn 2013), transfer of frontal plane balance control (Sawers et al. 2013a), and decreased the cognitive demand during practice (Sawers et al. 2013b) compared to sudden training. Further, Criscimagna-Hemminger et al. (2010) have proposed that the difference in effects on motor learning between large and small errors may be due to the engagement of different neural pathways within the cerebellum. While small errors seem to improve retention performance of a given task, large errors improve transfer, possibly indicating a difference in how the cerebellum updates the forward model based on error size.

From these studies, it has been postulated that the minimization of error size experienced during practice positively impacts retention and transfer of a novel gait pattern. However, it may also be possible that in addition to error size, error variance may also have an impact. It has long been demonstrated that a more variable ordering of environmental conditions, termed contextual interference (Shea and Morgan 1979), has led to improved motor learning outcomes across a wide variety of motor skills. Lee and Magill (1983) have mentioned that one reason for the improved motor learning observed following a practice protocol using contextual interference is that a variable change in

environmental demands causes unpredictability that diminishes the cognitive aspect of motor planning. Therefore, individuals have to learn a skill by performing it and learning from sensory prediction errors, instead of cognitively predicting the required motor parameters. It has also been recently suggested that variable practice engages a trial-and-error learning mechanism that allows learners to explore the space of potential solutions to improve motor performance (Wu et al. 2014). In the case of the series of studies performed by Sawers and colleagues, it is possible that the gradual training group received a small dose of contextual interference during acquisition (Figure 1.1), where the increasing belt velocity of one limb made the practice session more unpredictable. This may have allowed for those individuals to undergo the trial-and-error learning process to some degree.

Contextual interference can be thought of in terms of a spectrum, ranging from low to high (Figure 1.1). On the low end of the spectrum is constant practice, or repeated practice trials of a motor skill with no change in practice conditions. On the high end is random practice, or repeated trials of practice with entirely random variations in practice conditions from trial to trial (Magill 2011). Many factors determine the most optimal level of contextual interference during motor skill acquisition, including the type of task and the skill level of the learner (Guadagnoli and Lee 2004). In the case of locomotor adaptation, it is still unknown where this optimal level is. The gradual training group in the series of studies by Sawers and colleagues experienced a lower amount of contextual interference (Figure 1.1), and therefore the connection between higher amounts of error variance and gait adaptation is still largely unknown. While Torres-Oviedo and Bastian (2012) used a variable practice paradigm, their study, like the Sawers studies, was

designed so that one treadmill belt was always faster than the other. This may limit the contextual interference effect to some degree, since another group has suggested that when adapting a gait pattern, individuals assign different roles to each limb. If one limb is always moving faster than the other, then that limb will consistently use a different mechanical strategy (Ogawa et al. 2014). This allows for some practice predictability in that subjects can predict which limb would be the faster moving one and apply the appropriate mechanical parameters to that limb. This could diminish their ability to utilize the trial-and-error learning process that is engaged through contextual interference. If it was unpredictable which limb would be moving faster than the other, then subjects would not be able to predict the necessary parameters.
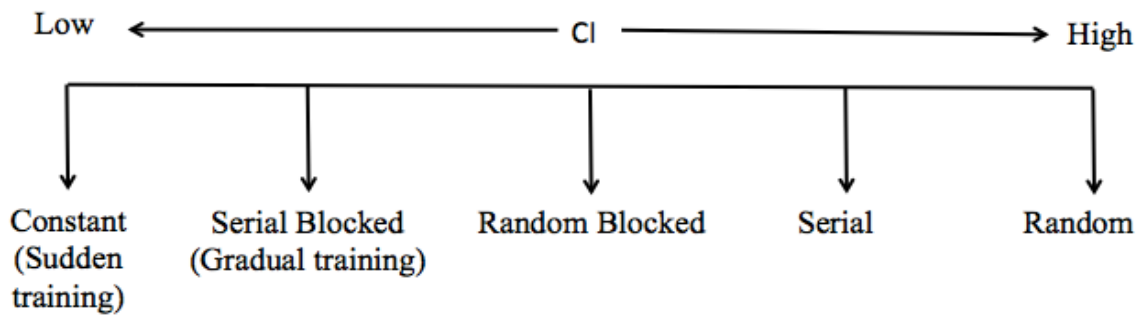
Fig 1.1. Continuum of contextual interference. On the left side, constant practice represents the least amount of contextual interference, as the practice environment does not change. On the right, random practice has the most contextual interference, as the practice environment changes randomly from trial-to-trial. Previous work has investigated the effects of the low end of the continuum (sudden training, gradual training), but the higher end's effects are still unknown.

One challenge facing the advancement of knowledge in gait adaptation is that measurement of walking performance is often ambiguous. In many sport or rehabilitative settings, motor learning of a skill can be measured by tracking performance over time,

such as the amount of putts made during a golf practice session. In the case of walking there is not as clear of a task goal. One way that gait adaptation can be explained behaviorally is that the CNS may attempt to minimize certain costs of walking, such as energy expenditure, balance, or pain (Bastian 2008; Emken et al. 2007; Todorov 2004). Therefore, if a sensory prediction error causes an increase in a specific cost, then a person's gait may be adapted in a way that specifically returns that cost to a minimal state. However, it is still unknown where, mechanically, that adaptation occurs given a certain gait perturbation.

If knowledge of where and when a person adapts their gait when learning a novel locomotor pattern, then a connection can be made between fundamental locomotor adaptation studies and clinical application. This has recently become an even greater possibility through development of inertial measurement units (IMUs). These devices are often equipped with three-dimensional accelerometers, rate gyroscopes, and magnetometers, thereby providing up to nine dimensions of kinematic data in a low-cost, portable format. Research has recently demonstrated that measurement of segmental kinematics with these devices is almost as accurate as an optical motion capture system (Bolink et al. 2016; Esser et al. 2012). Hence, newly developed devices and practice protocols that rehabilitate gait can be implemented in clinics or other locations where access to high-end motion capture equipment is not always possible.

General and Specific Aims

The overall goal of this study was to determine whether a variable practice paradigm could increase retention and transfer of an asymmetric gait pattern in able-

bodied individuals, and provide a basis of application to future gait rehabilitation protocols. The anticipated outcomes of this project would benefit those with gait deficiencies, clinicians, and the greater scientific community. First, knowledge of the effects of contextual interference on locomotor adaptation would help to fine-tune the current understanding behind the role of sensory prediction errors in gait adaptation. This would contribute to the scientific body of work on human gait. Second, this work would give a full description of the mechanical outcomes following adaptation to a variable practice paradigm, possibly detailing any beneficial or adverse gait mechanics that are adopted following a bout of asymmetric SBW. This would provide a framework for long-term prospective studies using an asymmetric SBW paradigm. Finally, this dissertation will seek to perform an analysis of gait adaptation kinematics, giving more information to researchers and clinicians about what specifically should be measured during gait adaptation.

This general goal will be addressed through four specific aims. In Aim 1, a new method for automation of a split-belt treadmill is detailed, as development of this methodology was essential to progress into the later Aims of this study. In Aims 2, 3, and 4, a variable practice paradigm was given to able-bodied individuals during an acute bout of asymmetric SBW. Three-dimensional motion capture data were collected, and different elements of this data set were used to address three different purposes in Aims 2, 3, and 4. These Aims were as follows:

Specific Aim 1. To detail and test a new methodology that allows for full automation of treadmill belt velocities. The process behind automated treadmill control was defined,

and its performance was evaluated during asymmetric SBW to determine its feasibility of use in the subsequent Aims.

Specific Aim 2. To test the effects of variable practice on the retention and transfer of frontal plane balance control. Three groups were compared, representing the three highest levels of contextual interference (from least contextual interference to most: serial, random blocked, random). It was hypothesized that 1a) random practice would be most unpredictable, and result in the highest amount of balance control variability during acquisition while 1b) serial practice would be least unpredictable, and have the least balance control variability during acquisition. It was further hypothesized that 2a) the minimal errors encountered during acquisition would allow for serial practice to have the least amount of balance control variability on a retention test, while 2b) the large errors encountered by random practice would make for the most variability on a retention test. Finally, it was hypothesized that 3a) random practice would allow for high generalizability, demonstrated by the least balance control variability on a transfer test while 3b) serial practice would have the most, indicating the least amount of generalizability.

Specific Aim 3. From the same study cohort as Aim 2, to determine the effects of variable practice on the biomechanical gait adaptations that occur during acquisition, retention, and transfer of a novel gait pattern. Using outcome measures previously noted in other locomotor adaptation studies, it was hypothesized that: during acquisition, 1a) random practice would result in the largest changes in gait biomechanics compared to symmetric

walking, while 1b) serial practice would have the least changes. Second, it was hypothesized that 2a) random blocked practice would result in gait mechanics most reflective of symmetric walking early in a retention test due to the similarity between acquisition and retention, but by 2b) the end of the retention test all groups would have similar gait patterns as they all had re-adapted. Third, it was hypothesized that 3a) serial practice would show the most different gait mechanics compared to symmetric walking on a transfer test, but like retention 3b) all groups will re-adapt by the end of transfer, with no observable differences in gait biomechanics among them.

Specific Aim 4. a) To use a principal component analysis (PCA) to reduce the large kinematic data set to a small one that identifies the kinematic coordination patterns during acquisition, retention, and transfer of asymmetric SBW. b) To observe the contextual interference effects across the three practice groups through this reduced data set. The same study cohort from Aims 2, and 3 were used here. It should be noted that this was not a hypothesis-driven study, but rather an exploratory one that sought to find the most salient aspects of the data set.

Organization of Dissertation

This dissertation is written in a journal format style, where Chapters III-VI have been or will be submitted for publication to peer-reviewed journals. The following explains how these chapters fit together into a coherent body of work. A bridge is present at the conclusion of Chapters III-V to provide context to the flow from one chapter to the next.

The current chapter (Chapter I) has provided the background information and significance necessary to detail how the research questions of this dissertation were formulated, as well as described the general and specific aims that guided the overall study. Next, Chapter II will detail the methodology implemented for each study, while explaining the similarities and differences between each. Chapter III will give a detailed overview of how a controller for a split-belt treadmill was designed to automatically and reliably carry out a given practice paradigm. Development of this controller was essential in order to implement the designed practice paradigms, since they all require accurate changes in treadmill belt velocity in very short time frames.

Once the study design was able to be implemented, the research detailed in Chapters IV-VI could be carried out. In Chapter IV, the effect of variable practice on retention and transfer of frontal plane balance control was examined. This analysis was performed first in order to make direct comparisons with other groups who have done similar studies, and to determine practice group performance when applied to a specific task-related goal. Chapter V delves deeper, in order to determine the biomechanical gait strategies utilized by each practice group during acquisition, retention, and transfer. Results from this study would help to further solidify findings from Chapter IV, while providing a biomechanical description of the actual strategies implemented by each practice group. Chapter VI will then provide a translation of these findings into something more clinically interpretable, by finding outcomes indicative of gait adaptation that are measureable outside of a research laboratory. In doing so, this chapter also provides a description of the practice group effect from this new perspective. The final chapter, Chapter VII, summarizes the key results from the overall body of work, giving a

larger-picture view of this set of studies while mentioning limitations and suggesting directions for future work.

This dissertation includes co-authored work, some of which has already been published in peer-reviewed journals. Chapter III has already been accepted for publication into the *Journal of Biomechanics*. Chapter IV is currently under second review for acceptance into *Experimental Brain Research*. Chapter V is under first review in the *Journal of Experimental Biology*, and Chapter VI will be submitted for publication in the near future to an appropriate journal. For all work in this dissertation, Jacob W. Hinkel-Lipsker was the primary contributor, including being responsible for designing the study, subject recruitment, data collection, data analysis, and dissemination. Michael E. Hahn, the other co-author on this set of studies, oversaw all aspects of the dissertation process from a mentorship role and also participated in study design.

CHAPTER II

GENERAL METHODOLOGY

Subjects

To address Specific Aim 1 (Chapter III), one able-bodied male (28 years old, 185 cm tall, 84 kg) was recruited. To address the remaining Specific Aims (Chapters IV-VI), 48 able-bodied participants were recruited (Table 2.1). For a subject to be included in this cohort, she or he was required to be between the ages of 18 and 50 years of age, and be able to walk on a treadmill for up to 30 minutes without assistance. Exclusion criteria were any self-reported cardiopulmonary or neurological disorders, or chronic or acute (within the last 6 months) musculoskeletal injuries. Subjects were also excluded from participation if they had any experience walking asymmetrically on a split-belt treadmill. For Chapters IV-VI, informed consent was obtained from subjects, and study protocols were approved by the University of Oregon Institutional Review Board.

Table 2.1 Group demographics, organized by acquisition practice group (serial, random blocked (RB), random) and whether they completed a retention or transfer test. Sex, age, height, weight, limb dominance (Limb Dom), and self-selected walking speed (SSWS) were recorded.

Group Demographics						
Group	Sex	Age (mean yrs ± SD)	Height (mean cm ± SD)	Weight (mean kg ± SD)	Limb Dom	SSWS (mean m/s ± SD)
Serial Retention	3 F/5 M	25.0 ± 5.4	176.8 ± 10.7	70.2 ± 9.8	8 R/0 L	1.31 ± 0.16
Random Retention	5 F/3 M	22.9 ± 3.0	169.9 ± 15.9	75.0 ± 14.0	8 R/0 L	1.28 ± 0.09
RB Retention	5 F/3 M	24.6 ± 5.8	175.5 ± 6.0	75.0 ± 14.5	7 R/1 L	1.29 ± 0.13
Serial Transfer	4 F/4 M	23.9 ± 5.5	177.1 ± 6.4	78.9 ± 14.4	7 R/1 L	1.35 ± 0.18
Random Transfer	4 F/4 M	24.1 ± 5.7	175.2 ± 8.6	72.6 ± 9.8	8 R/0 L	1.29 ± 0.12
RB Transfer	3 F/4 M	23.5 ± 3.3	173.0 ± 8.0	67.4 ± 13.7	7 R/0 L	1.30 ± 0.21
Mean and Totals	**25 F/23 M**	**24.0 ± 4.8**	**174.6 ± 9.3**	**73.2 ± 12.7**	**46 R/2 L**	**1.30 ± 0.15**

Study Design and Experimental Protocol

Chapter III

A treadmill control algorithm was designed to automate control of the velocity of the treadmill belts. The details of that algorithm are explained in detail in Chapter III. In general, this algorithm was designed to use data from the force plates embedded underneath each belt of the split-belt treadmill (Bertec, Columbus, OH) to detect when a person's limb is in swing phase (or when the ground reaction force is equal to zero). Time constraints were placed on the algorithm, since acceleration of the treadmill belt in question needed to occur while the person's leg was in swing phase to prevent additional perturbations. To ensure the required performance, the control loop was separated into discrete time points and timed over 100 strides.

To track control loop performance, each step in the loop was separated and timed individually. Some of these steps were deemed to be instantaneous, such as the time it takes for the analog signal to travel from the force plate to the Analog/Digital (A/D) converter. The non-instantaneous time points included the sampling rate of the Arduino Mega 2560 A/D converter (a constant 25 Hz), the input/output time of the MATLAB (Mathworks, Natick MA) script running the control loop, and the acceleration of the treadmill belt to the new velocity.

Chapters IV-VI

Subjects completed two consecutive days of testing, separated by 24 hours. The first day began with collection of anthropometric data, limb dominance, and subjects' self-selected walking speed (SSWS; Table 2.1). Limb dominance was determined by

asking the subject which leg she or he would use to kick a soccer ball, and SSWS was

calculated as the average of four times walking across a 20 m walkway. Next, subjects

were asked to walk for 15 minutes on the treadmill with both belts set to their SSWS.

This acclimation phase was used to collect motion capture data during symmetric

walking, and to ensure gait consistency on the treadmill (Zeni and Higginson 2010).

Immediately following the acclimation phase, the automated treadmill control

program implemented a 720-stride acquisition phase. Here, each subject completed an

asymmetric SBW practice protocol in accordance with their randomly-assigned practice

group. For all practice groups, their non-dominant limb was termed the constant limb,

and was driven at subjects' SSWS for all 720 strides of acquisition. The dominant limb

was termed the variable limb, and was driven at different velocities according to the

practice protocol. Subjects in the serial practice group began with the variable limb belt

velocity at SSWS-0.5 m/s on the first stride and, over the course of the acquisition phase,

this belt velocity increased every stride until it reached SSWS+0.5 m/s on the 720th stride.

Hence, each variable limb step was 1/720 m/s faster than the previous one. The random

blocked practice group began on the first stride with the variable limb belt set to a

random velocity within ±0.5 m/s of SSWS. This belt velocity remained constant for 20

strides, and then switched to a new random velocity within ±0.5 m/s of SSWS and ±0.5

m/s of the previous stride. Therefore, this group experienced 36 different belt velocities

in blocks of 20 strides over the course of acquisition. Finally, the random practice group

started acquisition at a random velocity within ±0.5 m/s of SSWS, and this belt velocity

changed every stride to a new random velocity within ±0.5 of SSWS and ±0.5 m/s of the

previous stride (Figure 2.1).

n = 48 → **Acclimation** → **Acquisition** → **Retention (n = 24)** / **Transfer (n = 24)**

Serial Training (n = 16) — Limb Variable / Constant

	Acclimation	Acquisition	Retention/Transfer
Variable	SSWS	Linear increase from -0.5 m/s of SSWS to +0.5 m/s of SSWS	1.5*SSWS (n = 8) / 2*SSWS (n = 8)
Constant	SSWS	SSWS	SSWS

Random Blocked Training (n = 16) — Limb Variable / Constant

	Acclimation	Acquisition	Retention/Transfer
Variable	SSWS	Random velocity within ± 0.5 m/s of SSWS, constant for 20 strides	1.5*SSWS (n = 8) / 2*SSWS (n = 8)
Constant	SSWS	SSWS	SSWS

Random Training (n = 16) — Limb Variable / Constant

	Acclimation	Acquisition	Retention/Transfer
Variable	SSWS	Random velocity within ± 0.5 m/s of SSWS	1.5*SSWS (n = 8) / 2*SSWS (n = 8)
Constant	SSWS	SSWS	SSWS

15 minutes — 10 s — 720 strides — 24 hrs — 400 strides

Fig 2.1. Study design for Chapters IV-VI. 48 able-bodied individuals were recruited for this set of studies, and assigned to complete either a serial, random blocked, or random practice protocol. Following a 15-minute acclimation phase where both constant and variable limb belt velocities were tied to SSWS, subjects completed a 720-stride acquisition protocol. In the case of serial practice, this meant that the variable limb belt velocity increased linearly over the course of this phase. For random blocked practice, belt velocity was set to a random velocity and changed every 20 strides to a new random velocity. The random practice group had the variable limb belt driven at a random velocity with every step. After 24 hours, subjects completed either a retention test, where they experienced a consistent 1.5:1 (variable:constant asymmetry), or a transfer test of a 2:1 asymmetry.

Twenty-four hours later, subjects returned to complete either a retention or transfer test (Figure 2.1). Twenty-four hours were given between the acquisition and retention or transfer phases to allow for consolidation of motor memories (Brashers-Krug et al. 1996) and to allow for washout of the adapted asymmetric gait pattern through

symmetric overground walking. The retention test, completed by half of the entire study cohort, was given to measure how well subjects formed a relationship in memory between sensory feedback and motor output at a given walking asymmetry during the acquisition phase. As such, retention tested for individuals' memory recall of that relationship and how they applied it to re-adapt their gait (Newell 1991; Schmidt 1975; van Kesteren 2012). This phase consisted of 400 strides of walking at a 1.5:1 (variable:constant) of SSWS asymmetry (Figure 2.1). This asymmetry was chosen because it was large enough to create a significant challenge during re-adaptation, but also was close to the maximum variable limb belt velocity that subjects experienced the previous day (thereby testing for recall).

The transfer test, which the other half of the study cohort completed, was used to measure how well subjects could generalize their learned gait pattern. Previous work has demonstrated that during motor skill learning individuals can use their previous practice experiences to apply their skill in a novel context (Newell 1991; Schmidt 1975; van Kesteren 2012). For this test, a 2:1 (variable:constant) of SSWS asymmetry was chosen because no subjects experienced this asymmetry during acquisition, but the context would still be as novel and challenging as possible without forcing subjects to run (Figure 2.1).

Data Collection

Chapter III

In order to measure treadmill control loop performance, GRF data were simultaneously sampled by a second A/D converter (National Instruments, Austin, TX)

and collected on the same machine running the control loop using Cortex software (Motion Analysis, Santa Rosa, CA).

Chapters IV-VI

Fifty-four reflective markers were placed on participants' bony landmarks (Sawers and Hahn 2012) prior to implementation of the experimental protocol on both days. During data collection, three-dimensional marker coordinate data were collected at 60 Hz for the final 20 strides of acclimation, and throughout the 720-stride acquisition and 400-stride retention or transfer phases using an 8-camera motion capture system (Motion Analysis, Santa Rosa, CA). These data were synchronized with GRF data collected from two force plates, one underneath each treadmill belt (Bertec, Columbus OH) using Cortex motion capture software (Motion Analysis, Santa Rosa, CA).

Raw marker coordinate data were low-pass filtered using a 4th order Butterworth with a 5 Hz cut-off frequency, and GRF data were low-pass filtered with a 4th order Butterworth using a 45 Hz cut-off frequency (Sawers et al. 2013a). These data were then used to build a 13-segment whole-body model using Visual 3D (C-Motion, Germantown, MD).

Data and Statistical Analysis

Chapter III

After the trial, swing phase time for each stride was calculated as the sum of the number of samples collected while GRF = 0. In doing so, the treadmill control loop time could be compared to swing phase time, where if the control loop was shorter than swing

phase time then performance would be deemed successful. In order to further quantify this margin, a factor of safety was then calculated.

Chapter IV

Using Visual 3D, the whole-body center of mass (COM) position was calculated as the weighted sum of the 13-segment model. Then, the frontal inclination angle (FIA) during heel strike was calculated as the angle of a vector from the COM to the lateral malleolus of the heel-striking foot with respect to vertical. A more in-depth explanation of the choice of dependent variables is given in Chapter IV. The standard deviation of these FIA values were found for every 20 strides of the acclimation, acquisition, and retention/transfer phases. Then, the FIA SD from the last 20 strides of acclimation was subtracted from each 20-stride FIA SD during acquisition and retention/transfer, thereby quantifying a difference in variability between symmetric gait and the learning of an asymmetric one. These values were then averaged across each test (acquisition, retention, transfer) to reflect the overall variability of a given test. This metric has been previously termed the Average Uncertainty Residual (AUR; Sawers and Hahn 2013; Sawers et al. 2013a).

To compare the effects of each practice protocol on balance control variability during each test, a three-way analysis of variance (ANOVA) was performed using SPSS statistical software (IBM, Armonk, NY) with practice group, limb, and test as independent variables and AUR as the dependent variable. Bonferroni-adjusted pairwise comparisons were made when significant main effects were revealed.

Chapter V

In order to take a deeper look at the underlying gait strategies adopted by each practice group, ten spatiotemporal, kinematic, and kinetic variables were calculated. The reasoning and explanation of each variable is further discussed in Chapter V. Five different time windows were used for analysis: acquisition, early retention, late retention, early transfer, and late transfer. These data were analyzed in two ways. First, in a more qualitative fashion, each measurement was normalized to one gait cycle (1-100%), and ensemble plots were generated to compare the group differences for each time-series measurement. Second, discrete peak values were calculated from each gait cycle and averaged, thereby giving the mean peak value for all strides in a given time window. Kinematic and kinetic calculations were performed using Visual 3D, and internal joint moments were estimated using an inverse dynamics approach. Peak value extraction was performed using MATLAB.

To determine the effect of practice group on all variables, five two-way multivariate analyses of variance (MANOVAs) were run using SPSS, one for each of the five aforementioned time windows. Within these MANOVAs, practice group and limb were included as independent variables, and each of the ten mechanical gait measures were set to be dependent variables. Where significant main effects or interactions were found, Bonferroni-adjusted pairwise comparisons were made.

Chapter VI

Lower-limb kinematic data were extracted using Visual 3D, including frontal and sagittal plane segmental linear velocities and accelerations, frontal and sagittal plane angular velocities and accelerations, frontal and sagittal plane pelvic orientation, frontal plane COM velocity and acceleration, and specifically chosen ankle, knee, and hip joint angles. Peak values for each full gait cycle for each variable were then calculated. For more description on variable selection and analysis, see Chapter VI.

This large data set was then standardized and reduced to a lower dimensionality using three PCAs (one each for acquisition, retention, transfer). A larger discussion on PCA is given in Chapter VI. This method was chosen in order to remove the bias of the researcher by minimizing the amount of *a priori* decisions needed before analysis about which variables to examine. A scree plot test was used to determine how many dimensions of data should be used for analysis. The contribution of each input variable to a given dimension, or principal component (PC) was then measured using the absolute value of the standardized coefficients of each PC. Finally, each subject's data was projected onto the reduced PC space in order to qualitatively examine any effect of practice group.

CHAPTER III

A METHOD FOR AUTOMATED CONTROL OF BELT VELOCITY CHANGES

WITH AN INSTRUMENTED TREADMILL

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Jacob W. Hinkel-Lipsker designed this study, collected the data, and analyzed it. Michael

E. Hahn provided mentorship activities, including assistance with study design, general

oversight of the project, and editing and finalizing of the journal manuscript.

Introduction

Split-belt treadmill training has been shown to be effective in normalizing gait

symmetry by inducing motor adaptation to an asymmetry in belt velocity (Bastian 2008;

Stubbs and Gervasio 2012). This adaptation is likely a central nervous system response to

minimize the kinematic variability and effort costs associated with gait perturbations

(Bastian 2008). As a result, split-belt treadmill training has been shown to have positive

gait outcomes in populations with asymmetrical gait patterns, such as those who have

suffered a stroke (Reisman et al. 2007). This method of training has also been used in

conjunction with virtual reality systems in order to combine walking asymmetry with

various sensory stimuli (Feasel et al. 2011; Marques et al. 2007; O'Connor and Kuo

2009).

Going forward, it is possible that split-belt treadmill training can be used with

variable practice as another form of rehabilitation. This theory postulates that when

practice of a motor skill is varied, the practice session becomes more challenging due to

the lack of predictability of the required parameters to successfully perform the motor skill (Shea and Morgan 1979). However, this lack of predictability drives storage of the relationship between the outcome and the sensory consequences in memory as a part of that motor skill's generalized motor program (Schmidt 1975). In the context of split-belt treadmill training, variable practice would require one belt to remain at a set speed, while the other belt would drive an individual's leg at a random speed on a stride-to-stride basis. To date, the effects of variable practice on acquisition, retention, and transfer of a novel gait have not been studied.

The split-belt treadmill training methods that have utilized blocked (gradual) training, or changes in belt velocity between training blocks, have required the treadmill operator to manually adjust belt velocities through the controlling device (Sawers et al. 2013). This form of manual control can become a source of error and even impossible if the belt velocity changes are frequent (stride-by-stride, in the case of variable practice). Further, timing of velocity changes is of crucial importance to insure that the adjustment happens during the swing phase, so that the limb is moved at a constant velocity during stance phase.

Thus, in order to implement practice schedules with frequent changes in belt velocity, the need has arisen for automated treadmill operation. While some virtual reality interfaces have utilized kinematic data (Kim et al. 2012; Yoon et al. 2012) or a combination of ground reaction force (GRF) and kinematic data (Feasel et al. 2011) for user-driven control schemes, there is currently a lack of operator-driven schemes that can be pre-set to change speeds given a specified gait event. Therefore, an approach was designed to automate an operator-driven control system for split-belt treadmill walking.

The purpose of this study was to define the process of an automated treadmill control loop and evaluate its performance during a trial of variable asymmetrical split-belt training, which would test the functionality of this control loop across its entire range of velocity changes.

Methods

A variable practice protocol, representing the most challenging practice difficulty according to contextual interference theory (Shea and Morgan 1979), was implemented. This practice method involved the non-dominant limb being driven at the user's self-selected walking speed (SSWS) while the speed of the dominant limb was randomly changed on a stride-by-stride basis within a range of ± 0.5 m/s of the previous step, and also within a ± 0.5 m/s velocity range of SSWS for every step. These ranges were chosen to test the ability of both the treadmill hardware and the control algorithm to make large negative and positive changes in belt velocity between strides, without causing a safety risk for the participant. However, the researcher can alter these ranges and the direction of velocity changes (i.e. only above SSWS) if a different methodology is required for a future study. To determine SSWS, the participant was asked to walk naturally four times across a 20 m walkway and was timed using a stopwatch. Using the MATLAB (version 2014b, Mathworks, Natick, MA) RANDI function, stride-to-stride velocities were randomized prior to the trial (eg., velocity (m/s) = {1.91, 1.48, 1.34, 1.23, 1.65, …}) to decrease computation time. One male (185 cm, 84 kg, SSWS = 1.57 m/s) walked for 100 strides on the treadmill, and GRF data were collected by the force plate embedded under the dominant leg treadmill belt at 1200 Hz.

A Bertec split-belt instrumented treadmill (Bertec, Columbus, OH) was used for this study. This treadmill allows for programs to remotely control the belt motors through TCP/IP. The control scheme was designed as follows (Figure 3.1): analog force plate data (in volts) were detected (T1) by an Arduino Mega 2560 sampling at 25 Hz (T2), which then interfaced with a Windows 7 machine (2.7 GHz, 8 GB RAM) using a USB serial connection (T3). These data were then streamed into MATLAB using the Data Acquisition Toolbox (T4). As the analog data were streamed, a custom-written program detected swing phase for the dominant foot and issued a command at the first sample where GRF = 0 volts to change speeds (T5) from the pre-set speed randomization file to a TCP/IP controller using MATLAB Instrument Control Toolbox commands via USB (T6). The embedded Bertec treadmill control software was set to allow for remote application control, which interfaced with the treadmill motor to drive the belt. For TCP/IP commands to be issued, the Bertec C^{++} treadmill control library was loaded into the MATLAB script. The acceleration of the belt (T7) was set at 20 m/s^2 for each velocity change to be fully accelerated during swing phase, prior to the subsequent foot contact.
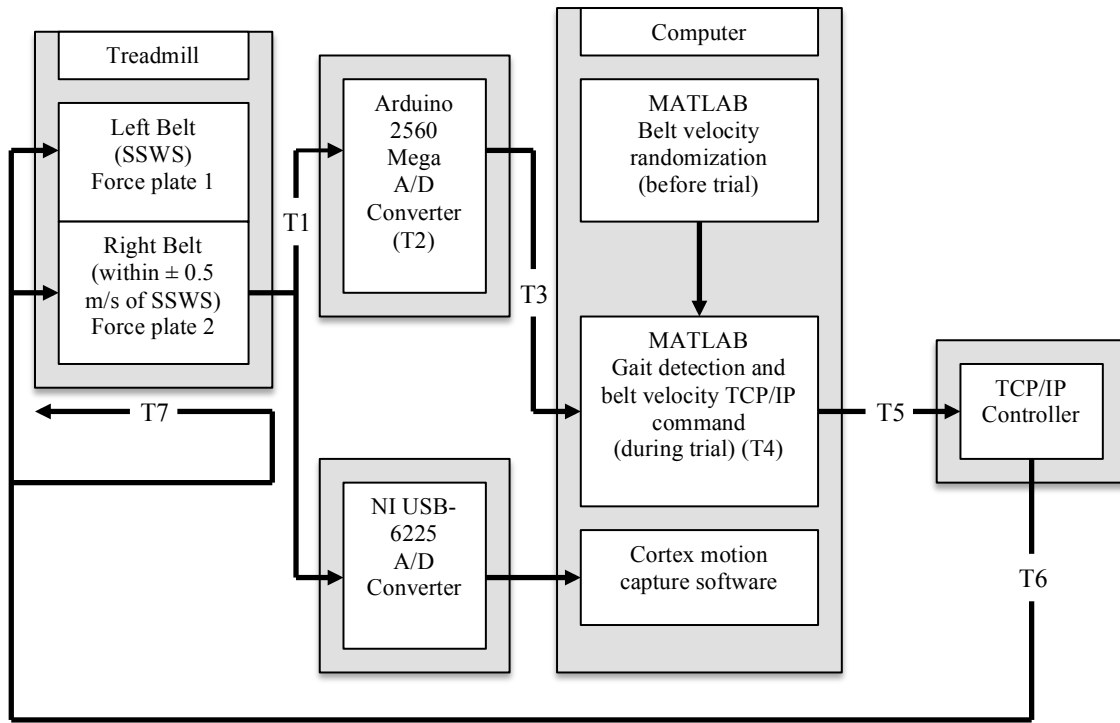
Fig 3.1. Treadmill control block diagram. Analog force plate data (T1) were sampled by an Arduino A/D board (T2), then streamed in real-time (T3) into custom written MATLAB software. Force plate data were also sampled using a National Instruments A/D board, and streamed into motion capture software on the same machine. Once swing phase was detected by the MATLAB software (T4), a command for a pre-set velocity change (within ± 0.5 m/s of self-selected walking speed) was sent to a TCP/IP controller (T5), which controlled the motor (T6) to accelerate the treadmill belts (T7). The treadmill belts were driven at self-selected walking speed for the left, non-dominant limb and at the pre-set stride-by-stride velocity for the right, non-dominant limb.

To assess algorithm performance, the total time (TT) for processing and execution of velocity change was calculated as the accumulation of the system's time points (T1-7). Assuming T1, T3, T5, and T6 to be nearly instantaneous, only T2, T4, and T7 were summed to calculate TT. T2 was set as a constant value of 40 ms, to represent the longest possible time for the Arduino board to capture a GRF = 0 signal while sampling at 25 Hz. T4 was calculated using MATLAB timing functions to compute the time between signal input and output. After the first stride was removed from analysis, since this was an acceleration from 0 m/s to the first pre-set speed, T7 was calculated as the change in belt

velocity for each step divided by the 20 m/s^2 acceleration of the treadmill belt (Equation 3.1, where n = stride number):

$$T7 = \left| \frac{velocity_n - velocity_{n-1}}{20} \right|$$

<div align="right">(3.1)</div>

GRF data were simultaneously sampled by a second A/D converter (NI-USB 6225, National Instruments, Austin, Texas) and collected on the same machine using Cortex software (Motion Analysis, Santa Rosa, CA). Following the walking trial, the swing phase time was calculated as the sum of samples for each stride on the dominant leg where GRF = 0 and 1 sample = 1/1200 seconds. The minimum swing phase time (swing$_{min}$) over the 100 strides was then calculated.

Failure to complete this control loop would represent a scenario where an individual's foot makes contact before the treadmill belt has fully accelerated to the desired velocity. To assess failure risk, we calculated a factor of safety (FOS) value, dividing swing$_{min}$ by TT for each step over the 100 strides (Equation 3.2, where n = stride number):

$$FOS = \frac{swing_{min}}{TT_n}$$

<div align="right">(3.2)</div>

Results

An evaluation of the belt velocity randomization protocol revealed that the mean absolute velocity change was 0.23 ± 0.15 m/s, with a range of -0.49 m/s to 0.47 m/s, indicating that the velocity randomization function provided acceptable representation of an ideal range of belt velocities for experimental protocols. Calculation of T4 (MATLAB processing time) resulted in a mean time of 1.2 ± 0.7 ms, while T7 (time to achieve

velocity change) was calculated to be 11.3 ± 7.5 ms. Combining these two values with the constant sampling rate of the Arduino A/D board (T2 = 40 ms), average TT was calculated to be 52.5 ± 7.7 ms, ranging from 41.3 to 66.0 ms.

With a constant value of T2, only T4 and T7 were affecting timing changes on a stride-to-stride basis. To confirm this observation, a polynomial was fit to the relationship between velocity change and TT (Figure 3.2). An examination of this polynomial indicated that belt velocity change had a strong relationship with TT ($R^2 = 0.93$). Given this result, it appears that changes in TT are almost entirely dependent on time needed to accelerate the treadmill belt.
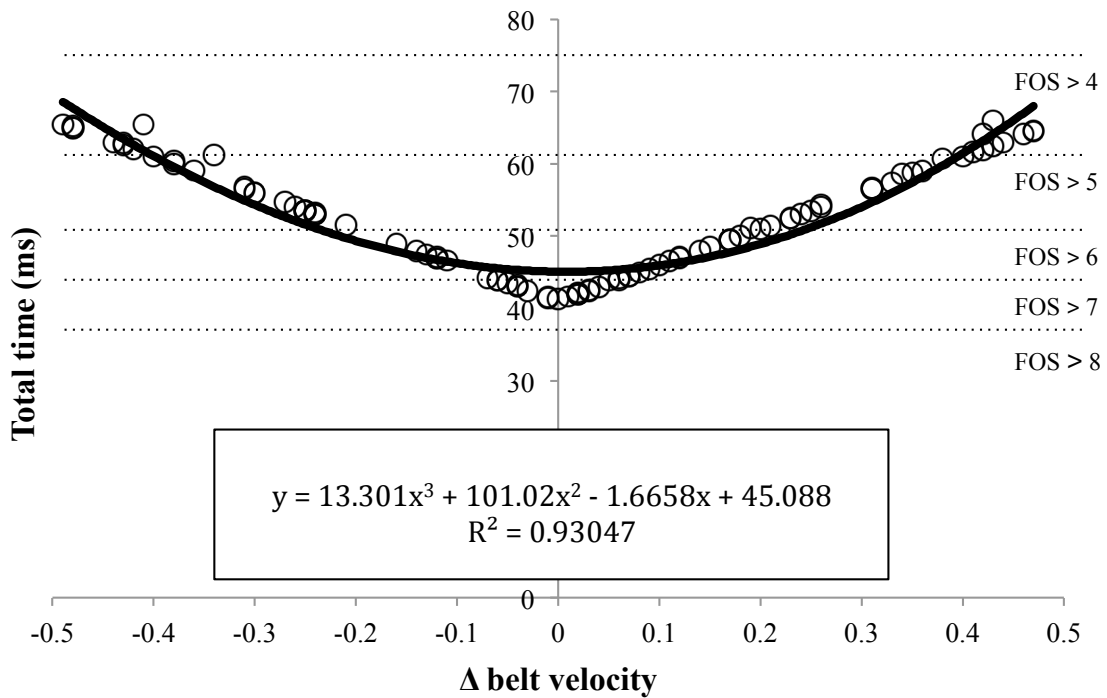
Fig 3.2. Total time as a function of belt velocity change. Total time increased as treadmill velocities reached their upper and lower limits. Polynomial fit analysis indicates a strong relationship between these two factors ($R^2 = 0.93$). FOS ranged from 4.54 – 7.26.

From the asymmetrical walking trial, $swing_{min}$ was calculated to be 300 ms. Using this value to calculate a FOS for each stride resulted in a minimum FOS of 4.54 and a maximum of 7.26 across all strides (Figure 2). While there is a lack of published data using FOS to determine treadmill control loop performance, it seems that this approach performed within an acceptably safe range to prevent gait imbalances which would be likely if a treadmill belt accelerated during stance phase. Further, if the ± 0.5 m/s limit was removed, and the derived polynomial were applied, this approach could reasonably accommodate treadmill velocity changes ranging from -1.77 m/s to +1.47 m/s while remaining at or above a FOS of 1. However, it is important to note that a FOS of 1 would likely indicate that this control loop is operating close to failure, as small changes such as individual differences, computing power, or treadmill brand could cause the FOS to move under 1.

Discussion

These results indicate that, with a maximum TT of 66 ms, this control scheme is sufficient to accommodate treadmill belt velocity changes within the ± 0.5 m/s limit imposed on this study. The participant used to test this system was healthy and did not have any gait or neurological disorders. However, the present timing analysis indicates that this method would also function well for patient populations with much shorter swing phase times, such as individuals with a hemiplegic stroke, where swing phase on the affected limb only occupies between 20-30% of the gait cycle (Olney and Richards 1996; Kramers de Quervain et al. 1996).

Limitations

There are a few limitations in the development and testing of this treadmill control method. First, only one participant was used for testing, therefore any potential gait pattern differences between individuals were not accounted for in this method development. However, this participant was only used in order for the control algorithm to complete its loop through detection of gait events and was not considered to be a representative sample of any particular population. Also, the equipment and computing resources used for this study are specific to a single research laboratory. Therefore, the results may vary somewhat when the method is used with a different equipment setup. Finally, while it has been mentioned that this method would function for populations with unilateral gait disorders, it is important to note that additional safety considerations such as harnesses should be implemented in any future studies investigating these populations, and therefore the results and validity of this method could be compromised.

Future Work

The developed treadmill control method has the possibility to be applied in at least two different types of gait research. First, this approach can be implemented in future split-belt treadmill studies that require automated belt velocity changes. Second, the developed approach could be implemented in a virtual reality interface to detect gait events and implement operator-controlled gait rehabilitation or training programs. While some studies have combined virtual reality interfaces with split-belt treadmills as a means for gait rehabilitation (Feasel et al. 2011; Marques et al. 2007; O'Connor and Kuo 2009), these have been either user-controlled or manually controlled by the operator. Future

studies combining these two training paradigms can utilize an automated control system as presented here for gait event detection or mid-trial progressions in velocity. Finally, with pre-set velocity changes, the use of an automated treadmill control loop will allow for researchers to manually operate other simultaneous data collection software, such as motion capture systems.

Bridge

The results of this study indicate that the designed automated treadmill controller is suitable for safe and reliable use. This controller provided the researcher with the ability to customize and preset the acquisition, retention, and transfer protocols for each subject in the study cohort based on his or her SSWS. Also, this algorithm removes the need for accurate treadmill control by the researcher, allowing the researcher to focus on other elements of the data collection process. In all, this study provided a framework for other types of research to automate treadmill control. More important to this dissertation, the experimental design for the following chapters was implemented with the knowledge that the belt velocity changes on the treadmill were being accurately controlled.

CHAPTER IV

THE EFFECTS OF VARIABLE PRACTICE ON LOCOMOTOR ADAPTATION TO A

NOVEL ASYMMETRIC GAIT

This work is, at the time of writing, under second review for publication in *Experimental Brain Research*. Jacob W. Hinkel-Lipsker designed this study, collected the data, and analyzed it. Michael E. Hahn provided mentorship activities, including assistance with study design, general oversight of the project, and editing and finalizing of the journal manuscript.

Introduction

The human central nervous system (CNS) utilizes a multi-layered control strategy to maintain crucial aspects of locomotion when gait symmetry is compromised due to a changing environmental context, such as uneven terrain, neurological injury, or unilateral lower-limb amputation. One control center, the cerebellum is responsible for modulation of the locomotor rhythm and postural muscle tone, thereby recalibrating the walking pattern to accommodate new terrains and environments (Bastian 2008; Middleton and Strick 2000). Also, the premotor and supplementary motor areas use sensory information integrated in the posterior parietal and vestibular cortices to generate motor programs (Massion 1992; Takakusaki 2013). These control centers are therefore responsible for feed-forward adjustments to the locomotor pattern. As such, the cortical and cerebellar control areas provide predictive control of certain gait parameters, which are adjusted with practice when novel environmental walking conditions are presented.

One way to experimentally test this predictive control of gait is through use of asymmetric split-belt treadmill walking (SBW), a locomotor task where two belts on a treadmill are driven at different velocities. To those with a naturally symmetric gait, this task can be considered novel. Therefore, these individuals must adapt their gait pattern when belt velocities are different and subsequently de-adapt when treadmill belt speeds are tied, returning the subject to walking symmetry. Over the last two decades, many studies have used this task to address a variety of questions related to how individuals adapt to a novel gait pattern. Dietz et al. (1994), Reisman et al. (2005), and Morton and Bastian (2006) were the first to recognize specific predictive adaptations over time during performance of this task, namely changes in step length, double support time, and interlimb coordination. The role of the cerebellum has been clearly elucidated in these studies, as subjects with cerebellar damage have demonstrated an inability to make these predictive adjustments during asymmetric SBW (Morton and Bastian, 2006). Further, the potential to use this task as a rehabilitative tool has been demonstrated. Subjects with hemiparetic stroke have shown improved step length and double support symmetry when split-belt treadmill belt speeds are tied (Reisman et al. 2007), and during overground walking (Reisman et al. 2010) following a bout of asymmetric SBW. Also, Lauziere et al. (2014) have demonstrated that individuals with hemiparetic stroke increase their plantarflexion moment post-adaptation on the paretic side when that limb is driven faster than the contralateral one during adaptation.

Despite these recent advances, it remains unknown how these predictive adaptations are stored. It is likely that the manner in which a practice paradigm introduces predictive errors during a bout of asymmetric SBW ultimately affects

retention and transfer of this novel gait. When large errors are introduced during asymmetric SBW subjects may attribute them to environmental conditions rather than their own internal errors, limiting transfer to overground walking (Torres-Oviedo and Bastian, 2012). Also, a small, gradual introduction of asymmetry results in improved retention and transfer of lower-limb endpoint control (Sawers and Hahn 2013) and balance control (Sawers et al. 2013a), and reduced cognitive demand (Sawers et al. 2013b), compared to a sudden, large introduction of asymmetry. However, outside of these studies it is unknown how further manipulation of error influences locomotor outcomes during and after acquisition of a novel gait task.

While Sawers and Hahn (2013) and Sawers et al. (2013a; 2013b) have argued that minimization of errors improves gait performance while reducing practice difficulty, it is also possible that gradual training is more effective than sudden because of contextual interference. This noisy ordering of environmental conditions induces an error in task outcomes during motor skill practice due to a discrepancy between predicted and expected sensory feedback during acquisition of a novel motor task (Shea and Morgan, 1979). However, the gradual training paradigm implemented in these studies was introduced in a linear fashion, which potentially allowed for subjects to predict the velocity of the treadmill belts prior to foot contact. Further, Criscimagna-Hemminger et al. (2010) have postulated that while small errors seem to better drive retention during adaptation, large errors allow for better generalization of that task.

Interventions that utilize contextual interference as a training tool often induce a variable practice paradigm, where the task parameters from trial to trial are altered in an unpredictable fashion. The role of variable practice in motor learning has investigated

across a variety of sport-specific tasks. For example, Henz and Schollhorn (2016) have observed different brain activation patterns during variable practice of badminton racquet swings compared to constant practice. Wrisberg and Liu (1991) have shown how badminton players can increase accuracy on retention and transfer tests of different serves following a variable practice paradigm. Additionally, Landin et al. (1993) used a variable practice paradigm that increased retention (but not transfer) of a basketball shot at the task goal level. In a rehabilitative setting, Hanlon (1996) showed how variable practice increased retention of a functional reaching task after stroke, while a review by Krakauer (2006) discussed how contextual interference is critical to increase transfer of rehabilitated motor skills post-stroke. These studies demonstrate how the role of variable practice in retention or transfer (or both) of a given task changes depending on the task itself and the skill level of the learner. Wu et al. (2014) have recently suggested that variability (or "noise") in different experiments that alter practice conditions (such as force-feedback) during various reaching tasks allows for neurologically intact individuals to explore the space of potential solutions to errors incurred during practice. This exploration induces a trial-and-error learning mechanism that ultimately improves retention of various motor learning outcomes such as accuracy of hand trajectory. In the context of motor learning of predictive gait parameters during an asymmetric SBW task, variable practice would require belt velocities to change in a way that is unpredictable. Theoretically, this paradigm would allow individuals to explore the space of possible learning outcomes and determine solutions to sensory discrepancies.

To date, the role of variable practice in locomotor adaptation to asymmetric SBW has not been studied. Rhea et al. (2012) do demonstrate how variable speed single-belt

treadmill training does not promote increased retention of consistent gait dynamics in individuals who suffer from stroke, but their paradigm induced variable speed changes every minute. This effectively made for blocked practice. This group did recommend that future studies investigate the role of variable practice when treadmill belt speeds change stride-by-stride rather than every minute. While Torres-Oviedo and Bastian (2012) introduced a somewhat variable practice paradigm during a novel asymmetric SBW bout, the belt with varying velocities was consistently faster than the other. This made for some predictability in that subjects could determine that one limb would be moving faster than the other. The predictability inherent in this study could have influenced the limited amount of overground transfer noted. Recently, it has been demonstrated that during acquisition of a novel asymmetric SBW task with one limb consistently faster than the other individuals assign a different role to the fast limb compared to the slow limb (Ogawa et al. 2014). It is possible that if it was unpredictable which role each limb would take during practice, then subjects could learn to walk asymmetrically context-free— where they would be able to effectively adapt their motor pattern to a novel context regardless of the velocity of each treadmill belt.

The purpose of this study was to examine the effects of a variable practice paradigm on retention and transfer of balance control during asymmetric SBW. To implement this paradigm, subjects were recruited to undergo practice paradigms with varying levels of unpredictability and contextual interference (from most predictable to least, and least contextual interference to most: serial practice, random blocked practice, random practice). It was hypothesized that 1a) serial practice would be most predictable, and therefore individuals completing this paradigm would exhibit the least amount of

balance control variability (the outcome measure of motor learning for this study, see *Methods* section) during acquisition. Also, it was hypothesized that 1b) random practice would be most unpredictable, demonstrated through the highest amount of balance control variability during acquisition. Second, it was hypothesized that 2a) serial practice would allow for minimization of errors during practice, leading to the least amount of balance control variability during a retention test. Conversely, 2b) random practice would demonstrate the highest amount of balance control variability during retention as step-to-step errors would be highest during acquisition. Finally, it was hypothesized that 3a) random practice would demonstrate the best generalizability of balance control variability during a transfer test, shown through the lowest variability. On the other hand, 3b) serial practice would have the least amount of generalization, demonstrated through the highest amount of variability.

Methods

Recruitment

Forty-eight able-bodied individuals were recruited for this study (Table 2.1). To be included in this study, subjects were required to be between the ages of 18 and 50 years old, and have the ability to walk on a treadmill for up to 30 minutes without assistance. Subjects were excluded from this study if any cardiopulmonary, neurological, chronic lower-limb musculoskeletal, or acute lower-limb musculoskeletal injuries within the last 6 months were self-reported. Additionally, subjects were excluded if they had any experience walking asymmetrically on a split-belt treadmill. Informed consent was

obtained from all individual participants included in the study, and the university

Institutional Review Board approved all study protocols.

Study Design and Experimental Protocol

Subjects were asked to attend two days of experimental testing. On the first day,

their self-selected walking speed (SSWS) was measured as the average time it took them

to walk across a 20 m walkway 4 times. Next, all subjects underwent a 15-minute

acclimation phase on an instrumented split-belt treadmill (Bertec, Columbus, OH) where

the velocity of both belts were tied to their SSWS. This phase was used to ensure gait

consistency during treadmill walking (Zeni and Higginson 2010) and to measure

symmetric balance control variability (*see Data Analysis*). Next, subjects were randomly

selected to undergo a serial, random blocked, or random training protocol of 720 strides,

where their non-dominant limb (constant limb) was driven for all strides at their SSWS

while the dominant limb (variable limb) was driven according to the protocol they were

assigned. Limb dominance was determined as the limb that subjects would prefer to use

to kick a soccer ball.

For serial practice, the subjects' variable limb began at SSWS-0.5 m/s for the first

stride and increased linearly by 1/720 m/s until belt velocity reached SSWS+0.5 m/s on

the 720th stride. Subjects in the random blocked practice group began with their variable

limb set to a random velocity within ± 0.5 m/s of their SSWS. This velocity remained

constant for 20 strides, and then changed to a new random velocity within ± 0.5 m/s of

their SSWS and ±0.5 m/s of the previous stride to limit the magnitude of changes in

velocity. Finally, the random practice group experienced random velocity changes on

their dominant limb every step within ±0.5 m/s of their SSWS and ±0.5 m/s of the previous stride. All protocols were preset and randomized according to their SSWS and the assigned protocol (Figure 2.1). For the random and random blocked practice groups, belt velocities were randomized using a RANDI function in MATLAB with the aforementioned boundaries with regards to SSWS and the previous stride included. Control of treadmill velocities was automated using a custom-written MATLAB (Mathworks, Natick, MA) script previously established by Hinkel-Lipsker and Hahn (2016a, or Chapter III) as a way to ensure that belt velocities changed while the individual's dominant limb was in swing phase and fully accelerated prior to the subsequent heel strike to avoid additional perturbations, as well as remove any effect of errors by the treadmill operator in manually changing treadmill belt velocities. To analyze the effectiveness of the belt velocity randomizations and ensure that the range of belt velocities was the same for all groups, the mean variable limb belt velocity for each group for each stride was calculated (Figure 4.1).
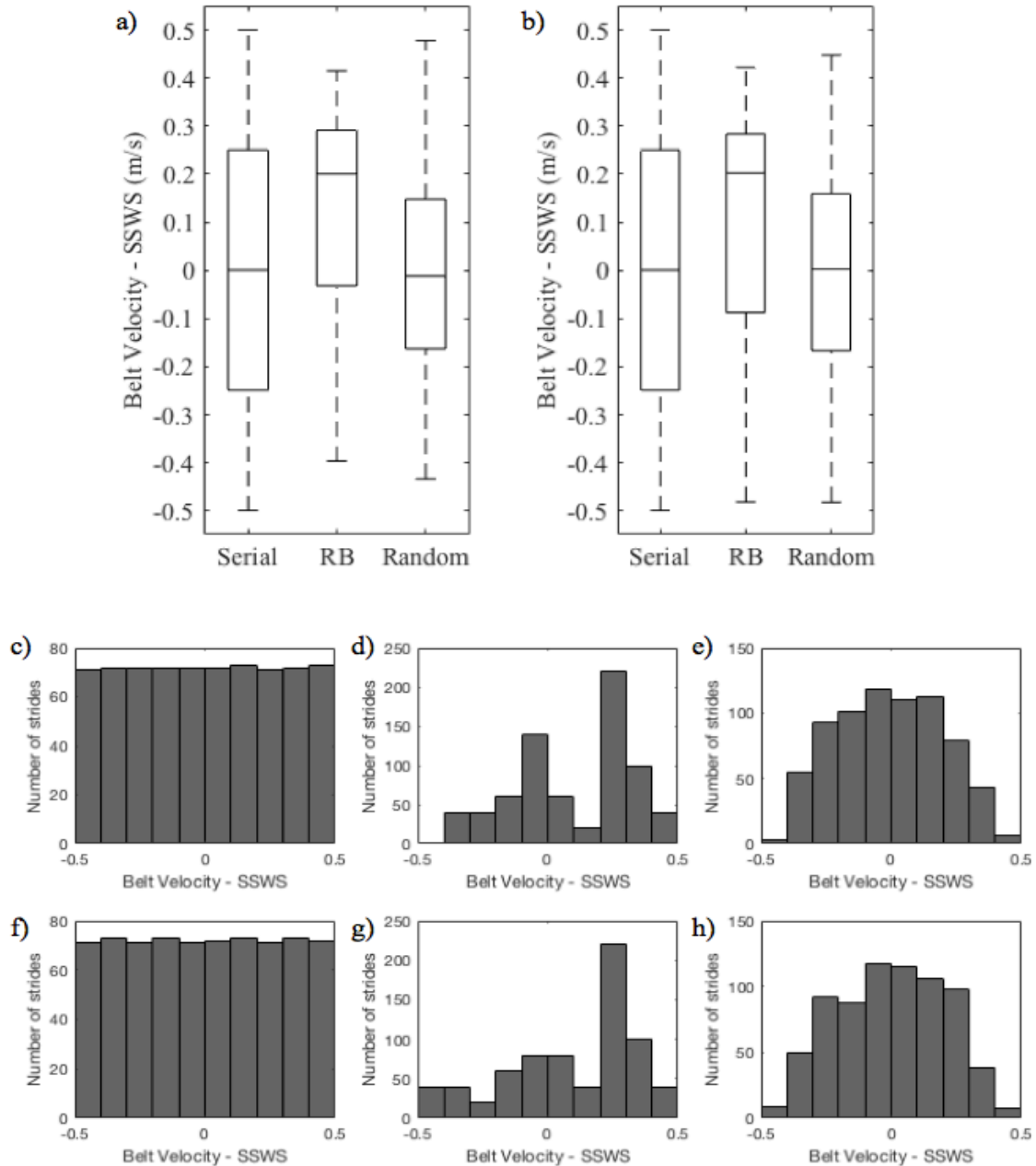
Fig 4.1. Distribution of variable limb belt velocities for serial, random blocked (RB), and random practice groups that completed either a) a retention test or b) a transfer test. Serial practice experienced a nonparametric distribution for both the c) retention and d) transfer groups on the. Random blocked practice experienced a non-Gaussian distribution of belt velocities for both d) retention and g) transfer, as there were only 36 possible belt velocities that the randomization function could use. This resulted in most belt velocities being above SSWS. Random practice had an approximately Gaussian distribution for both e) retention and h) transfer, due to 720 different strides being randomized.

On the second day of testing, subjects were randomly assigned to complete either a retention or transfer test (Figure 2.1). These tests occurred exactly 24 hours after the start of testing on the first day to allow for consolidation of motor memories (Brashers-Krug et al. 1996) and to allow the adapted locomotor pattern time for washout during overground walking in 24 hours between tests. In combination with the three acquisition protocols, this effectively made for six experimental groups: Serial Retention (SR), Serial Transfer (ST), Random Blocked Retention (RBR), Random Blocked Transfer (RBT), Random Retention (RR), and Random Transfer (RT). The retention test was assigned to measure how well subjects could recall an asymmetry experienced during acquisition. Within the area of motor skill learning, retention tests for the ability of individuals to form a relationship in memory between past outcomes and motor parameters of the current task, termed recall schema (Newell 1991; Schmidt 1975; van Kesteren 2012). Thus retention must reflect an environmental context previously experienced (Anguera et al. 2010; Galea et al. 2011). To test for retention in this study, a 1.5:1 (dominant:non-dominant) of SSWS asymmetry was applied for 400 strides. This asymmetry was chosen because all practice groups experienced it on the previous day for at least one stride (thereby testing for recall), while making the task as difficult as possible by using the largest asymmetry at the fastest velocity. The transfer test was used to measure generalizability of this task to a novel context, as individuals apply their previous experiences in a way where task performance is still possible using recognition schema (Newell 1991; Schmidt 1975; van Kesteren 2012). As such, a 2:1 (dominant:non-dominant) of SSWS asymmetry was applied for 400 strides. It should be noted that the term "transfer" here refers to the transfer of this learned gait asymmetry to an unpracticed

walking context on a split-belt treadmill. Other groups who have used SBW as a rehabilitative tool have also investigated the transfer of this skill from the treadmill to overground walking, which effectively is testing for a different form of skill generalization (Reisman et al. 2007). This asymmetry was chosen to make the context as novel and challenging as possible while ensuring that subjects' dominant limb was not moving so fast as to cause them to run, which is a different motor pattern not influenced by an enhanced recognition schema for walking.

Data Collection

Prior to the acclimation phase on the first day, demographic data including age, sex, height, and weight were recorded (Table 2.1). Before implementation of the experimental protocol on both days, 54 reflective markers were placed on participants' bony landmarks (Sawers and Hahn 2012) and 3D marker coordinate data were collected at 60 Hz for the final 20 strides of acclimation and throughout the acquisition and retention/transfer phases using an 8-camera motion capture system (Motion Analysis, Santa Rosa, CA). These data were synchronized with ground reaction force (GRF) data collected from two force plates (Bertec, Columbus, OH), one underneath each treadmill belt, at 1200 Hz using Cortex motion capture software (Motion Analysis, Santa Rosa, CA).

Data Analysis

3D marker coordinate data were low-pass filtered using a 4th order Butterworth with a 5 Hz cut-off frequency, and used to build a 13-segment whole-body model using

Visual 3D (C-Motion, Germantown, MD), while GRF data were low-pass filtered using a

4th order Butterworth with a 45 Hz cut-off frequency (Sawers et al. 2013a). Next, whole-

body COM position was calculated as the weighted sum of body segments. Then, the

frontal inclination angle (FIA) was calculated using a custom-written MATLAB script

(Mathworks, Natick, MA) as the angle between a vector from the COM to the lateral

malleolus of the heel striking foot with respect to vertical, projected onto the frontal

plane, or (Equation 4.1; Figure 4.2):

$$\sin \theta = \left(\frac{\overrightarrow{COMa} \times \overrightarrow{COMv}}{\overrightarrow{COMa}} \right)$$

(4.1)

, where $\overrightarrow{COMa}$ is the vector from the whole-body COM to the lateral malleolus, $\overrightarrow{COMv}$

is the vertical vector from the whole-body COM, and θ is the angle between the two.

This measure was taken at heel strike. Heel strike was determined as the first GRF

sample of that stride where vertical GRF > 10 N. The FIA was chosen as a measure of

balance control because foot placement in the frontal plane is crucial for maintaining

mediolateral balance control and altering frontal plane COM position (Bauby and Kuo

2000; MacKinnon and Winter 1993; Sawers et al. 2013a) and is capable of detection of

gait imbalances (Chen and Chou 2010; Huang et al. 2008). These discrete FIA values at

heel strike were calculated for each stride and each limb (constant and variable), and

were averaged for every 20 strides. Next, the standard deviation (SD) of each block of 20

FIA values for acclimation, acquisition, and retention/transfer was calculated as a

measure of variability in the balance control system.
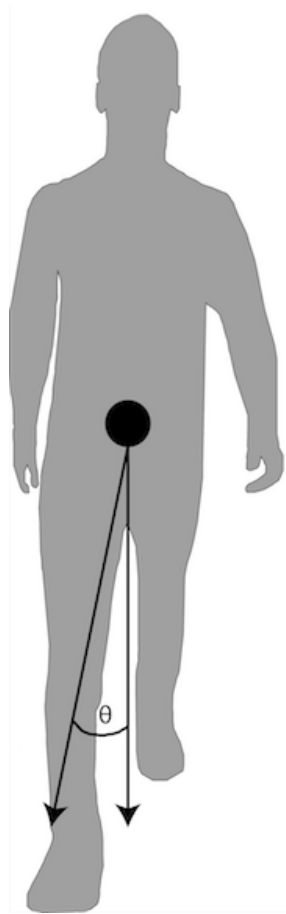
Fig 4.2. The frontal inclination angle during walking, measured as the angle between a vertical vector from the whole-body center of mass (see vector on right) and a vector from the whole-body center of mass to the lateral malleolus of the heel-striking leg projected onto the frontal plane (see vector on left).

To make comparisons on the effects of practice group on balance control variability, the average FIA SD for all blocks throughout acquisition and retention/transfer was calculated. Then, the average FIA SD during the last 20 strides of acclimation was subtracted from each block during acquisition and retention/transfer as a way to find the difference between natural gait variability during symmetrical walking (Winter 1984) and variability during acquisition and retention/transfer. Thus, this metric, previously termed the Average Uncertainty Residual (AUR), reflects the overall amount of variability in foot placement during the different tests (Sawers and Hahn 2013; Sawers

et al. 2013a) relative to symmetric gait. It should be noted that this measure is not necessarily one that is optimized by the CNS during adaptation, but rather was chosen as a metric of motor learning due to the aforementioned reasons.

Statistical Analysis

To compare the effect of practice schedule on balance control during acquisition, retention, and transfer of this novel gait pattern, a three-way ANOVA ($\alpha = 0.05$) was performed using SPSS v.23 (IBM, Armonk, NY) with practice schedule (serial, random blocked, random), limb (constant, variable), and test (acquisition, retention, transfer) as independent variables and AUR as the dependent variable. Assumptions of no outliers, normality, and homogeneity of variance were tested for (*see Results*). When significant main effects were revealed, Bonferroni-adjusted pairwise comparisons were made.

Results

Forty-eight able-bodied participants were enrolled in this study. In testing for assumptions for the ANOVA comparing practice schedules, it was noted that there were two extreme outliers in the data set. One, a subject in the RBT group, had an extremely high AUR for both limbs during the transfer test. It is likely that this was the case because their SSWS was measured to be 1.64 m/s, making the treadmill velocity for their variable limb during the transfer test to be 3.28 m/s, which is a typical slow running velocity. Since they had one limb at a walking velocity and one at a running velocity, this provided a methodological reason to remove AUR for both limbs for this participant from the data set as comparisons could not be made with other participants who had walking velocities

on both limbs. The other extreme outlier was for the constant limb for a subject in the RT

group during acquisition. This subject had a SSWS within the normal range for that

group, and therefore no methodological reason could be provided to remove this subject

from analysis. As such, the assumption of normality was violated for this group (RT,

acquisition, constant limb; Shapiro-Wilk test, $p < 0.05$). However, ANOVA is robust to

violations of the normality assumption (Schmider et al. 2010). Additionally, the

assumption of homogeneity of variance was also violated (Levene's test, $p < 0.05$), which

could possibly be due to the unequal sample sizes observed when the RBT outlier was

removed, or a relatively small overall sample size (Rogan and Keselman 1977). To

maintain an ability to interpret these data clinically, no transformations were made on the

data set and the RBT outlier remained excluded. Thus, it should be noted that due to the

heterogeneity of variance in this data set, the probability of Type I error might be inflated

by 2-4% (Rogan and Keselman 1977).

The model effects of the ANOVA revealed significant main effects of test ($F =$

12.622, $p < 0.05$, $\eta_p^2 = 0.132$) and group ($F = 14.667$, $p < 0.05$, $\eta_p^2 = 0.150$), and

significant test*group ($F = 12.197$, $p < 0.05$, $\eta_p^2 = 0.227$) and test*limb $F = 4.801$, $p <$

0.05, $\eta_p^2 = 0.055$) interactions. The main effect of limb was not statistically significant,

nor were the limb*group and test*limb*group interactions. Based on the significant main

effects and interactions, Bonferroni-adjusted pairwise comparisons were made between

each pair of groups (serial, random blocked, random) within each test (acquisition,

retention, transfer), as well as within-subject comparisons to examine the difference

between acquisition and retention/transfer, as a measure of learning. Due to a main effect

of limb or the limb*group and test*limb*group interactions not being statistically significant, no between-limb pairwise comparisons were made.

For acquisition, the random practice group had a significantly higher AUR compared to the serial practice group ($p < 0.001$; Figure 4.3) and random blocked training group ($p < 0.001$; Figure 4.3, 4.4a, 4.4b). AUR for the serial and random blocked practice groups was not significantly different (Figure 4.3, 4.4a, 4.4b). During retention, random blocked practice had a significantly lower AUR compared to serial practice ($p < 0.05$; Figure 4.3) and random practice ($p < 0.05$; Figure 4.3). During retention, neither serial nor random practice groups had significantly different AURs from each other and had similar re-adaptation trends over time (Figure 4.5a and 4.5b). Finally, during transfer serial practice resulted in a significantly higher AUR compared to both random blocked practice ($p < 0.05$; Figure 4.3, 4.5c, 4.5d) and random practice ($p < 0.05$; Figure 4.3, 4.5c, 4.5d). Further, the adaptation trends over time reflect that serial practice resulted in an overall larger and more variable FIA SD during transfer (Figure 6c, 6d).
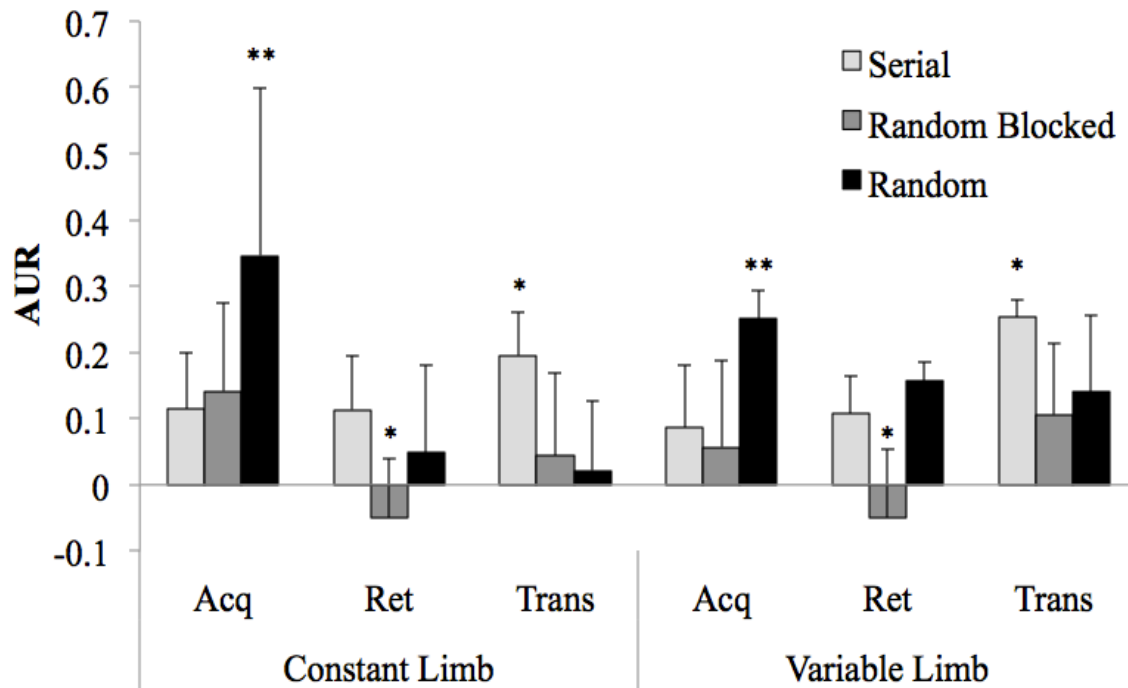
Fig 4.3. Average uncertainty residual of acquisition, retention, and transfer of asymmetric split-belt treadmill walking during and following either serial, random blocked, or random practice. Random practice was most difficult during acquisition, as evidenced by a significantly (** = $p < 0.001$) greater AUR compared to serial and random blocked practice groups, who did not have a significantly more or less challenging practice experience than each other. Random blocked practice resulted in a significantly (* = $p < 0.05$) lower AUR compared to the other two groups during retention, while serial practice resulted in a significantly higher AUR during transfer compared to both groups.
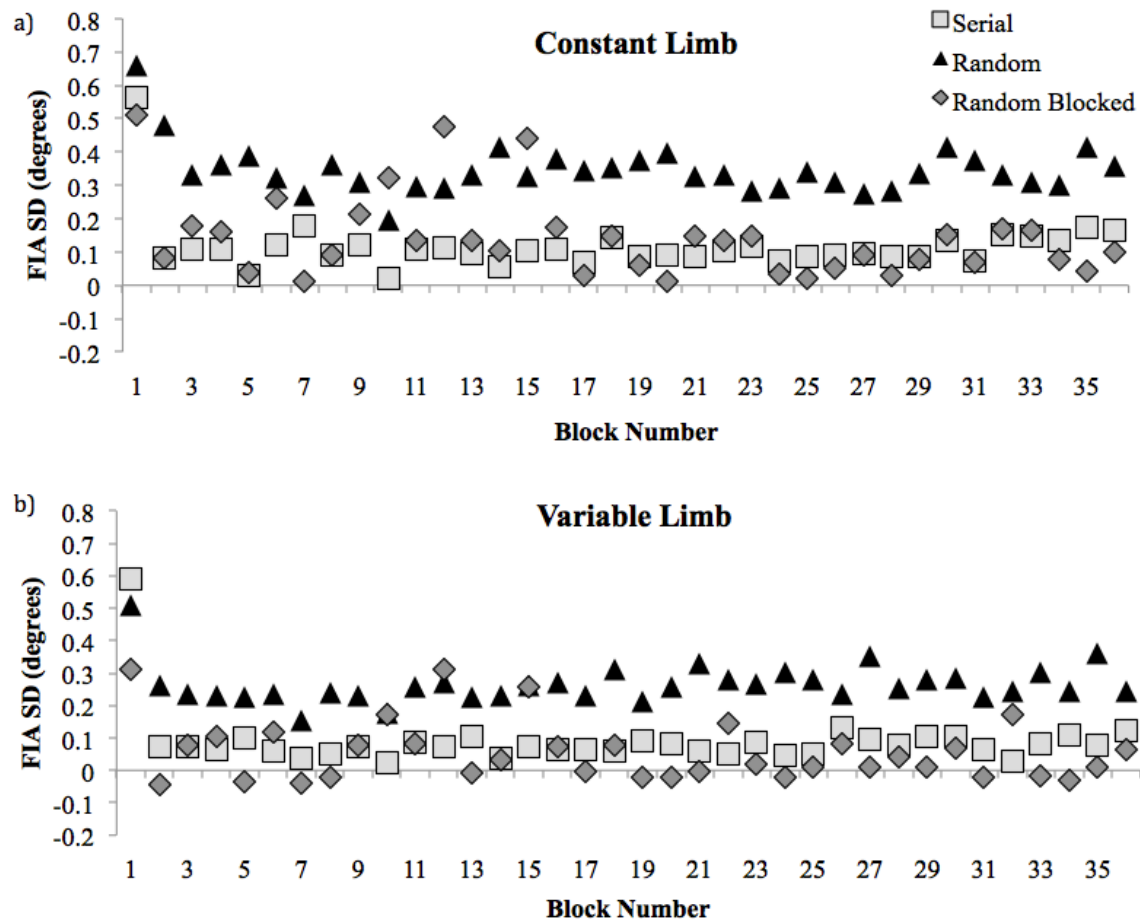
Fig 4.4. Group mean frontal inclination angle standard deviations (FIA SDs) during the 720-stride acquisition phase in blocks of 20 strides for a) the constant limb and b) the variable limb. After the initial perturbation, both the serial and random blocked (RB) practice groups demonstrated FIA SDs close to zero, reflecting variability in mediolateral foot placement close to that of natural, symmetric gait variability. The RB practice group had occasionally larger FIA SDs on both limbs due to the sometimes large changes in variable limb velocity from block to block. The random practice group had a consistently large FIA SD, due to the variable limb belt velocity changing with every stride. These data indicate that random practice was more challenging to frontal plane balance control on a step-to-step basis compared to the other two practice groups, and serial practice was least challenging
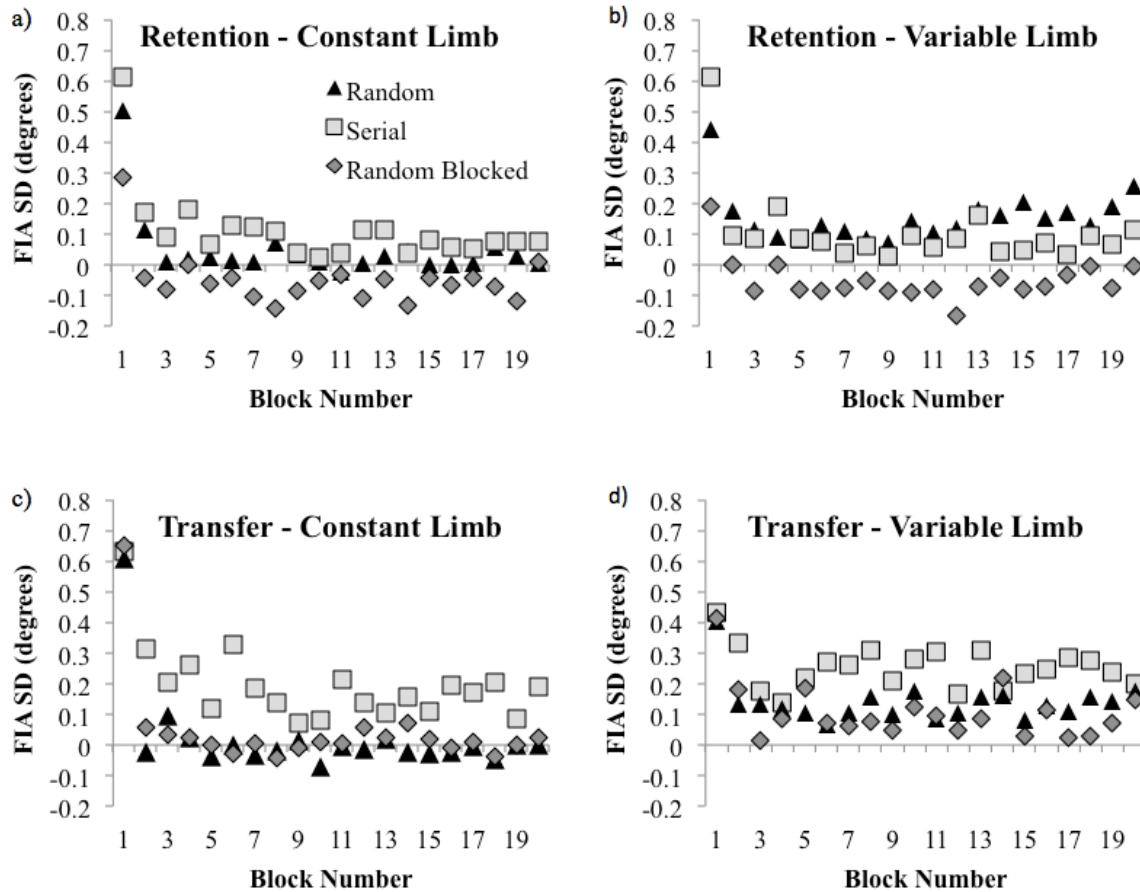
Fig 4.5. Group mean frontal inclination angle standard deviations (FIA SDs) in blocks of 20 strides during the 400-stride retention phase for the a) constant limb and the b) variable limb and 400-stride transfer phase for the c) constant limb and d) variable limb. The serial practice group had a larger initial variability during retention for both limbs, possibly due to the difference in perturbation size from that of their acquisition experience, and generally higher variability throughout the retention test. Random blocked (RB) resulted in retention values lower than 0, indicating less variability than natural, symmetric gait. Random practice resulted in variability near 0 for the constant limb, and higher variability for the variable limb. For transfer, both RB and random practice groups exhibited low (close to 0) variability on the constant limb, and slightly higher values on the variable limb. The serial practice group demonstrated high variability on both limbs during the transfer test

Discussion

The three groups experienced a very similar range of belt velocities on their dominant limb during acquisition (Figure 4.1). This analysis indicates that the randomization protocols that were set prior to the acquisition phase were effective in

51

implementing a practice schedule within the boundaries set, and that no subject

experienced a range of belt velocities outside of ±0.5 m/s of their SSWS. Thus, for all

groups, the 1.5:1 (dominant:non-dominant) retention protocol tested for an asymmetry

that subjects had experienced the day before, while the 2:1 transfer protocol tested for a

novel asymmetry not experienced the day before. However, both the RBR and RBT

practice groups had a median velocity greater than SSWS, and a slightly smaller range of

values (Figure 4.1a and 4.1b). Additionally, the belt velocities were clustered for both

random blocked practice groups more towards the faster end of the range of possible

values (Figure 4.1d and 4.1g). This is likely because the velocities were only randomized

36 times (36 blocks of 720 strides), while the serial and random practice groups had 720

different velocities. This, in addition to the constraints placed on the randomization

function (where the next random velocity had to be within ±0.5 m/s of SSWS and ±0.5

m/s of the previous stride's velocity, likely resulted in the non-Gaussian distribution

shown here.

During acquisition, it was revealed that the random practice group had a

significantly greater AUR compared to the serial and random blocked practice groups.

This supports hypothesis 1a. While it is not surprising that balance control was adversely

affected when belt velocities changed randomly with every step, this finding does align

with Schmidt's (1975) original idea that the challenge presented during variable practice

should be difficult and noisy in order to promote exploration of the task goals (Cohen and

Sternad 2009). However, hypothesis 1b is not supported, as AUR for serial practice was

not significantly lower than that of random blocked practice. An examination of the time

series plots for acquisition and the AUR SD for the serial and random blocked groups

(Figure 4.4a and 4.4b) reveals that serial practice resulted in a more consistent AUR for each block of 20 strides, while random blocked practice was more variable, likely because of the possibility of a large change in belt velocity every 20 strides. This indicates that while the magnitude of errors experienced by serial practice was lower, it did not result in an overall lower AUR than random blocked practice. As the main effect of limb and the limb*group interaction were not significant, there did not seem to be a strategy for error minimization on one limb compared to the other. Previous studies have revealed asymmetric limb differences during adaptation to SBW, such as step length and double support time (Reisman et al. 2005), braking GRF (Ogawa et al. 2014), lower-limb muscle activation (MacLellan et al. 2014; Ogawa et al. 2014), and phase shift between limbs (Torres-Oviedo and Bastian 2012). However, these studies were designed so that one limb was always faster than the other. Since this study involved all groups' variable limb spending approximately equal time moving faster and slower, one limb could not adapt to becoming the fast or the slow limb in this context.

The retention data does not support hypothesis 2a or 2b, since AUR for random blocked practice was significantly lower than both serial and random practice. Moreover, serial practice had the highest AUR (although not significantly higher than random). These findings are somewhat aligned with those of Roemmich and Bastian (2015) albeit with frontal instead of sagittal plane outcome measures. They found that gradual training (slowly incrementing the belt speeds) resulted in significantly less retention than abrupt training (one large perturbation followed by a constant belt speed) during a second bout of asymmetric SBW adaptation. This group attributed these findings to the notion that abrupt training allowed participants to form a more accurate perception of their walking

53

environment during acquisition. In the case of random blocked practice in this study, a similar interpretation can be made. Since this group had large perturbations followed by a round of constant belt velocities, this environment mimics that of the retention test, which abruptly went to a 1.5:1 asymmetry on the first step and remained there throughout the test. As seen in the first block of 20 strides during retention (Figure 6a and 6b), serial practice resulted in a FIA SD 2-3 times that of random blocked practice, followed by a consistently greater set of FIA SDs. Overall, these results indicate that random blocked practice performed best on retention with respect to balance control, possibly because the retention task mimicked that of their acquisition experience, allowing for a process in the cerebellum and prefrontal cortex to recall the same context as the practice environment (Galea et al. 2011; Anguera et al. 2010; Roemmich and Bastian 2015).

However, because AUR for random blocked practice was less than zero for both limbs, this means that these individuals walked with less variability in frontal plane foot placement than their natural, symmetrical gait. One possible explanation for this phenomenon may be increased attentional focus due to increased task difficulty, and therefore greater cognitive control of balance (Wulf et al. 2007). Another reason for this result is that the reduction in variability may have occurred as a result of this group having additional practice during acquisition where the variable limb was moving faster than the constant limb. To expand on this, Herzfeld et al. (2014) have recently shown that individuals have the capacity to form a memory of errors experienced during practice of a given motor task. Since the random blocked group here experienced more errors closer to the retention belt velocities, it is possible that that they were better able to recognize those errors during the retention test. It should also be noted that too little step width variability

is also associated with imbalance and fall risk (Brach et al. 2005). Ultimately, it is possible that the low AUR demonstrated by the random blocked group is not necessarily equivalent to better walking performance. Future studies should examine the lower-limb kinematic and kinetic adaptations of random blocked practice during asymmetric SBW in order to confirm that the low foot placement errors are not detrimental to long-term musculoskeletal health if this paradigm is used as a rehabilitative tool.

An examination of balance control performance during the transfer task reveals that hypotheses 3a and 3b are partially supported. While random practice did not result in a significantly lower AUR than random blocked practice, it was significantly lower than serial practice (Figure 4.3). Additionally, serial practice had a higher AUR than random blocked practice on this test. Thus, it seems that serial practice is not an effective paradigm to generalize the newly acquired gait pattern to new contexts, as previously noted in other studies observing motor learning of other tasks (Magill and Hall 1990). This result further indicates that the trial-and-error learning system described by Wu et al. (2014) was not engaged due to the small magnitude of errors incurred during practice. Conversely, the high level of contextual interference during both random blocked and random practice did allow for this trial-and-error mechanism to occur, supporting previous postulations by Criscimagna-Hemminger et al. (2010). In examining changes in FIA SD over the course of the transfer test (Figure 4.5c and 4.5d), it appears that both random and random blocked practice resulted in these groups limiting balance control variability on the constant limb, while allowing more on the variable limb. There may have also been a difference in cognitive engagement during acquisition that adversely affected the serial practice group's transfer performance, as it has been reported that large

errors during acquisition (as experienced during random blocked and random training) invoke a greater cognitive challenge, thereby allowing the CNS to acquire greater explicit information during practice and apply it to the new context (Roemmich and Bastian 2015; Sawers et al. 2013a). This was likely the case for the random blocked and random groups.

Taken together, it seems that random blocked practice is effective in engaging the two learning mechanisms associated with large and small errors (Criscimagna-Hemminger et al. 2010) in performance of a novel asymmetric gait pattern, as balance control variability was similar to that of serial practice during acquisition, and significantly lower during retention compared to both groups and transfer compared to the serial practice group. This advances the idea that predictive elements of locomotor adaptation can be trained through specific practice scheduling (Sawers and Hahn 2013; Sawers et al. 2013a). Although there was no difference in AUR between random blocked and random practice during transfer, it is evident that the greater challenge to balance control presented by random practice is unnecessary to optimally drive motor learning, as random blocked AUR was lower during acquisition. It is also possible that random blocked practice meets the optimal challenge point discussed in previous motor learning literature, where too much or too little noise during practice is detrimental to learning performance (Guadagnoli and Lee 2004).

Future Work

There are some notable clinical implications for rehabilitation of asymmetric gait given the results of this study. First, powered ankle-foot prostheses, which restore ankle

power in those with lower-limb amputation to nearly biomimetic levels, are now commercially available (Herr and Grabowski 2012). However, it is unknown what the long-term adaptation strategies to a restoration of ankle power are for those with amputation that have adapted to using a passive-elastic prosthesis (which do not fully restore ankle power). It may be necessary to train these individuals to control their device in a metabolically efficient and safe manner, especially since the next step for these prostheses is to use myoelectric controllers to proportionally actuate ankle power (Huang et al. 2014). In this case, training these individuals to acquire a new, symmetrical gait pattern with these prostheses may involve random blocked training for generalizability (transfer), where they can control the prosthesis in new environmental contexts. Second, those with neurological unilateral gait deficiencies, such as individuals with stroke, have shown improved overground walking symmetry following asymmetrical SBW practice (Reisman et al. 2007). While the possibility exists, given the results described here, that they may demonstrate even greater overground transfer following a random blocked SBW intervention, overground transfer was not measured in this study. However, the results of this study may not be applicable to these individuals, as it was previously discussed that random blocked practice may have been most effective for retention due to the abrupt perturbation every 20 strides during acquisition and at the beginning of retention, something that would not happen during overground walking, thereby limiting the generalizability of this task to overground walking.

Limitations

Some limitations may have affected the results of this study. First, in comparing the effects of practice group on acquisition, retention, and transfer, there was one outlier left in the data set, causing a violation of the normality assumption. This outlier was not removed from the data set because there was no methodological reason to remove it, and therefore this data point is representative of a learning experience from an able-bodied sample population. Another outlier was removed, causing unequal sample sizes between groups, which is possibly the reason for violation of the homogeneity of variance assumption. This data was removed for methodological reasons (*see Results*), and would have caused a further violation of normality if left in. Second, AUR was used as a metric for motor learning in this study, as it reflects a predictive (and therefore trainable) element of gait that has previously been shown to be sensitive to changes in balance. Since it was calculated as the mean across all strides for each phase of testing, it is possible that it did not capture enough resolution to identify small adaptive changes.

On the other hand, given the time series of FIA SD across all strides, it seems that the rate of adaptation did not differ between groups, and therefore it was deemed that detailed time series analyses were not necessary. Also, due to the study design, the random blocked practice group had the ability to practice multiple strides of the same asymmetry, while the serial and random groups did not. Because of this, the median velocity during acquisition being closer to the variable limb retention velocity, and the greater clustering of belt velocities above SSWS, it is possible that they received more practice at an asymmetry closer to that of the 1.5:1 retention test. However, serial practice had the benefit of always practicing a 1.5:1 asymmetry for the final stride of acquisition,

and random practice experienced asymmetries at or close to 1.5:1 at some point during their acquisition experience. Additionally, the retention and transfer tests were designed so that the variable limb was going at a faster velocity than the constant limb in order to make those tasks as challenging as possible, while during acquisition all subjects experienced variable limb velocities slower and faster than the constant limb to increase contextual interference and unpredictability. Thus, these data are not generalizable to recall and recognition of asymmetries where the variable limb is moving at a slower velocity than the constant limb.

The distribution of belt speeds (Figure 2) and subjects' measured walking speeds (Table 1) also caused a discrepancy in the implementation of the retention test. Since the average SSWS for all groups was greater than 1.0 m/s, this meant that the 1.5*SSWS experienced during the retention test caused a faster variable limb belt velocity than experienced during acquisition. However, this 1.5:1 asymmetry was chosen to maintain consistency for all groups; if the velocity was set to 0.5+SSWS on the variable limb, than the overall asymmetry would differ between individuals during retention. Moreover, all groups had a similar SSWS, so the retention experience was roughly equivalent for all groups. Still, the retention test here may not have truly reflected recall of a previously experienced walking context for all individuals. Finally, this study did not set the belt velocities to be equal for all groups, but rather set them to be a function of each individual's SSWS. Thus, individuals with a fast SSWS and short leg length may have experienced a walking gait on the constant limb and running gait on the variable limb, which is a different motor pattern likely not saved by these practice paradigms. However,

there were no differences in SSWS or height between groups (Table 1), therefore if this occurred then it likely did not affect one group more than the other.

Conclusions

This study sought to determine if a variable practice paradigm is applicable to improved performance of a predictive gait parameter, mediolateral balance control variability, during learning of a novel asymmetric gait pattern. It was found that random practice results in a significantly higher challenge to balance control during acquisition, but that random blocked and serial practice are not more challenging than each other. On a retention test, random blocked practice had a significantly lower amount of balance control variability compared to random and serial practice. While this may indicate that random blocked practice results in the best retention, this variability was lower than that of symmetric gait, raising questions as to whether gait strategy was actually indicative of better performance. Transfer test data reveal that serial practice resulted in much higher balance control variability compared to the other two groups, indicating the limited generalizability that this practice paradigm provides. Overall, random blocked practice presents a lesser challenge during acquisition, while performing better than random practice during retention and similarly during transfer. Thus, it is likely that random blocked practice meets the optimal challenge required to best drive motor learning during acquisition of this task. These results may help to provide a framework for future rehabilitative protocols using a split-belt treadmill, and help to further clarify the role of error magnitude and direction in locomotor adaptation. Future studies should further investigate this phenomenon by assessing specific biomechanical variables that are

altered as a result of changing practice paradigms, to determine if the balance control differences noted here are the result of a differing kinematic and kinetic strategy invoked by the CNS.

Bridge

This chapter demonstrated that a higher level of contextual interference does indeed promote improved retention and transfer of mediolateral balance control variability, but only to an extent. These findings help to further clarify the role of error variance in locomotor adaptation. However, before making a clinical recommendation about the use of contextual interference in a rehabilitative setting, it is necessary to investigate the gait strategy adopted by each practice group. Such information will lend insight to how error variance may influence mechanical output during and after locomotor adaptation. Using the same data set, Chapter V will provide this analysis.

CHAPTER V

SENSORY PREDICTION ERRORS DURING WALKING RESULT IN RETENTION

AND TRANSFER OF UNIQUE MECHANICAL ADAPTATIONS

This Chapter is, at the time of writing, under first review for publication in the *Journal of Experimental Biology*. Jacob W. Hinkel-Lipsker designed this study, collected the data, and analyzed it. Michael E. Hahn provided mentorship activities, including assistance with study design, general oversight of the project, and editing and finalizing of the journal manuscript.

Introduction

Locomotion is a task that humans can adapt rapidly in an environment that demands a change in lower limb mechanical function. Generally, a locomotor adaptation serves as a means by which the central nervous system (CNS) can minimize a specific cost of walking, such as energy expenditure, balance, or pain (Bastian 2008; Todorov 2004). Also, this adaptation can reflect flexibility within the locomotor control system that allows for the ability of humans to maintain walking performance in the face of new or difficult conditions. While flexibility of gait mechanics may manifest as a permanently different pattern after unilateral lower-limb amputation (Sanderson and Martin 1997) or hemiparetic stroke (Olney and Richards 1996), it has also been reported to be acutely observable within the first 12-15 strides of a new walking context in able-bodied individuals (Prokop et al. 1995). Additionally, biomechanical gait adaptations may occur

due to uneven terrain (Voloshina et al. 2013) or physical constraints such as an active exoskeleton (Banala et al. 2010).

Neurophysiologically, rapid adaptability may occur through the cerebellum, where a sensory discrepancy during locomotion between expected and actual proprioceptive feedback is dynamically detected and corrected through the spinocerebellar tract (Morton and Bastian 2007), providing the cerebellum with the means for direct override of the basic locomotor rhythm provided by spinal pattern generators (Anderson and Grillner 1983; Takakusaki 2013). The cerebellum may also be responsible for updating a feed-forward model as a result of this sensory discrepancy, which is then relayed to premotor cortical areas for updating of the motor plan for locomotion (Blakemore et al. 2001; Galea et al. 2011; Seidler et al. 2013). Therefore, sensory prediction errors during locomotion may be directly responsible for how an individual adapts to a novel gait pattern, as they can be immediately corrected and more permanently planned for through separate processes.

Researchers have made note of this effect during observation of human adaptation to asymmetric split-belt treadmill walking (SBW), an experimental paradigm where two belts on a treadmill are driven at different velocities as a method for inducing a gait asymmetry. For able-bodied individuals who normally walk symmetrically, this method can be viewed as a way to introduce a novel context for walking, and therefore a gait adaptation can be observed over time. During this process, the type of sensory prediction errors encountered during walking seems to affect how individuals adapt their gait pattern. For example, Torres-Oviedo and Bastian (2012) proposed that the distribution of errors incurred during adaptation to SBW ultimately affects the transfer, or

generalizability, of an asymmetric walking pattern to overground walking. Also, Sawers and Hahn (2013) and Sawers et al (2013a; 2013b) have discussed how a gradual introduction of asymmetry (where the belt velocity for one limb increases walking asymmetry over time) leads to better gait performance and reduces practice difficulty compared to a large, sudden introduction of asymmetry (which would create one large stepping error).

Sensory prediction errors have been discussed in the context of motor learning for decades. Shea and Morgan (1979) were among the first to introduce the idea of contextual interference as a way to increase motor learning, where environmental conditions during practice are ordered in a noisy fashion to intentionally induce sensory prediction errors. When contextual interference is used as a training tool for learning of a motor skill, it creates an unpredictability that requires the learner to solve sensory prediction errors instead of solely predicting the required movement parameters for optimal task performance (Lee and Magill 1983). As such, noisy environmental conditions may induce a trial-and-error learning mechanism, where unpredictable sensory feedback ultimately drives the need for individuals to explore the space of potential learning solutions (Wu et al. 2014). Indeed, even in simulations, a noisy optimization algorithm can increase the rate of learning in artificial neural networks (Burton and Mpitsos 1992), highlighting an adaptive learning process that may be applicable to biological systems.

In humans, the method of learning referred to as variable practice has been demonstrated to be an effective tool for the acquisition of novel motor skills, ranging from bimanual coordination tasks (Tsutsui et al. 1998) to basketball shooting (Landin et

al. 1993). In addition, it has been used effectively as a means to refine already acquired motor skills or increase their generalizability to conditions outside of the practice context, with an increased ability for an individual to scale movement parameters following variable practice. Specifically, a positive learning effect of variable practice has been noted in reaching and grasping tasks (Hanlon 1996; Krakauer 2006) and stepping (Pollock et al. 2014) following a hemiparetic stroke, indicating its potential for use in rehabilitative settings. From a motor planning perspective, this enhanced generalizability of a newly learned motor skill to other novel learning contexts may occur because it allows the learner to better refine the abstract rules inherent in a generalized motor program and extract those rules when needed (Wulf and Schmidt 1997).

It remains largely unknown how variable practice influences human locomotor behavior when individuals are asked to adapt their walking pattern to novel contexts. While the studies previously mentioned here by Torres-Oviedo and Bastian (2012), Sawers and Hahn (2013), and Sawers et al. (2013a; 2013b) investigate the effect of sensory prediction errors on locomotor adaptation during SBW, one belt was always driven at a faster velocity than the other. This may have allowed some predictability of sensory feedback and motor parameters. Recent work has shown how, during locomotor adaptation, individuals seem to organize the roles of the two lower limbs into a slow limb and fast limb—with each exhibiting different mechanical output (Ogawa et al. 2014). One way to further increase the amount of noise in the adaptation experience may be to vary the roles of the limbs to prevent one from moving at a consistently fast velocity, thereby preventing the assignment of limb roles.

Recently, we have demonstrated that some error variance during novel gait acquisition allows for optimization of the trial-and-error learning process (Chapter IV). This recent work involved a healthy population, with a group that underwent a random asymmetric SBW acquisition experience, where one belt was driven at random velocities faster and slower than the other belt on a step-to-step basis. This group demonstrated the same amount of generalizability with regards to balance control as a group that was given random blocked practice, where belt velocities changed randomly every 20 strides. In addition, random blocked practice resulted in better retention than serial practice, as shown through lower variability in balance control. This finding was surprising as we expected serial practice to demonstrate the best recall of a gait asymmetry due to the relatively small errors experienced during practice (Crisimagna-Hemminger et al. 2010). One possible explanation for this was that the random blocked practice experience mimicked the retention experience by providing individuals a large error followed by constant belt velocities, allowing for better recall of that process when the retention test began. Also, the large random perturbation induced large errors known to drive generalizability (Criscimagna-Hemminger et al. 2010), but the subsequent phase of constant belt velocities (for 20 strides) may have allowed individuals to find a solution to the presented walking asymmetry. It remains unknown if the mechanical mechanisms used by the random blocked practice group to achieve this balance control solution were different than the mechanical strategies used by the other practice groups. Such knowledge may further clarify the role of error size and variance on adaptability of gait in a novel context.

Thus, the purpose of this study was to explore the effect of variable practice on lower-limb gait mechanics during acquisition, early and late in a retention test, and early and late in a transfer test, for a novel asymmetric gait pattern. In order to test the effects of error size and variance on locomotor adaptation, subjects completed one of three acquisition protocols (from least contextual interference to most): serial practice, random blocked practice, or random practice. Based on previously reported observations with regards to balance control, the following hypotheses were made: 1) during acquisition, the highly variable treadmill belt velocities experienced during random practice would result in large changes in gait kinematics and kinetics, while serial practice would demonstrate gait biomechanics closest to that of symmetric walking. Next, 2a) the similarity between random blocked practice and the prescribed retention test would allow those individuals to have a more immediate recall of the acquisition experience, as demonstrated through differing gait mechanics during early retention compared to the serial and random practice groups. However, by late retention, 2b) the random blocked group's unique mechanics would not persist, as all groups would be fully adapted to the new pattern, with no biomechanical differences between groups. Finally, it was hypothesized that during early transfer 3a) the gait mechanics demonstrated in serial practice would be the most different from symmetric walking, and similar to the retention test 3b) this unique strategy would resolve by the end of the transfer test, with no difference in gait mechanics between groups.

Methods

Recruitment

Forty-eight individuals between the ages of 18 and 50 years old that had the ability to walk on a treadmill for up to 30 minutes were recruited for this study (Table 2.1). Subjects were excluded from participation if they self-reported any cardiopulmonary, neurological, acute (within 6 months) or chronic musculoskeletal injuries to the lower limbs, or if they had any previous experience in walking asymmetrically on a split-belt treadmill. The university Institutional Review Board approved all study protocols and all subjects provided informed consent prior to enrollment.

Study Design and Experimental Protocol

Each subject attended two consecutive days of experimental testing. On the first day, the average time across 4 trials it took them to walk 20 m overground was used to calculate a self-selected walking speed (SSWS). To ensure gait consistency during treadmill walking (Zeni and Higginson 2010) and to collect biomechanical gait data during symmetric walking, subjects were then asked to walk for 15 minutes for an acclimation phase on an instrumented split-belt treadmill (Bertec, Columbus, OH) where the velocity of both belts were tied to their SSWS. After 15 minutes, subjects completed one of three 720-stride acquisition protocols to which they were randomly assigned: serial, random blocked, or random practice. For all acquisition protocols, the non-dominant limb (constant limb) was consistently driven at SSWS (Figure 1), while the dominant limb (variable limb) was driven according to the assigned practice protocol.

Limb dominance was determined as the one the subject would prefer to use to kick a soccer ball.

For the variable limb, subjects in the serial practice group began with belt velocity set to SSWS-0.5 m/s on the first stride, and then the belt velocity increased linearly by 1/720 m/s on every subsequent stride so that on the 720th stride, variable limb belt velocity was SSWS+0.5 m/s. For the random blocked practice group, the variable limb belt began at a random velocity within ±0.5 m/s of SSWS, continued at that velocity for a block of 20 strides, and then randomly changed to a new velocity within ±0.5 m/s of SSWS and within ±0.5 m/s of the previous stride. For the random practice group, the variable limb belt velocity changed randomly every stride within ±0.5 m/s of SSWS and ±0.5 m/s of the previous stride. The belt velocities were preset and organized with respect to practice protocol and SSWS, and then deployed by a custom-written MATLAB script (Mathworks, Natick, MA) to automate control of the treadmill belts. This automation method has been previously established as a way to remove any effect of researcher error on changing belt velocities accurately on a step-by-step basis and ensure that treadmill belts were only accelerating during swing phase of gait as a way to prevent additional perturbations during walking (Hinkel-Lipsker and Hahn 2016a). We have recently demonstrated that the randomization protocols were effective in implementing the belt velocities according to the set boundaries, and that all groups experienced a similar mean and range of belt velocities (Chapter IV).

Subjects were given 24 hours to allow for consolidation of motor memories following the acquisition experience (Brashers-Krug et al. 1996) and for the adapted gait asymmetry to wash out through overground walking. Following the 24-hour period,

subjects were then asked to return, with half of each group completing a retention test and half completing a transfer test. They were only assigned one of two tests to prevent additional practice from occurring as a result of performing both. The retention test was used to measure the ability of individuals to recall a previous practice context and apply the correct motor parameters in that context (Newell 1991; Schmidt 1975; van Kesteren 2012). To apply a previous practice experience, we chose a 1.5:1 (variable:constant) belt velocity asymmetry. It should be noted that subjects with faster SSWS did not experience a full 1.5:1 asymmetry for any step during the acquisition experience. However, this test was chosen in order to maintain the same magnitude of belt velocity changes during acquisition, allow for all subjects to walk at the same asymmetry during retention, and introduce a challenging retention test with a large belt asymmetry. The transfer test was performed to measure how individuals can apply their previous practice experience to a novel walking context (Newell 1991; Schmidt 1975; van Kesteren 2012). We therefore chose a walking context, 2:1 (variable:constant), that had not been previously experienced but ensured that the subjects' dominant limb was not moving so fast as to induce a running gait.

Data Collection

Demographic data, including age, sex, height, and weight, were recorded on the first day of testing. Three-dimensional (3D) marker coordinate data were collected at 60 Hz from 54 reflective markers placed on participants' bony landmarks (Sawers and Hahn 2012) using an 8-camera motion capture system (Motion Analysis, Santa Rosa, CA). Additionally, ground reaction force (GRF) data were collected from two force plates

underneath the two treadmill belts (Bertec, Columbus, OH) at 1200 Hz. These data were synchronized with marker coordinate data using Cortex motion capture software (Motion Analysis, Santa Rosa, CA), and were collected during the final 20 strides of acclimation, and throughout acquisition and retention/transfer.

Data Analysis

Marker coordinate data were low-pass filtered using a 4th order Butterworth with a 5 Hz cut-off frequency, and GRF data were low-pass filtered using a 4th order Butterworth with a 45 Hz cut-off frequency (Sawers et al. 2013a). These data were used to build a 13-segment model with Visual 3D software (C-Motion, Germantown, MD).

Specific spatiotemporal, kinematic, and kinetic variables were calculated for each limb (constant and variable) to help describe the mechanical strategies that each group adopted as a result of their practice experience. In the case of the spatiotemporal and kinetic data, variables were chosen because of their ability to describe specific gait strategies that people adopt during asymmetric and/or novel gait, as previously noted in the literature. Kinematic variables were calculated to observe the changes in lower-limb motion resulting from gait adaptation. Internal joint moments were estimated using an inverse dynamics approach and normalized to body weight. Five different windows of time were used for analysis: acquisition, early retention, late retention, early transfer, and late transfer. The acquisition time window represented all 720 strides. Due to the organization of the practice protocols, specific times during acquisition for each group could not be extracted for analysis because the variable limb belt velocities were not

71

equal for each group. Similarly, gait behavior was not extracted for each velocity because the time during adaptation when a particular velocity was experienced was unique to each group. Therefore, analysis of data during acquisition represented the overall gait strategy adopted, when the variable limb belt was at times both slower and faster than the constant limb belt. Early retention and transfer windows included the first 20 strides for each limb during this test. Late retention and transfer windows included the last 20 strides. These windows were chosen to represent the immediate recall or generalization during early retention and transfer, respectively, while late retention and transfer would represent the ultimate adapted pattern that each group settles into. The descriptions and justifications for the choice of each variable are provided below.

Spatiotemporal – <u>Double support time</u>: This value was calculated as the length of time in which both limbs are in contact with the ground. It has been previously demonstrated that as individuals adapt their gait pattern to a novel asymmetry, double support time becomes more symmetric between limbs (Reisman et al. 2005), indicating predictive control of this parameter (i.e., not dependent on spinal feedback mechanisms). Thus, regardless of whether the faster moving or slower moving limb is leading, double support times would be virtually equivalent if an individual has fully adapted their gait to that asymmetry. <u>Step length</u>: This value was calculated as the anterior-posterior distance from the leading foot calcaneus making contact with the ground at heel strike to the trailing foot calcaneus. Similar to double support time, this metric has been previously demonstrated as one that is under predictive control (Reisman et al. 2005). The difference in step length between limbs becomes more symmetric as a person adapts their gait.

Mean double support time and step length for each analysis window (acclimation, acquisition, retention/transfer) were extracted as discrete values for statistical testing.

Kinetic – <u>Anterior-posterior GRF:</u> Peak braking force was measured as the minimum value for the GRF time series. This metric has been previously used as an indicator of predictive control of ankle stiffness, where more adapted individuals are better able to reduce braking force, increasing walking efficiency. In contrast, less adapted individuals have a higher braking force, slowing the forward velocity of the center of mass, at the expense of increased energy expenditure (Ellis et al. 2013; Mawase et al. 2013; Ogawa et al. 2014). <u>Hip extensor moment (HEM):</u> When measured during late swing phase (70-100% gait cycle), this metric indicates control of limb swing velocity, with associated increased energy absorption to slow the velocity of the swing leg (Winter 1992). It is likely that an adapted individual would control their leg swing velocity in a way where higher hip extensor energy absorption would not be necessary, thus minimizing energy expenditure, as higher leg swing velocity requires more work to be performed to slow it prior to heel strike (Doke et al. 2005). <u>Knee extensor moment (KEM):</u> When measured during stance phase, (0-60% gait cycle) the peak knee extensor moment can be used as a measure of loading asymmetry between the two limbs (Roemmich et al. 2012). Compared to using peak vertical GRF to measure limb loading, peak knee extensor moment gives a loading measure relative to the knee joint. It has been acknowledged previously that the knee extensors perform negative work during weight acceptance to prevent excess knee flexion from occurring (Kepple et al. 1997).

Kinematic – Sagittal-plane ankle, knee, and hip angles were calculated to provide descriptions of the overall motion of the lower limbs, and to determine if there were

differences in that motion according to practice group. <u>Peak ankle dorsi- and plantar flexion angles (ADA and APA)</u>: These values were calculated for each stride from 30-65% GC as the maximum and minimum angles, respectively. <u>Peak knee flexion angle (KFA)</u>: During stance this value was calculated as the minimum sagittal plane knee angle from 0-65% GC. <u>Peak hip flexion and extension angle (HFA and HEA)</u>: These values were calculated as the maximum value during swing (65-100% GC) and minimum value during stance (0-65% GC). Each measurement was normalized to one gait cycle (1-100%), or the time from heel strike on one limb to the subsequent heel strike on the same limb. To perform statistical analyses, discrete peak values were calculated from each gait cycle and averaged to find the mean peak value across all strides for each discrete variable. Ensemble curves were also calculated to provide a qualitative time-series average for each parameter during each of the five time windows. Kinematic and kinetic calculations were performed using Visual 3D (C-Motion, Germantown, MD), and variable extraction was performed using MATLAB (Mathworks, Inc., Natick, MA).

Statistical Analysis

To analyze the effect of practice group on biomechanical gait variables for each limb, five two-way multivariate analyses of variance (MANOVAs, $\alpha = 0.05$) were run using SPSS v.23 (IBM, Armonk, NY); one for each of the five time windows. Practice group (serial, random blocked, and random) and limb (constant and variable) were included as independent variables, and the ten aforementioned gait variables as dependent variables. Outliers and assumptions of univariate and multivariate normality, multicollinearity, homogeneity of covariance, and homogeneity of variance were tested

for and transformations were made if these assumptions were not met. If significant main effects or interactions were revealed, Bonferroni-adjusted pairwise comparisons were made. Gait behavior during the acclimation phase was included in all statistical tests to examine the difference between each practice group's gait behavior and during acquisition and retention/transfer.

Results

For acquisition, a MANOVA revealed a significant main effect of limb ($F = 3.842$, $p < 0.001$, $\eta_p^2 = 0.183$) and group ($F = 4.119$, $p < 0.001$, $\eta_p^2 = 0.218$), and a significant limb*group interaction ($F = 1.483$, $p < 0.05$, $\eta_p^2 = 0.8$). Pairwise comparisons indicate that random practice had a significantly greater peak HEM during swing on the constant limb compared to acclimation (Figure 5.1a), and on the variable limb (Figure 5.1b) compared to acclimation, serial, and random blocked practice. The random practice group also walked with a significantly greater KEM during stance on the constant limb compared to the other three groups (Figure 5.1c). This group also walked with a significantly shorter step length on the constant limb (Figure 5.1e) compared to all groups and on the variable limb (Figure 5.1f) compared to acclimation and the serial practice group. Finally, random practice resulted in a significantly greater KFA during stance on the constant limb (Figure 5.1d) compared to acclimation and the serial practice group (Table 5.1).

Table 5.1. Summary means of peak values for spatiotemporal, kinetic, and kinematic dependent variables during acquisition. Values were deemed statistically significant when compared to acclimation, when both belts were tied at self-selected walking speed (*, $P < 0.05$), or compared to other groups (†, $P < 0.05$). BF = Braking Force, HEM = Hip Extensor Moment, KEM = Knee Extensor Moment, DST = Double Support Time, SL = Step Length, ADF = Ankle Dorsiflexion, APF = Ankle Plantar Flexion, KF = Knee Flexion, HF = Hip Flexion, HE = Hip Extension

Variable	BF	HEM	KEM	DST	SL	ADF	APF	KF	HF	HE
Units	N/kg	Nm/kg	Nm/kg	s	m	°	°	°	°	°
Constant Limb										
Serial	-2.04	-0.38	0.88	0.12	0.60	10.64	-13.26	-16.48	30.41	-12.52
RB	-1.93	-0.42	0.83	0.12	0.58	10.24	-12.46	-20.57	34.60	-8.24
Random	-2.14	-0.48^{*}	$1.25^{*\dagger}$	0.11	$0.53^{*\dagger}$	9.29	-14.39	$-23.0^{*\dagger}$	31.22	-8.96
Variable Limb										
Serial	-2.02	-0.35	0.84	0.12	0.60	10.05	-14.98	-17.70	31.44	-11.76
RB	-1.93	-0.40	0.73	0.12	0.57	10.22	-14.63	-20.04	33.77	-11.05
Random	-1.72	-0.46^{*}	0.94	0.11	$0.54^{*\dagger}$	10.75	-16.89	-22.30	34.71	-8.18
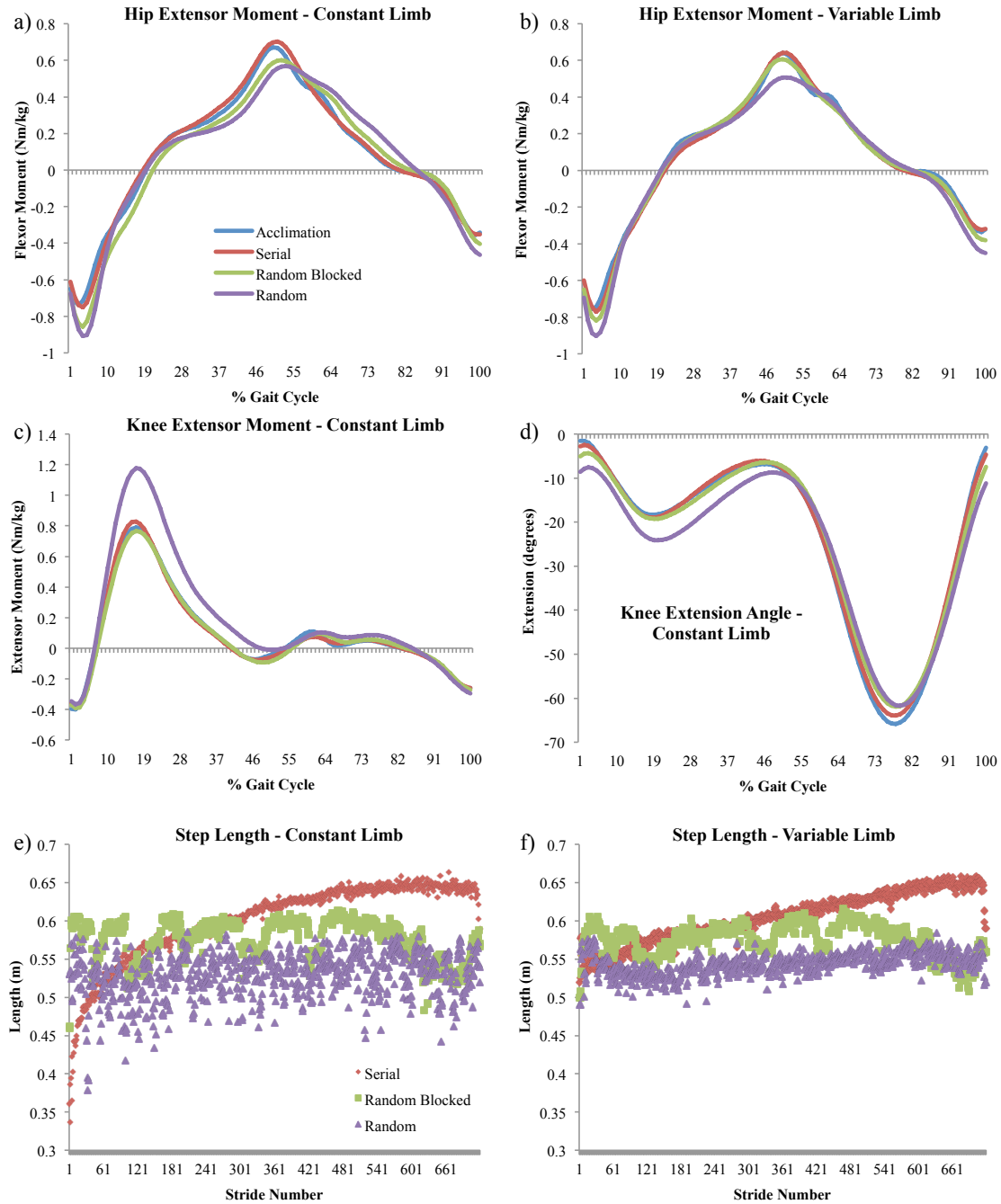
Fig 5.1. Selected ensemble curves (a-d) and step length plots (e-f) representing gait behavior of all practice groups during acquisition.

During early retention, there was a significant main effect of limb ($F = 16.601$, $p < 0.001$, $\eta_p^2 = 0.570$) and group ($F = 4.881$, $p < 0.001$, $\eta_p^2 = 0.278$), and a significant limb*group interaction ($F = 3.029$, $p < 0.001$, $\eta_p^2 = 0.193$). An examination of pairwise comparisons revealed that all groups had a significantly greater HEM during swing on the constant limb compared to acclimation, and all but the random blocked practice group showed the same effect on the variable limb. Random practice had a significantly higher KEM on the constant limb compared to acquisition, while the random blocked practice group's KEM was significantly higher than acclimation on the variable limb. Additionally, all groups had a significantly shorter double support time on both limbs compared to acclimation, and significantly greater plantar flexion during late stance on the variable limb compared to acclimation (Table 5.2).

Table 5.2. Summary means of peak values of all dependent variables measured during early retention (first 20 strides), and late retention (final 20 strides) on the constant (const) and variable (var) limbs. Statistical significance is denoted by * (value compared to acclimation, or symmetric gait, $P < 0.05$). BF = Braking Force, HEM = Hip Extensor Moment, KEM = Knee Extensor Moment, DST = Double Support Time, SL = Step Length, ADF = Ankle Dorsiflexion, APF = Ankle Plantar Flexion, KF = Knee Flexion, HF = Hip Flexion, HE = Hip Extension

Ret.	BF	HEM	KEM	DST	SL	ADF	APF	KF	HF	HE
Units	N/kg	Nm/kg	Nm/kg	s	m	°	°	°	°	°
Early - Const										
Serial	-1.94	-0.57*	1.01	0.09*	0.61	12.81	-10.51	-21.07	34.77	-2.49
RB	-2.03	-0.60*	0.97	0.08*	0.61	12.54	-9.96	-22.84	31.95	-7.55
Random	-1.99	-0.57*	1.27*	0.14*	0.57	12.00	-11.85	-22.80	33.87	-3.42
Early - Var										
Serial	-1.63	-0.52*	0.91	0.10*	0.58	11.73	-21.67*	-21.38	37.44	-7.62
RB	-1.89	-0.49	1.08*	0.10*	0.59	7.07	-23.24*	-23.45	35.49	-10.47
Random	-1.63	-0.52*	0.91	0.10*	0.57	8.25	-23.93*	-19.90	37.09	-5.32
Late - Const										
Serial	-2.05	-0.60*	1.20*	0.10	0.62	12.73	-9.35	-23.09	32.25	-7.59
RB	-2.00	-0.63*	1.01	0.10*	0.60	13.36	-9.25	-23.86*	31.10	-10.35
Random	-2.08	-0.60*	1.36*	0.09*	0.59	13.00	-10.20	-23.06	32.44	-7.73
Late - Var										
Serial	-2.78*	-0.47	1.00	0.11	0.67*	9.04	-19.05*	-21.07	37.87	-11.43
RB	-2.82*	-0.51*	1.15*	0.11	0.64*	5.40	-20.85*	-22.69	35.12	-13.72
Random	-2.69*	-0.53*	1.06	0.10*	0.64*	6.23	-19.56*	-20.24	36.58	-8.22

A MANOVA for the late retention analysis window showed a significant main effect of limb ($F = 15.163$, $p < 0.001$, $\eta_p^2 = 0.548$) and group ($F = 3.628$, $p < 0.001$, $\eta_p^2 = 0.222$), and a significant limb*group interaction ($F = 2.728$, $p < 0.001$, $\eta_p^2 = 0.177$). Pairwise comparisons showed a significantly greater peak braking force for all groups on the variable limb compared to acclimation, and a significantly greater HEM on the constant limb compared to acclimation. For the variable limb, however, only the random blocked and random groups walked with a significantly greater HEM compared to

acclimation. Subjects in the serial and random groups walked with a significantly greater

KEM compared to acclimation on the constant limb (Figure 5.2a), while only the random

blocked practice group had a significantly greater KEM than acclimation on the variable

limb (Figure 5.2b). The random blocked and random groups had a significantly greater

double support time than acclimation on the constant limb, while only random practice

resulted in a significantly greater double support time on the variable limb compared to

acclimation. All groups had a significantly shorter step length on the variable limb

compared to acclimation, significantly less plantar flexion during late stance, and the

random blocked practice group had a significantly greater KFA on the constant limb

(Figure 5.2c).
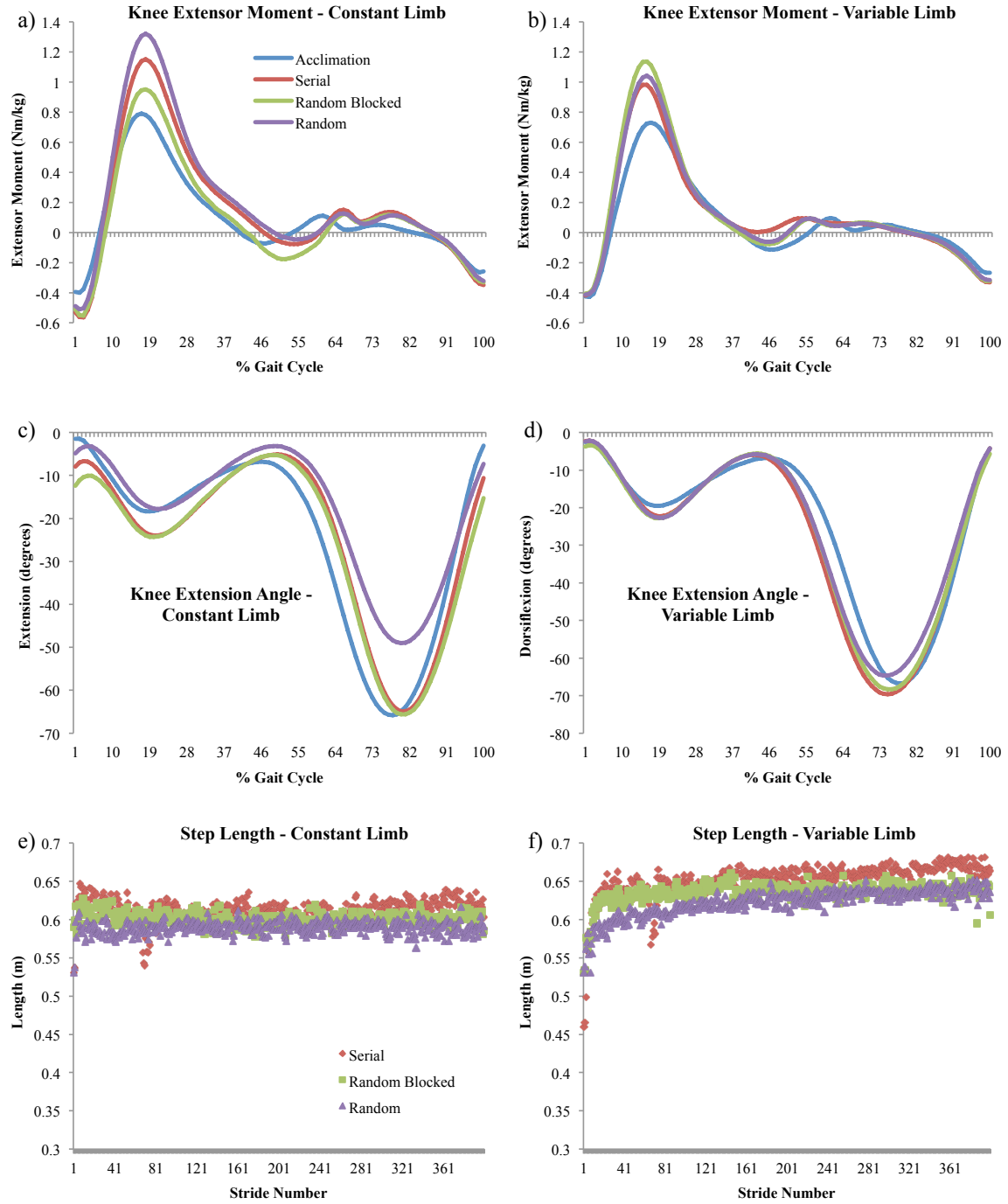
Fig 5.2. Selected ensemble curves (a-d) and step length plots (e-f) during retention of a 1.5:1 gait asymmetry. Ensemble curves represent late retention (final 20 strides) to show persistent adaptations that occurred.

During early transfer, a significant main effect of limb ($F = 21.704$, $p < 0.001$, $\eta_p^2 = 0.638$), group ($F = 6.506$, $p < 0.001$, $\eta_p^2 = 0.342$), and a significant limb*group interaction ($F = 3.598$, $p < 0.001$, $\eta_p^2 = 0.224$) was noted. On both limbs, all groups had a significantly higher HEM during swing compared to acclimation, and random practice resulted in a significantly higher HEM compared to serial practice on the variable limb. The random practice group also demonstrated a significantly greater KEM during stance on both limbs compared to acclimation. All groups had a significantly shorter double support time compared to acclimation on both limbs. The serial practice group had a significantly greater peak ADA during stance compared to acclimation on the constant limb, while the random blocked practice group had a significantly greater APA on the constant limb compared to acclimation, and all groups had significantly less plantar flexion during late stance compared to acclimation on the variable limb. Moreover, all groups walked with significantly greater knee flexion in both limbs during stance, and with significantly less hip extension during stance on the constant limb. However, only the serial practice group had a significantly less hip extension during stance on the variable limb compared to acclimation. Additionally, the serial and random blocked practice groups had a significantly greater peak HFA during swing compared to acclimation (Table 5.3).

Table 5.3. Summary means of peak values for all dependent variables measured during early transfer (first 20 strides), and late transfer (final 20 strides) for the constant (const) and variable (var) limbs. Statistical significance is denoted by * (compared to acclimation, or symmetric walking, $P < 0.05$) and/or † (compared to other groups, $P < 0.05$). BF = Braking Force, HEM = Hip Extensor Moment, KEM = Knee Extensor Moment, DST = Double Support Time, SL = Step Length, ADF = Ankle Dorsiflexion, APF = Ankle Plantar Flexion, KF = Knee Flexion, HF = Hip Flexion, HE = Hip Extension

Transfer	BF	HEM	KEM	DST	SL	ADF	APF	KF	HF	HE
Units	*N/kg*	*Nm/kg*	*Nm/kg*	*s*	*m*	°	°	°	°	°
Early - Const										
Serial	-1.85	-0.74*	1.19	0.09*	0.59	13.24	-11.92	-24.56*	38.22*	1.44*
RB	-1.54	-0.60*	0.96	0.08*	0.55	12.18	-8.04*	-23.78*	35.78*	0.39*
Random	-1.76	-0.78*	1.48*	0.06*	0.56	12.14	-10.90	-28.78*	32.57	-2.19*
Early - Var										
Serial	-1.63	-0.52*	1.21	0.09*	0.57	14.10*	-21.48*	-24.95*	42.03	-2.48*
RB	-1.68	-0.52*	0.96	0.10*	0.55	10.04	-25.41*	-25.52*	40.33	-5.57
Random	-1.75	-0.69*†	1.33*	0.08*	0.52	11.92	-26.39*	-28.62*	37.20	-7.99
Late - Const										
Serial	-2.04	-0.80*	1.65*	0.04*	0.58	12.22	-12.39	-29.48*	37.89	-0.87*
RB	-1.62	-0.62*	1.20*	0.06*	0.49*†	12.69	-7.78*	-28.11*	32.33	-5.02
Random	-1.73	-0.81*	1.79*	0.06*	0.52*	12.28	-9.54	-28.84*	29.10	-6.19
Late - Var										
Serial	-2.64*	-0.52*	1.83*	0.09*	0.63	14.16	-15.08	-30.93*	43.81*	-6.96
RB	-2.56*	-0.51*	1.20*	0.09*	0.65	10.48	-22.05*†	-28.79*	40.67*	-8.18
Random	-2.52*	-0.70*†	1.71*	0.08*	0.60	12.45	-17.96	-32.66*	36.92	-9.99

Finally, the late transfer MANOVA also demonstrated a significant main effect of limb ($F = 16.050$, $p < 0.001$, $\eta_p^2 = 0.566$) and group ($F = 6.204$, $p < 0.001$, $\eta_p^2 = 0.332$), and a significant limb*group interaction ($F = 3.371$, $p < 0.001$, $\eta_p^2 = 0.212$). These main effects are explained by multiple pairwise comparisons (Table 5.3). On the variable limb, all groups had a significantly greater peak braking force compared to acclimation, and a significantly greater HEM compared to acclimation on both limbs. Additionally, serial and random blocked practice resulted in a significantly lower peak HEM compared to random practice. All groups had a significantly greater KEM on both limbs compared to acclimation, as well as a significantly shorter double support time on both limbs. On the constant limb, the random blocked and random practice groups had a significantly shorter step length compared to serial practice and acclimation. Also, the random blocked practice group had a significantly greater amount of APF during late stance compared to acclimation on both limbs, and all groups had significantly greater knee flexion on both limbs compared to acclimation. Finally, compared to acclimation, the serial practice group walked with a more flexed hip throughout the gait cycle, as evidenced by a significantly lower peak hip extension angle during stance on the constant limb (Figure 5.3a) and a significantly greater hip flexion angle during swing on the variable limb (Figure 5.3b). The random blocked practice group also demonstrated a significantly greater hip flexion angle during swing on the variable limb compared to acclimation (Figure 5.3b).
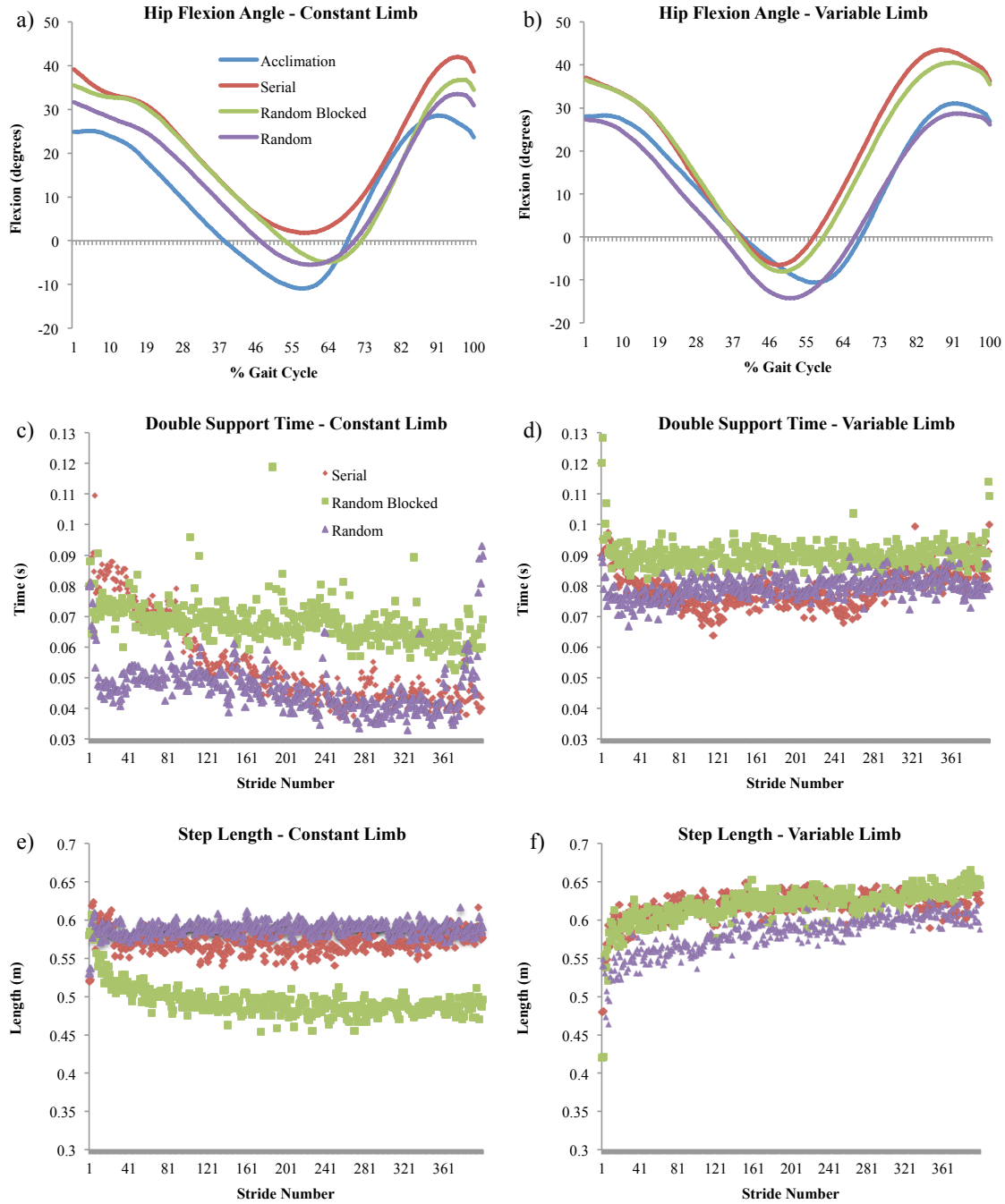
Fig 5.3. Ensemble curves (a-b), double support time (c-d), and step length plots (e-f) during the transfer test. Selected gait variables are shown here, with ensemble curves (Figs 5.3a and 5.3b) representing late transfer (final 20 strides), where differences were occurring after any re-adaptation.

Discussion

These results indicate that the cohort in this study utilized unique gait strategies to accommodate the novel practice experience, and it seems that these adopted practice strategies resulted in different strategies for recall and generalizability of gait asymmetry. With all spatiotemporal, kinematic and kinetic gait data taken together, a few broad narratives emerge that help to explain the overall gait strategy taken by each practice group during both the acquisition and retention/transfer experiences Since these adaptations likely occurred as a result of walking asymmetrically in general and not due to a specific acquisition experience, they are not discussed here. The first narrative is evident in the strategy adopted by the random practice group during acquisition. The second narrative seems to indicate that random blocked practice results in a different ability to recall the learned gait asymmetry. Third, while serial practice may allow for minimization of errors during acquisition, it may not allow a high level of generalizability, as this group demonstrated a careful, guarded gait pattern possibly indicative of sagittal plane imbalance.

To address the first narrative, it seems that the unpredictability associated with random practice resulted in a highly different gait pattern that may demonstrate an apprehension towards use of the variable limb. For example, the random practice group had a significantly greater HEM during swing of the constant limb compared to acclimation, and a greater HEM during swing of the variable limb compared to all practice groups. This may indicate greater hamstring activation in an attempt to slow the velocity of the swing limb prior to foot contact (Winter and Rogers 1992). As limb swing velocity is largely a function of ankle push-off power (Winter 1983; Winter and Rogers

86

1992), the random practice group may be generating less ankle power during terminal stance. This lack of swing control velocity could help to explain other gait adaptations which indicate that the random practice group's strategy is to move from the variable limb onto the constant limb as quickly as possible. When combined with a significantly greater KFA during stance on the constant limb, these values suggest that this group utilized a gait adaptation similar to that of wearing a ski boot or rigid ankle-foot orthosis, where ankle ROM is limited at the expense of greater knee flexion (Abel et al. 1998; Radtka et al. 2005), and thereby an increased KEM is needed to maintain support of body weight.

The ski boot strategy can be further understood if the possible intention of the random practice group was to favor the constant limb over the variable limb for support and propulsion. Ankle dorsiflexion during stance indicates tibial progression while the foot is fixed on the ground, and also eccentrically loads the ankle plantar flexors, storing strain energy. The return of this energy facilitates the push-off drive of the foot off during pre-swing (Don et al. 2007; Orendurff et al. 2005). Given the lack of ankle dorsiflexion exhibited by the random practice group, it is likely that they had reduced plantar flexor lengthening, which would limit strain energy storage and subsequent ankle power generation, thus reducing the forward velocity of the whole-body center of mass. This may represent a method to avoid moving at high velocity onto the variable limb during weight acceptance.

The first hypothesis of this study stated that random practice would be most difficult, and the results discussed here largely support this hypothesis. Additionally, these findings further explain our previous findings, which showed that random practice

posed a greater challenge to balance control compared to the other training groupsChapter IV). It should be noted that these adaptations by the random practice group occurred with approximately equal amounts of time with the variable limb belt moving slower and faster than the constant limb. Therefore, these adaptations are considered a response to a variable gait, not to a specific asymmetry.

The second narrative arising from the results of this study highlight the strategy utilized by the random blocked practice group during the retention test. As previously noted, the retention test involved treadmill belts set to a consistent 1.5:1 of SSWS (variable:constant limb) asymmetry for 400 strides for all groups. One notable aspect of this retention test is that despite all groups being given the same asymmetry, each group demonstrated the acquired gait pattern using different biomechanical patterns. This lends credence to the thought that practice scheduling specificity ultimately impacts how a novel gait pattern is acquired. For the random blocked group, this pattern was recalled in a number of ways. One, the serial and random practice groups seemed to adopt a strategy of using the constant limb as a reference (Ogawa et al. 2014; Hinkel-Lipsker and Hahn 2016b), where walkers favor the slower moving belt during a bout of asymmetric SBW. The serial and random practice groups used a significantly greater KEM during stance compared to symmetric walking conditions. Conversely, the random blocked practice group had a significantly greater KEM on the variable limb compared to the other groups. This pattern was demonstrated early in the retention test and persisted until the end of the test, indicating that this strategy did not change as these individuals experienced the asymmetric gait for a second day.

Increased KEM discussed above was likely the result of an increased GRF and a relatively stiff knee joint, as a result of these individuals placing more body weight on this limb and utilizing the knee extensors to minimize flexion during weight acceptance. An increase in knee joint stiffness helps to elucidate the strategy utilized by the random blocked practice group. It has been previously noted that a relationship exists between knee joint stiffness and running velocity, where a faster velocity results in increased joint stiffness as a way to maximize energy efficiency (Arampatzis et al. 1999; Butler et al. 2003; Kyrloainen et al. 2000). It is possible that the random blocked practice group was able to match their knee joint stiffness to the velocity of the treadmill belt on each limb as a way to maximize economy of motion in this asymmetric walking state. The relationship between gait adaptation and treadmill belt velocity has been recently demonstrated in the frontal plane, where individuals seem to match their lower limb kinetics during single limb support with the velocities of the treadmill belt over time (John et al. 2012; Roper et al. 2017). In the present study this strategy was recalled by the random blocked practice group and did not change during retention test, showing that this strategy was recalled from the acquisition experience. Since the other two practice groups had a higher KEM on the constant limb during retention, it appears that their practice experience was not conducive to this type of control of lower-limb kinetics.

The third narrative described above highlights the serial practice group's generalization of the learned gait asymmetry during a transfer test. The most striking finding in this narrative is that during the transfer test this group had significantly less hip extension during stance compared to acclimation. This was especially the case in the constant limb, where the hip remained mostly flexed throughout stance phase. This

adaptation may indicate a forward trunk lean, which has been observed previously in elderly walkers, who lean forward at the trunk during gait as a way to maintain balance and reduce the work performed at the knee and ankle (DeVita and Hortobagyi 2000). This adaptation is considered to be predictive, occurring proactively as a protective mechanism to reduce the likelihood of a backward loss of balance by maintaining a more anterior whole-body COM position (Bhatt et al. 2006; Pai et al. 2003). Our group has previously observed the serial practice group's inability to control foot positioning during the transfer test in the frontal plane, where they had significantly greater balance control variability compared to the other two groups (Chapter IV). , A strategy of a more anterior COM positioning may have been employed by the serial practice group to ensure sagittal plane balance. This has been described as a common means to achieve walking stability (Lockhart et al. 2003).

Remarkably, the conservative COM positioning mechanism was not in place for the serial practice group during acquisition, where very few biomechanical adaptations to the serial practice experience were observed. Changes in hip kinematics were the only notable adaptation occurring during the transfer test that separated the serial practice group's walking strategy from the others. It appears the predictability of the linear increase in variable limb belt velocity may have allowed this group to effectively predict the variable limb belt velocity from step to step, allowing them to essentially mimic a symmetric gait pattern. However, when presented with the novel 2:1 transfer test asymmetry on the next day, the serial practice group attempted to reproduce their symmetric gait pattern again. This was demonstrated by the lack of change in biomechanical measures, leaving them in a more unbalanced state, compensated for by

leaning forward with the trunk in the early portion of the transfer test. Once they reached a more balanced state, these individuals seem to have settled into the conservative pattern, as the forward trunk lean persisted until the end of the transfer test. These results highlight the inability of this group to generalize their learned gait asymmetry to a novel context, potentially due to the predictability of their acquisition experience allowing a minimization of stepping errors. The need for large errors during motor learning to drive generalizability has been well-documented (Crisimagna-Hemminger et al. 2010; Shadmehr and Mussa-Ivaldi 1994), but the relative efficacy seems to be task-specific. The results of this study lend support to the idea that large prediction errors may drive generalizability during adaptation specifically in a locomotor task (Torres-Oviedo and Bastian 2012).

Limitations

A few limitations may have impacted the results of this study. First, the measured gait parameters were averaged across the entire acquisition experience, which may have moderated the measured effect of some adaptations because the variable limb was at times slower and at times faster than the constant limb. However, group comparisons could not have been made if the acquisition analysis was separated into smaller time windows because the variable limb was not moving at the same velocity for all groups during any given window. Thus the time windows could not be matched for belt velocity because those specific gait asymmetries occurred at different points of time for each group. Analysis of the overall acquisition experience provides a snapshot of the overall strategy adopted by individuals due to variability on one belt, not necessarily a faster or

slower belt. Therefore, this study helps to address the role of error size and variance in locomotor adaptation, but not necessarily direction or timing of errors. A second limitation is that the study design allowed for the random blocked group to practice walking at only 32 different asymmetries, while the serial and random practice groups experienced up to 720 different asymmetries, with an equal amount of time where the variable limb belt was slower and faster than the constant limb belt. The randomization function used here and the boundaries placed on it may have made for an experience where the random blocked practice group walked more frequently at a faster velocity than a slow one, effectively making for more practice closer to the 1.5:1 retention asymmetry. Analysis from our previous work indicates that the median velocity for this group was slightly higher than the others and more clustered towards the higher end of the velocity boundaries (Figure 4.2). A third limitation was that subjects were not tested for recall or generalizability when the variable limb belt was slower than the constant belt, even though they received practice for about half of the acquisition phase at such an asymmetry. Therefore, these results cannot be extrapolated to all possible split-belt walking asymmetries. Finally, all subjects did not walk at the same absolute velocities for each belt, but rather the velocities were a function of their measured SSWS. It is possible that subjects with a faster SSWS and shorter leg length may have been more challenged at high velocities compared to other individuals. However, there were no differences in SSWS or body height among groups; therefore the group-wide comparisons were not likely affected. Making the practice protocols a function of SSWS also meant that not all subjects experienced the 1.5:1 asymmetry used for retention during acquisition. This means that the retention test may not have truly tested for recall. Still, the largest

difference for subjects between the maximum variable limb belt velocity during

acquisition and retention was about 0.3 m/s. Additionally, the difference in gait behavior

noted in this study between retention and transfer tests indicates that subjects during

retention were not generalizing their acquisition experience to a truly novel context.

Future Work

The three narratives discussed in this section highlight the differential gait

behavior exhibited as a result of the acquisition experience of a novel gait pattern. From

this behavior, multiple future research directions may help to further clarify the role of

sensory prediction errors on locomotor adaptation. First, certain gait parameters

previously established as clear markers of predictive locomotor adaptation, such as

double support time (Reisman et al. 2005), step length (Reisman et al. 2005), or braking

GRF (Mawase et al. 2013) were not as evident in the present study. However, the

previous studies utilized a post-adaptation washout period on the treadmill, where the

predictive adaptations are considered evident once a gait asymmetry is removed. The

post-adaptation period was not measured in the present study. Future studies investigating

the effect of variable practice on the ability to de-adapt may be better suited to utilize

these parameters. Second, the study cohort in the present study represented a young,

healthy population, and therefore the effect of variable practice may not be applicable to

other populations such as the elderly or individuals with gait deficiencies. If these

populations have a loss of somatosensory information (or a decreased ability to integrate

and process it), the ability of these individuals to adapt to a novel gait pattern may be

reduced (Bunday and Bronstein, 2009). In turn, future studies could help to elucidate

whether the variable practice effect demonstrated in the present study can positively affect locomotor adaptation in other populations. Finally, this study observed learning in an acute sense, with subjects being tested for retention or transfer 24 hours after a novel acquisition experience. It remains unknown how a novel gait pattern is adapted to and stored when individuals are given multiple bouts of practice over longer periods of time. It is possible that a repeated training intervention could be used as a rehabilitative tool, where populations with gait deficiencies could be trained to walk overground with a new locomotor pattern after frequent practice bouts.

Conclusions

This study investigated the effects of serial, random blocked, and random training conditions on locomotor adaptation to a novel gait. It was found that 1) random practice, the most variable condition, resulted in the greatest challenge during acquisition, 2) random blocked practice, with large perturbations followed by brief periods of constant belt velocities, resulted in the best retention of a learned gait asymmetry, and 3) serial practice, which allows for error minimization during acquisition, did not lead to a high level of generalizability to a novel context on a transfer test. Taken as a whole, these results support previous findings from Chapter IV, which showed that random blocked practice led to the best ability to recall and generalize a novel walking pattern with regards to lateral balance control. In the present analysis, the random blocked practice group was observed to walk in an efficient manner during a retention test, indicating high recall, and better than the serial practice group during a transfer test. In addition, very few mechanical differences existed between the random blocked and random practice groups

on the transfer test, indicating an equal amount of generalizability. This information, combined with the observation that random practice was substantially more challenging during practice, may indicate that random blocked training represents an optimal amount of prediction error during acquisition. The findings of this study support the idea that error size and variance does affect an individual's ability to adapt to a novel gait pattern and can greatly alter the mechanical strategies employed by these individuals when asked to recall or generalize their acquisition experience. Random blocked practice may represent the most optimal level of error size and variance, indicating that individuals may need to be given time to find solutions to large sensory prediction errors during locomotor adaptation.

Bridge

Chapter IV provided analysis of the contextual interference effect during gait adaptation when applied to a task-related outcome, mediolateral balance control variability. This chapter helped to reveal some of the underlying biomechanical strategies adopted by each group. Next Chapter VI will attempt to make these noted group effects more applied, by reducing this large data set to a clinically measurable level. If this data set could be reduced to a small amount of important variables that describe the adaptation and group effects noted in Chapters IV and V, then recommendations can be made with regards to how to apply this work to a rehabilitative protocol.

CHAPTER VI

A CONTEXTUAL INTERFERENCE PARADIGM DRIVES NOVEL KINEMATIC

SOLUTIONS DURING ASYMMETRIC SPLIT-BELT TREADMILL WALKING

This Chapter is currently unpublished. Jacob W. Hinkel-Lipsker designed this study, collected the data, and analyzed it. Michael E. Hahn provided mentorship activities, including assistance with study design, general oversight of the project, and editing and finalizing of the journal manuscript.

Introduction

Human locomotion requires a certain amount of coordinative flexibility in order to accommodate changing environmental demands such as uneven terrain while maintaining balance. In highly acute situations, such as a rapidly applied resistance to the leg (Noble and Prentice 2006; Reisman et al. 2010), the human central nervous system (CNS) must quickly implement a new coordination solution for all degrees of freedom that still maximizes walking ability. This phenomenon has been reported as evidence of gait adaptation (Bastian 2008), which can become more permanent over time following a musculoskeletal injury, neurological injury, or following repeated bouts of gait rehabilitation. As repeated exposure to a specific environmental condition occurs, individuals become more capable of quickly switching to that adapted pattern, and back to the original pattern when the stimulus is removed (Bastian 2008).

Experimentally, gait adaptations can be studied using an asymmetric split-belt treadmill walking (SBW) protocol. This protocol involves driving the two belts of a split-

belt treadmill at different velocities, effectively inducing a limp. When subjects enrolled in this type of experiment are able-bodied and naturally walk symmetrically, a forced asymmetry can be viewed as a novel walking environment to which subjects must adapt over time. In recent decades, researchers have used this paradigm to describe gait adaptation in terms of changes in lower-limb mechanics over time. For example, Dietz (1994), Reisman et al. (2005), and Morton and Bastian (2006) noted that when able-bodied individuals are given a novel gait asymmetry, they make alterations to their step length, time spent in double support, and interlimb coordination even when belt velocities do not change. Feed-forward adaptations such as these are likely mediated in the cerebellum, since individuals with cerebellar damage do not exhibit changes when given an asymmetric SBW paradigm (Morton and Bastian 2006).

Evidence of specific feed-forward adaptations and their neural control has led to a more applied approach, where asymmetric SBW has been explored as a potential way to rehabilitate populations with gait asymmetries. For example, when those with hemiparetic stroke are given a bout of asymmetric SBW (where their paretic limb is driven faster than the other limb), there have been measurable improvements in step length (Reisman et al. 2007), double support (Reisman et al. 2007), and plantar flexor moment (Lauziere et al. 2014) symmetry. As a whole, asymmetric SBW research on able-bodied individuals has provided the fundamental knowledge for design of interventions to bring asymmetric walkers closer to the ability to walk symmetrically.

Other recent work has sought to fine-tune the asymmetric SBW exposure in order to maximize its effect. This work has helped to demonstrate that the manner in which a gait asymmetry is introduced influences how it is ultimately acquired and stored. This

idea stemmed from previous findings on the role of sensory prediction errors in motor learning, where a discrepancy between predicted and actual sensory feedback drives a correction process to mechanical limb output (Miall and Wolpert 1996; Tseng et al. 2007). In the case of gait adaptation, repeated exposure to sensory prediction errors over time induces a change in mechanical gait parameters in an attempt to find a coordination solution that best minimizes sensory discrepancies (Bastian et al. 2008; Tseng et al. 2007). In a recent study by Torres-Oviedo and Bastian (2012), it was noted that subjects who experience large sensory prediction errors often attribute those errors to environmental conditions rather than their own internal errors. It was further postulated that large sensory prediction errors impact how the new asymmetry is learned, as treadmill to overground transfer was limited in the individuals who experienced these errors during the adaptation process. These findings have been generally supported, by recent demonstration that a gradual introduction of small errors during an acute bout of asymmetric SBW leads to improved retention and transfer of frontal (Sawers et al. 2013) and sagittal plane (Sawers and Hahn 2013) balance compared to a sudden introduction of large errors.

Though it has been shown that sensory prediction error size during gait adaptation can impact the mechanical strategy used, it is necessary to better understand the relationship between sensory prediction errors and gait performance. Some researchers have speculated that it is possible that error variance, in addition to error size, may also impact how individuals adapt their gait (Davidson and Wolpert 2003; Torres-Oviedo and Bastian 2012). This concept has been studied in motor learning literature for decades as contextual interference, representing a noisy ordering of practice conditions (Shea and

Morgan 1979). While this training tool has positively influenced motor learning of sport-specific tasks such as badminton serve accuracy (Wrisberg and Liu 1991) and basketball shooting (Landin et al. 1993), and rehabilitative tasks such as reaching after stroke (Hanlon 1996; Krakauer 2006), it has rarely been studied in the context of gait adaptation. During motor skill practice, variability in practice conditions makes feed-forward prediction of successful movement parameters challenging, inducing a trial-and-error exploration of potential coordination solutions (Wu et al. 2014). One way to apply this paradigm to asymmetric SBW would be to require one belt to move at random velocities with every step while the other is held constant. This would force the walker to use the trial-and-error process to explore a range of experienced gait asymmetries, possibly allowing them to find a solution at each combination of belt velocities. One other study introduced a similar paradigm, however in that study the belt with variable velocities was always moving faster than the constant belt (Torres-Oviedo and Bastian 2012). This consistency may have allowed for individuals to assign a predictable role to the limb that is moving faster compared to the slower limb (Ogawa et al. 2014; Roper et al. 2017), in essence making parameter selection more predictable. If the belt with varying speeds provided a range of both faster and slower speeds than the constant belt, then this role assignment would be less achievable, in turn making parameter selection less predictable.

There is currently some debate among research groups regarding how to best measure gait adaptation and learning. When investigating motor learning of a task with a more concrete goal, such as shooting a basketball, success can be measured in terms of how many shots are made. However, during walking the task goals are not as obvious.

99

This has led to researchers taking different approaches towards quantification of walking performance. Some have sought to quantify walking performance through the use of simulations, where different task goals can be modeled as a cost function that the CNS would seek to optimize; such as energy expenditure, balance, or pain (Bastian 2008; Emken et al. 2007; Todorov 2004). Many other studies, some of which have been mentioned here, have used a variety of spatiotemporal, kinematic, or kinetic measures to describe gait adaptation. The ambiguity behind measurement of gait performance has created a need to clarify which outcome measures are most demonstrative of the underlying coordination strategy implemented by the CNS. This clarification would help to provide a bridge between what is currently understood about the fundamental nature of gait adaptation and its application to clinical implementation.

One way to clarify the most demonstrative measures of coordination strategy is to make use of the large amount of kinematic information available during a gait analysis; separating the coordinative features which indicate the underlying motor control of the system from random noise. Because the CNS affects many degrees of freedom leading to a coordinated solution during walking, a reduction of available kinematic data to a set that helps to explain more important coordination patterns among these variables may allow for future research to be more targeted in measuring gait adaptation outcomes. Many studies have used principal component analyses (PCA) for data reduction to answer a number of different clinical gait analysis questions in populations with walking deficiencies. For example, Olney et al. (1998) used PCA to reduce a large set of kinematic gait data collected from a sample of post-stroke individuals. Deluzio and Astephen (2007) used a similar analysis to reduce a data set from patients with knee

osteoarthritis. For each of these studies, a list of underlying coordinative structures were extracted to better explain the overall gait strategy adopted by these populations.

Once these underlying structures are known, there is an additional challenge of how to assess them in a clinical setting where access to the laboratory-based optical motion capture systems may be limited. Recent technological developments in inertial measurement units (IMUs) may provide a portable, lower-cost alternative to these systems. These devices, equipped with accelerometers, rate gyroscopes, and magnetometers, can provide segmental kinematic data almost as accurately as the gold standard optical motion capture systems (Bolink et al. 2016; Esser et al. 2012). In addition, recent work has provided algorithms for accurate calculation of joint angles from IMU data (Seel et al. 2014), making use of these devices outside of a research laboratory more feasible. Prior to use of IMUs in measurement of gait adaptation, there is a need to solidify what, in terms of lower-limb kinematics, clinicians should be measuring. Of particular interest is whether specific coordinative structures change depending on the rehabilitation protocol.

Therefore, there were two main purposes of this study. First, this study sought to identify the underlying kinematic coordination patterns during acquisition, retention and transfer of a novel bout of asymmetric SBW in able-bodied individuals. The second purpose of this study was to observe whether sensory prediction error variance through contextual interference during acquisition had an influence on how individuals structure those patterns, and if it affects structuring during retention and transfer. Such information would help to clarify the relationship between sensory prediction errors and gait adaptation, and explain the most important coordinative structures that are implemented

as a response to those errors. These outcomes would provide a means to apply fundamental behavioral knowledge of human gait adaptation to a clinical rehabilitation setting.

Methods

Recruitment

Forty-eight able-bodied individuals were asked to participate in this study. Inclusion criteria for participation required subjects to be between 18 and 50 years of age and be able to walk unassisted on a treadmill for up to 30 minutes. Exclusion criteria were any self-reported musculoskeletal, cardiopulmonary, or neurological injuries, as well as any experience walking asymmetrically on a split-belt treadmill. The university Institutional Review Board approved all study protocols, and all subjects provided written informed consent prior to enrollment in this study.

Study Design and Experimental Protocol

Subjects attended two days of testing separated by 24 hours. On the first day of testing, subject's self-selected walking speed (SSWS) was measured by calculating the average of 4 times walking across a 20 m walkway. Once this was recorded, all subjects were given a 15-minute acclimation phase where both belts on an instrumented split-belt treadmill (Bertec, Columbus, OH) were driven at their SSWS to promote gait consistency (Zeni and Higginson 2010). Following this phase, subjects completed a 720-stride asymmetric acquisition phase, where their non-dominant limb was driven at their SSWS for all strides (termed the constant limb), while the dominant limb was driven according

to one of three randomly assigned practice paradigms (termed the variable limb). Each subject's dominant limb was recorded as the one that they would use to kick a soccer ball.

The three practice protocols were designed to reflect different levels of contextual interference. As the second purpose of this study was to determine the role of error variance in the structuring of lower-limb coordination, the assumption was made that higher levels of contextual interference would result in more error variance. This assumption is justified by our recent work, which showed that increasing contextual interference resulted in more variability in frontal plane balance control (Chapter IV). One of the three practice paradigms, serial practice, was the protocol with the lowest amount of contextual interference. Subjects in this practice group began with their variable limb being driven at SSWS-0.5 m/s for the first stride. Over the 720-stride acquisition phase, this belt velocity increased linearly until it reached SSWS+0.5 m/s on the final stride. Hence, for each stride the variable limb belt velocity increased by 1/720 m/s. The random blocked practice group represented the next lowest level of contextual interference. These individuals had their variable limb driven at a random velocity that remained consistent for 20 strides and then changed to a new random velocity. In total, subjects in this group were exposed to 36 blocks of 20 strides, with each block at a random velocity within ± 0.5 m/s of their SSWS and ± 0.5 m/s of the previous block to limit the magnitude of velocity changes to a safe range. The third group, random practice, had their variable limb belt driven at a random velocity that changed with every stride. This group represented the highest level of contextual interference in the study (Figure 2.1). All protocols were preset and randomized according to each subject's SSWS and

assigned practice group. Treadmill belt velocities were automatically controlled by a custom-written MATLAB script that commanded the treadmill belts to change speeds while the subject's foot was in swing phase to prevent additional perturbations (Hinkel-Lipsker and Hahn 2016a; Chapter III).

Subjects were asked to return 24 hours later to allow for consolidation of motor memories following the acquisition period (Brashers-Krug et al. 1996), and time for the gait adaptation to wash out through over ground walking. On the second day, half of the subjects were assigned to a retention test and half to a transfer test. The retention test was used to measure how well subjects recalled the parameters required to successfully walk a previously experienced practice context (Newell et al. 1991; Schmidt 1975; van Kesteren et al. 2012). Therefore, all subjects were asked to walk for 400 strides at a 1.5:1 (variable:constant limb) asymmetry. The magnitude of this ratio was chosen as it represented the fastest possible variable limb belt velocity and the largest asymmetry between belts experienced during acquisition, thereby perhaps requiring the most unique coordination pattern solutions. The transfer test, was used to test for how well subjects generalized their acquisition experience to a novel walking context (Newell 1991; Schmidt 1975; van Kesteren 2012). To induce a novel walking context that was challenging, but did not require a different gait pattern (e.g., where the variable limb belt was at a running velocity), a 2:1 (variable:constant limb) asymmetry was chosen. One subject in the random blocked group that completed a transfer test was *a priori* removed from analysis because their measured SSWS was above 1.6 m/s, making their variable limb velocity above 3.2 m/s for the transfer test, which is typically a running velocity.

Data Collection and Analysis

On the first day, demographic data such as age, sex, height, and weight were recorded (Table 2.1). Prior to the start of experimentation on both days, 54 reflective markers were placed on participants' bony landmarks (Sawers and Hahn 2012). Three-dimensional marker coordinate data were collected at 60 Hz using an 8-camera motion capture system (Motion Analysis, Santa Rosa, CA) during the acquisition and retention/transfer phases. Simultaneously, ground reaction force (GRF) data were collected at 1200 Hz from two force plates (Bertec, Columbus, OH), one underneath each treadmill belt. These data were collected and synchronized using Cortex motion capture software (Motion Analysis, Santa Rosa, CA). Raw marker coordinate data were low-pass filtered with a 4th order Butterworth using a 5 Hz cut-off frequency, and GRF data were low-pass filtered with a 4th order Butterworth using a 45 Hz cut-off frequency (Sawers et al. 2013). These data were used to build a 13-segment whole-body model using Visual 3D (C-Motion, Germantown, MD).

From this model, lower-limb kinematic data were extracted from Visual 3D. One purpose of this study was to reduce data to a small set that could be measured outside of a research laboratory. Therefore, one criterion for variable selection was the ability of a variable to be measured by a typical IMU. Variables were extracted from seven segments (foot, shank, and thigh of each leg, and the pelvis) in two planes of motion (sagittal and frontal) to describe the segmental linear velocities and accelerations, angular velocities and accelerations, or orientations (in the case of the pelvis). Sagittal plane ankle and knee joint angles, as well as sagittal and frontal plane hip joint angles were also calculated. Additionally, pelvic orientation data were extracted for sagittal plane (tilt) and frontal

plane (obliquity). Lastly, whole-body center of mass (COM) velocity and acceleration were extracted. For a full list of variables, see Table 6.1.

Table 6.1. List of variables chosen for principal component analysis.

Center of Mass:	**Thigh (both limbs):**	**Shank (both limbs):**	**Foot (both limbs):**
M/L linear velocity	+ Linear velocity	+ Linear velocity	+ Linear velocity
M/L linear acceleration	– Linear velocity	– Linear velocity	– Linear velocity
Pelvis:	+ Linear acceleration	+ Linear acceleration	+ Linear acceleration
Tilt	– Linear acceleration	– Linear acceleration	– Linear acceleration
Obliquity	+ Angular velocity	+ Angular velocity	+ Angular velocity
Hip Joint (both limbs):	– Angular velocity	– Angular velocity	– Angular velocity
Flexion (swing)	+ Angular acceleration	+ Angular acceleration	+ Angular acceleration
Extension (stance)	– Angular acceleration	– Angular acceleration	– Angular acceleration
Abduction (swing)			
Adduction (stance)			
Knee Joint (both limbs):			
Flexion			
Extension			
Ankle Joint (both limbs):			
Plantar flexion			
Dorsiflexion			

Next, peak values from each kinematic variable were calculated using MATLAB (Mathworks, Natick, MA) for each full gait cycle, defined as the time between the heel strike on one limb to the subsequent heel strike of the same limb. For segmental linear and angular velocities and accelerations, both the positive and negative peaks were extracted without any temporal restrictions. For joint angles, peak ankle plantar flexion and dorsiflexion during stance, knee flexion and extension during stance, hip flexion during swing and extension during stance, and hip abduction during swing and adduction during stance were calculated. These angles were chosen based on their overall ability to

106

describe gait, and therefore restricted to certain temporal windows. Peak pelvic anterior and posterior tilt, obliquity towards the constant and variable limbs, COM velocity in the direction of the constant and variable limbs, and positive and negative COM acceleration were also extracted. Peak values for each gait cycle were averaged across each test (acquisition, retention, transfer), making for 120 total variables for each subject for each test.

Statistical Analysis

To reduce this high-dimensional data set, a PCA was performed on each of the three tests (acquisition, retention, transfer). This method was chosen as it represents an unbiased approach to reduction of gait data, where the researcher is not required to make *a priori* decisions about which variables are of most interest (Daffertshofer et al. 2004). Briefly, this analysis works by transforming a set of input data into orthogonal variables known as principal components (PCs). Each PC is composed of a linear combination of the original input data, and is ranked compared to the other PCs according to how much variance in the original data set it explains. Each PC is calculated through an eigenvalue decomposition of the covariance matrix derived from the original data set. As such, the PC associated with the highest eigenvalue has an axis that explains the most variance in the data set, the PC with the second highest eigenvalue explains the second most variance, and so on. For a more in-depth explanation of the PCA methodology applied to gait, please see Daffertshofer et al. (2004).

Prior to the PCA implementation, all data were centered to a zero mean and standardized using inverse variable variances as weights. To determine how many PCs to

retain for further analysis, a scree plot for each test (acquisition, retention, transfer) was

generated and used for extraction of PCs for further analysis. There were a number of

reasons why the scree plot test was chosen as the method for determining which PCs to

retain. This decision occurred as a part of the *post hoc* analysis of the PCA, and is

presented in greater detail in the discussion section. The cut-off point on the scree plot

was determined as the point where the first major inflection point occurs (Zhu and

Ghodsi 2006). This point often distinguishes PCs with meaningful information from

those representing random variation (Olney et al. 1998). Following these decisions, a

varimax rotation on the new, reduced data set was performed. The varimax method of

factor analysis, which rotates the subspace of the retained data set (Abdi 2003), was used

to minimize the number of variables with a high amount of loading on each PC

(Milovanovic and Popovic 2012). Variable loading represents how much each input

variable explains a single PC, or its relative weight on a PC, and was measured using the

absolute value of the standardized coefficients previously calculated. All coefficients

greater than or equal to 0.32 were deemed to be "non-trivial", or variables that have at

least a minimal level of influence on the amount of variance that a PC explains (Brown

2009; Comrey and Lee 1992). Finally, each subject's PC score, or the projection of each

observation onto the PC subspace, was calculated and used to further examine group

differences, where the spread of each group along two PC axes could help to explain a

specific coordinative strategy implemented by that group.

Results

The PCA performed on the acquisition data set revealed that while many PCs explained a portion of the variance and had eigenvalues greater than 1, two PCs had substantially higher eigenvalues (to the left of the inflection point) on the scree plot (Figure 6.1a). These PCs explained approximately 30% of the total variance in the data set, and were retained for further analysis. Similar to the acquisition phase, many PCs in the retention data set combined to form 90% of the variance and had eigenvalues greater than 1. The two PCs to the left of the eigenvalue inflection point were retained for analysis (Figure 6.1b). These PCs combined to contribute to about 45% of the total variance in the data set. Finally, two PCs were also retained from the transfer test based, using the same inflection point eigenvalue threshold (Figure 6.1c). Combined, these PCs explained approximately 35% of the variance in the transfer data set.
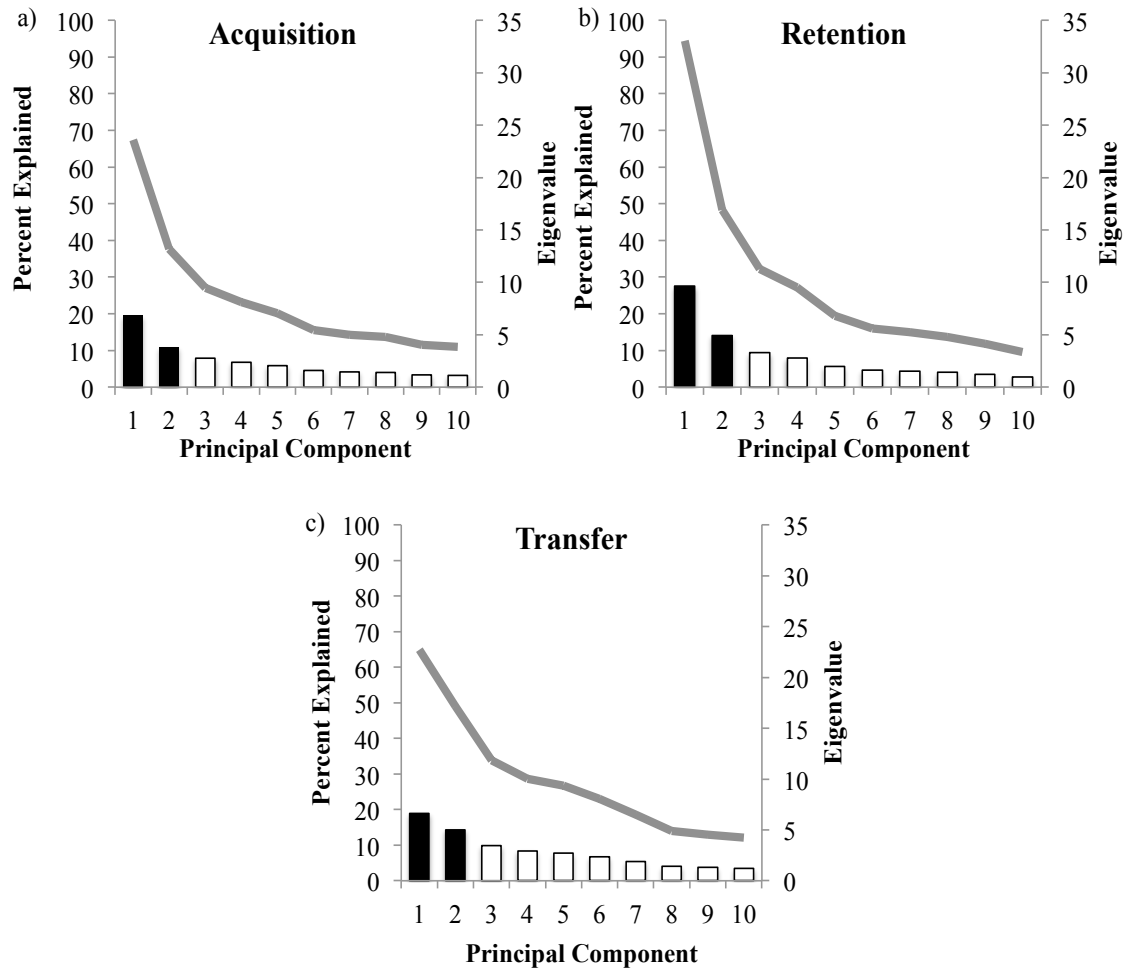
Fig 6.1. Scree plots of principal components (PCs) for acquisition, retention, and transfer of a novel asymmetric gait. Each plot describes the percentage of variance of the entire data set explained by each PC (bars), and the associated eigenvalue of each PC (gray line). For all three tests, many PCs contributed to 90% of the total variance, and many had eigenvalues > 1. Therefore, PC retention was determined using these plots, as the point where the eigenvalues flatten or every PC to the left of the first major inflection (black bars = retained). For acquisition, the first two PCs were retained, explaining ~30% of the variance. Two PCs were also retained for the retention test, explaining ~45% of the variance. Two were also retained for transfer, explaining ~35% of the variance.

Variable loadings on each retained PC show that between 0-3 variables had coefficients greater than 0.32. During acquisition, PC1 (19.7% total variance explained) had two variable coefficients above the threshold; variable and constant limb positive peak thigh angular velocity in the sagittal plane (Table 6.2; Figure 6.2a). The acquisition PC2 (11.0% total variance explained) was loaded by frontal plane measures; positive and negative peak linear frontal plane acceleration of the constant limb thigh, and peak positive frontal plane linear velocity of the constant limb thigh (Table 6.2; Figure 6.2a). During retention, PC1 (27.6% total variance explained) was loaded by peak positive linear velocity of the constant limb foot, the only variable with a coefficient greater than 0.32 for this PC (Table 6.2; Figure 6.3a). For retention PC2 (14.1% total variance explained), linear frontal plane negative acceleration of the whole-body COM in the negative direction had the highest loading coefficient, while frontal plane velocity of the COM in the positive direction (towards the variable limb) had the next highest coefficient (Table 6.2; Figure 6.3a). It should be noted that while a negative COM acceleration was labeled as the direction towards the constant limb, it is actually a decreasing COM velocity in a positive direction (towards the variable limb) that results in this peak (Figure 4d). Finally, PC1 for the transfer test (18.9% total variance explained) was not loaded by any variables greater than 0.32, but PC2 (14.3% total variance explained) had two non-trivial variables: positive peak angular velocity of the variable limb foot and shank in the sagittal plane (Table 6.2; Figure 6.4a).

Table 6.2. Variable loading on retained principal components (PCs) for acquisition, retention, and transfer tests. Variables were considered to be non-trivial if their component loading exceeded 0.32. All three tests (acquisition, retention, transfer) retained 2 PCs. PC1 for acquisition was loaded by two variables, positive sagittal plane angular velocity of the thigh for the variable limb (VThiωSagP) and constant limb (CThiωSagP). PC2 was loaded by constant limb thigh frontal plane positive linear acceleration (CThiAFroP) and negative linear acceleration (CThiAFroN), as well as positive linear velocity (CThiVFroP). PC1 during retention is loaded by constant limb foot positive linear velocity (CFooVFroP), and PC2 is loaded by center of mass mediolateral acceleration towards the constant limb (COMAC), and velocity towards the variable limb (COMVV). For transfer PC1, all variables were below the 0.32 loading threshold, and therefore considered to be trivial (N/A). PC2 for transfer was loaded by variable limb positive sagittal plane angular velocity of the foot (VFooωSagP) and shank (VShaωSagP).

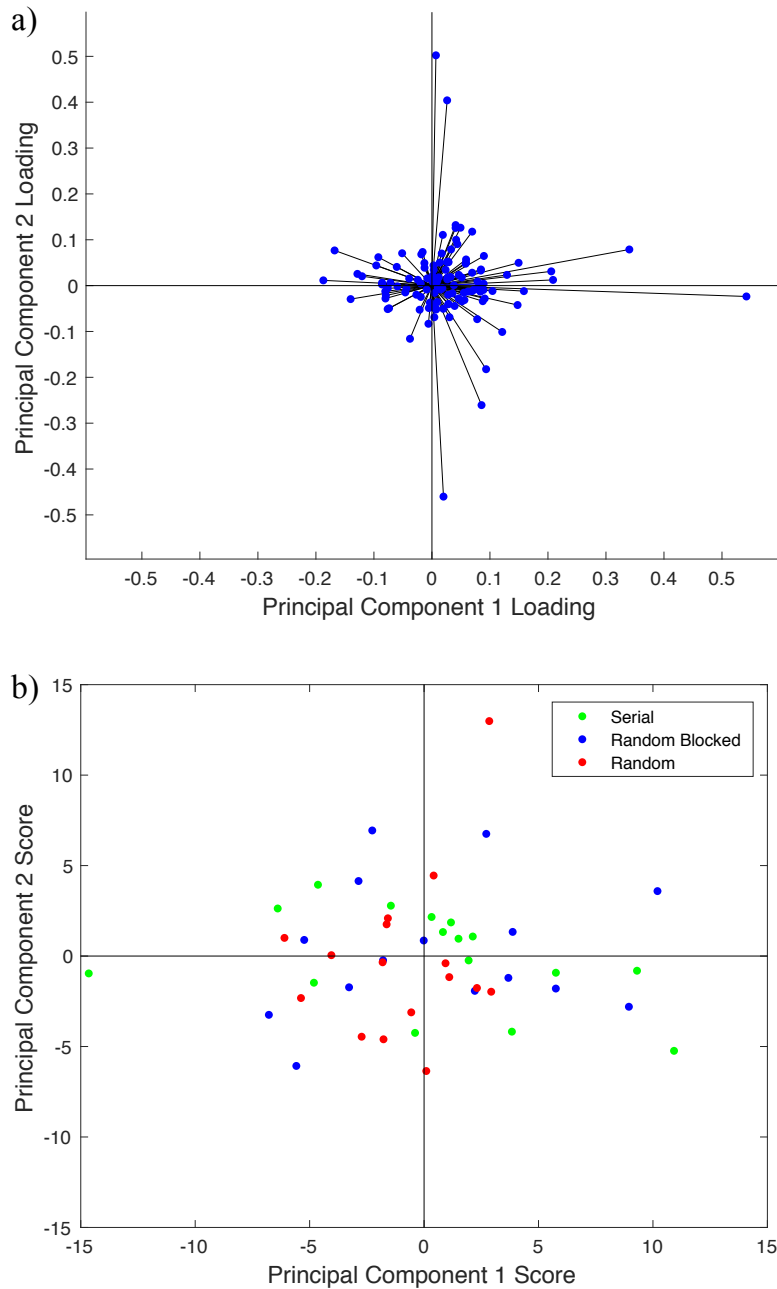|	PC1		PC2	
	Variable	Loading	Variable	Loading
Acquisition	VThiωSagP	0.5421	CThiAFroP	0.5023
	CThiωSagP	0.3403	CThiAFroN	-0.4602
			CThiVFroP	0.4040
	Variable	Loading	Variable	Loading
Retention	CFooVFroP	0.3358	COMAC	-0.3400
			COMVV	0.3204
	Variable	Loading	Variable	Loading
Transfer	N/A	N/A	VFooωSagP	0.4280
			VShaωSagP	0.3313

Acquisition

Fig 6.2. Variable loading (a) and projected individual scores (b) for acquisition of a novel asymmetric gait. During acquisition, a) variable loading is clustered such that two variables dominantly load PC1 in the positive direction (constant and variable limb thigh angular velocity in the sagittal plane). PC2 is predominantly influenced by three variables, two positive and one negative, all of which are related to frontal plane thigh motion on the constant limb. When individual values are b) projected onto the PC space, group effects are apparent as serial practice is mostly spread along PC1, while random practice is spread along PC2.
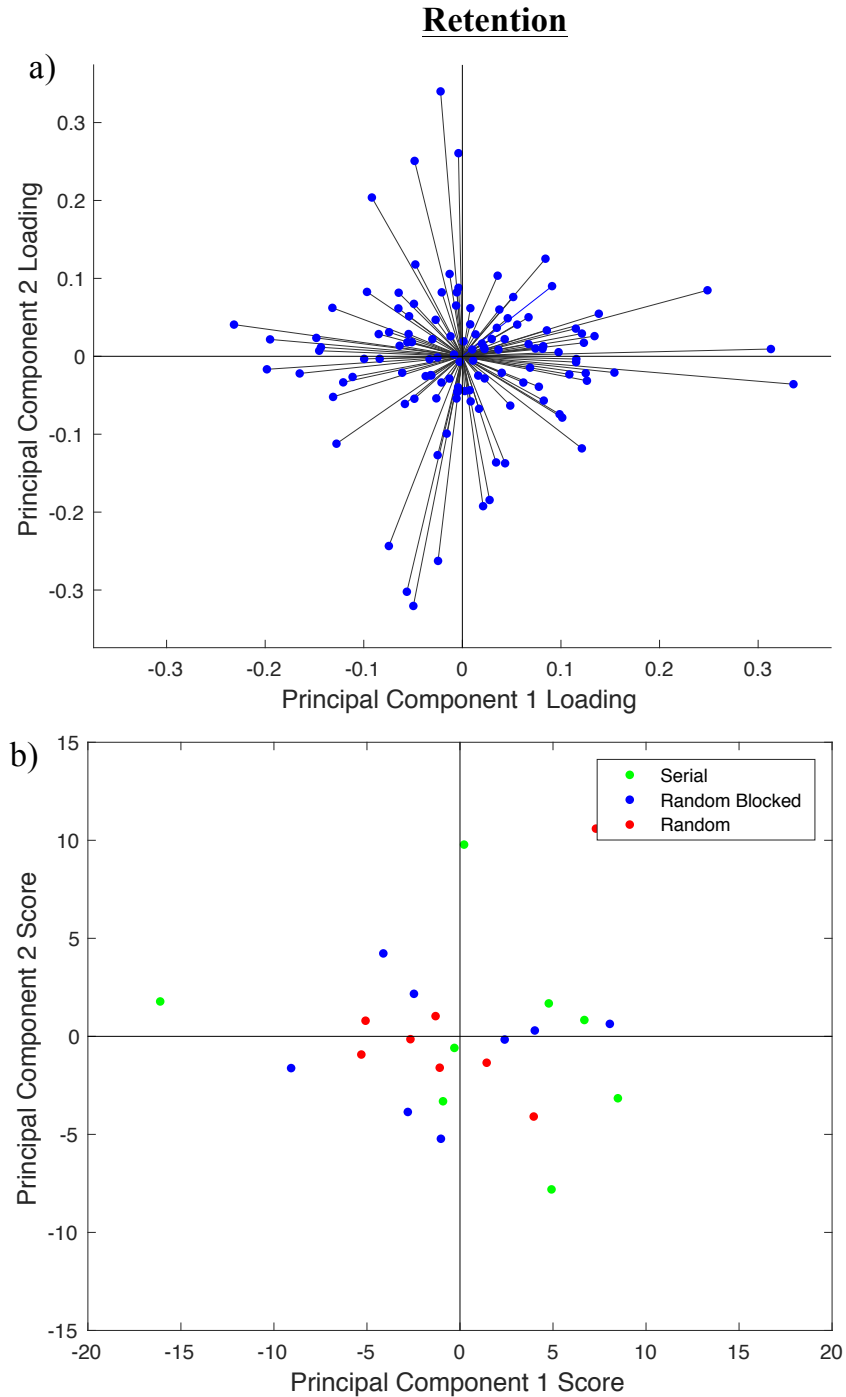
Fig 6.3. Variable loading (a) and projected individual scores (b) for retention of a novel asymmetric gait. a) A handful of variables dominantly load PC1 in both the positive and negative directions, but only frontal plane constant limb foot positive linear velocity is considered non-trivial. A few variables also predominantly load PC2, with the non-trivial ones being related to center of mass motion. B) projected scores for each individual demonstrate that serial practice has a high level of variance along both PC axes, while random blocked practice has the least. Random practice is mostly scattered along PC2.
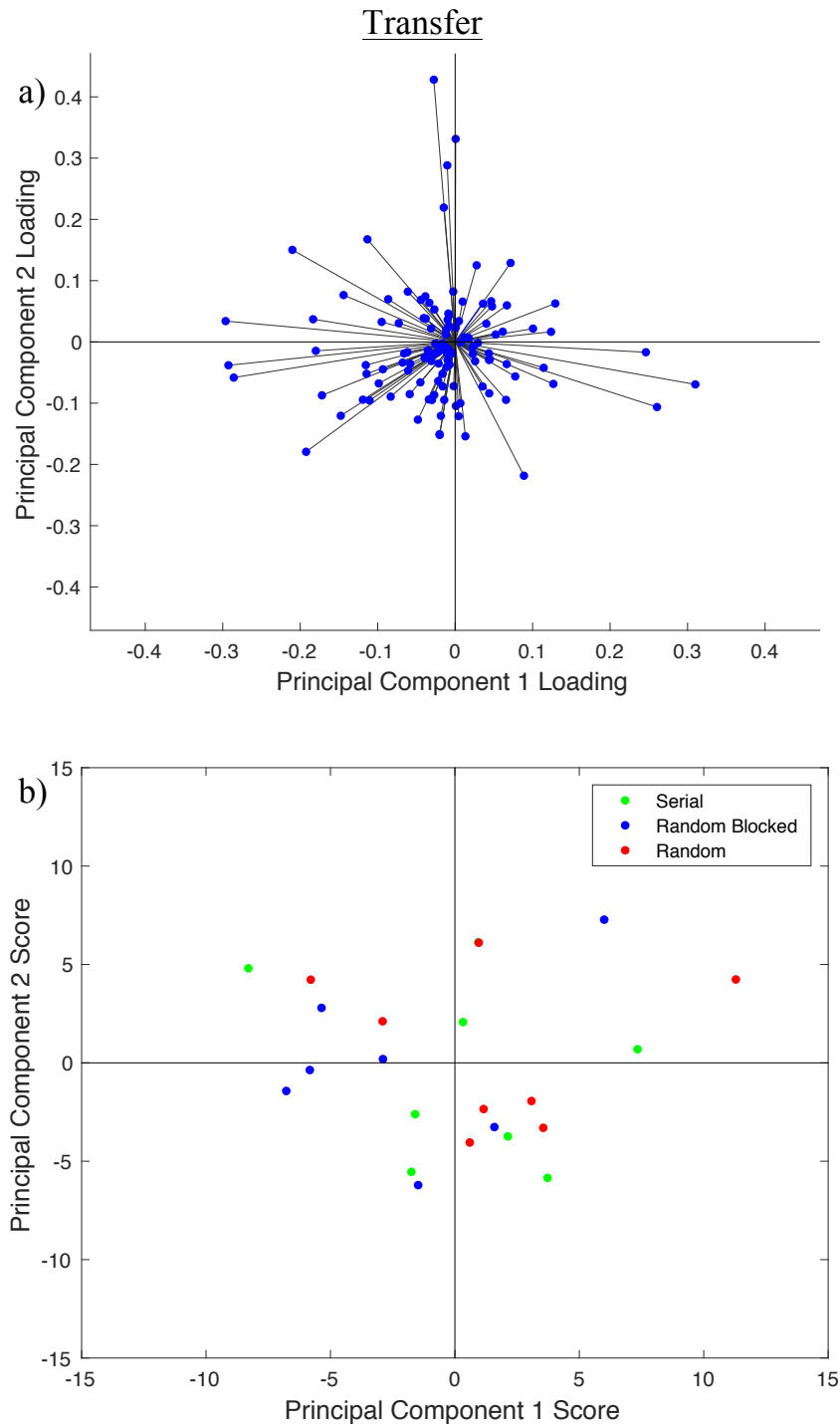
Fig 6.4. Variable loading (a) and projected individual scores (b) for transfer of a novel asymmetric gait. a) The clustering of variables along PC1 demonstrates the lack of a dominant loading. PC2 has non-trivial variables that load positively, related to sagittal plane angular velocity of the foot and shank on the variable limb. b) projected scores for each individual do not indicate a specific group strategy, as evidenced by the approximately equal scatter on the PC domain by all groups.

Further examination into time series plots of the kinematic peak values lends additional information as to individual variable loading on each PC. For PC1 during acquisition, peak positive sagittal plane angular velocity of the thigh occurs during swing phase, at approximately 70% of the gait cycle (GC; Figure 6.5a). The three peak values for PC2 during acquisition also occur between 50 and 90% GC, most of which is during swing phase (Figure 6.5b). For the retention test, the one peak value that loads PC1, peak positive frontal plane linear velocity of the thigh, occurs during late swing phase (approximately 90% GC; Figure 6.6a) while the two COM measures that load PC2 occur during pre to early swing phase on the constant limb (60-70% GC; Figure 6.6b). The two variables that load PC2 for transfer, variable limb peak positive sagittal plane angular velocity of the foot and shank, occur during mid to late swing phase (from 80-90% GC; Figure 6.7).

Fig 6.5. Timing of peak values for variables with loading coefficients greater than 0.32 for both PCs selected from acquisition. Peak values used in analysis are denoted by large points. The a) first PC for acquisition was loaded by peak positive thigh angular velocity in the sagittal plane for both the variable and constant limbs, both of which happen during swing phase. The b) second PC was loaded by peak positive and negative thigh linear acceleration in the frontal plane and positive linear velocity in the frontal plane. All of these peaks occurred during late stance or swing phase.
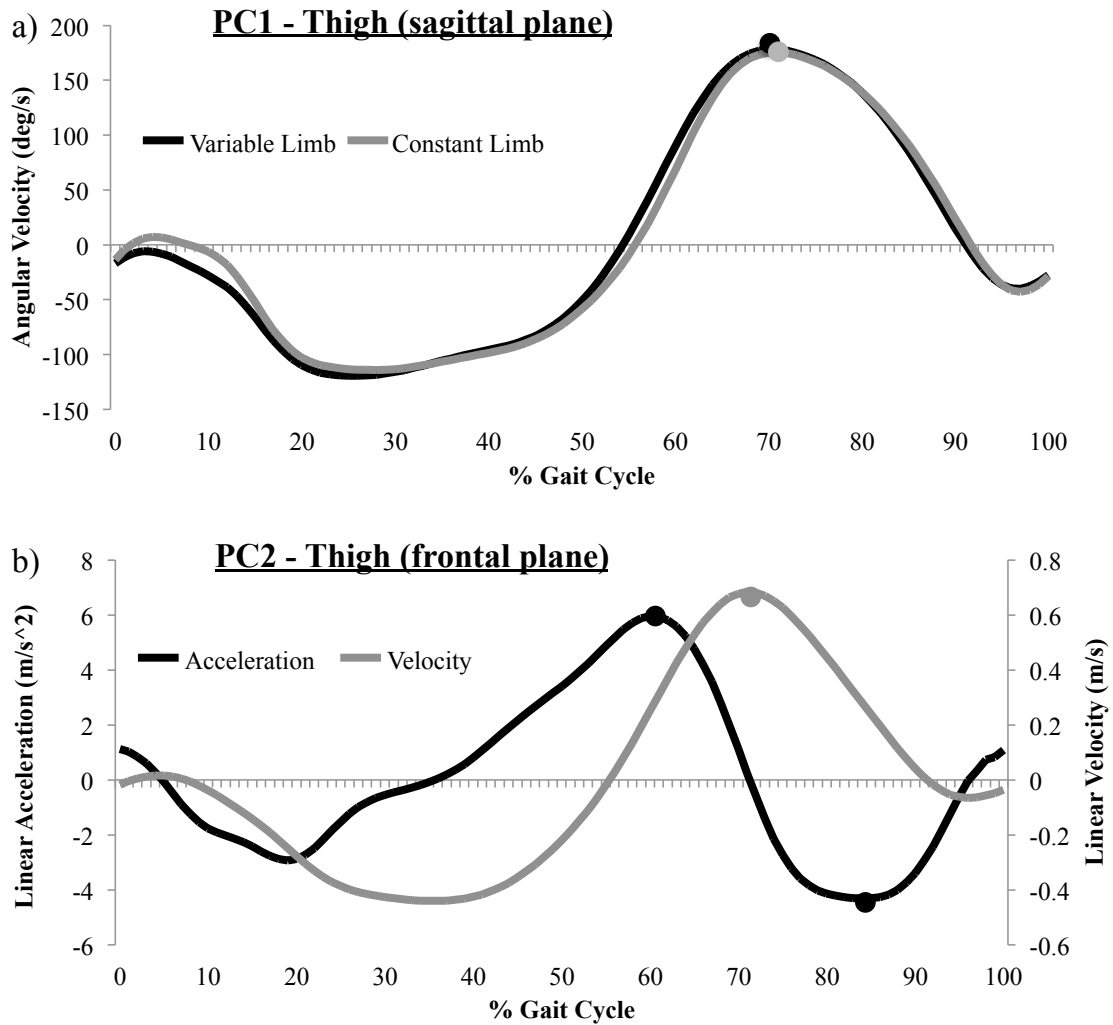
Fig 6.6. Timing of peak values for variables with loading coefficients greater than 0.32 for both PCs selected from retention. Peak values are denoted by large points. The a) first PC for retention was constant limb foot positive linear velocity in the frontal plane, which occurred during mid-swing phase. The b) second PC is loaded by peak center of mass acceleration in the (negative) direction towards the constant limb, and peak center of mass velocity in the (positive) direction of the variable limb. Both of these peaks happened during variable limb single-leg stance.

PC2 - Foot and shank (sagittal plane)

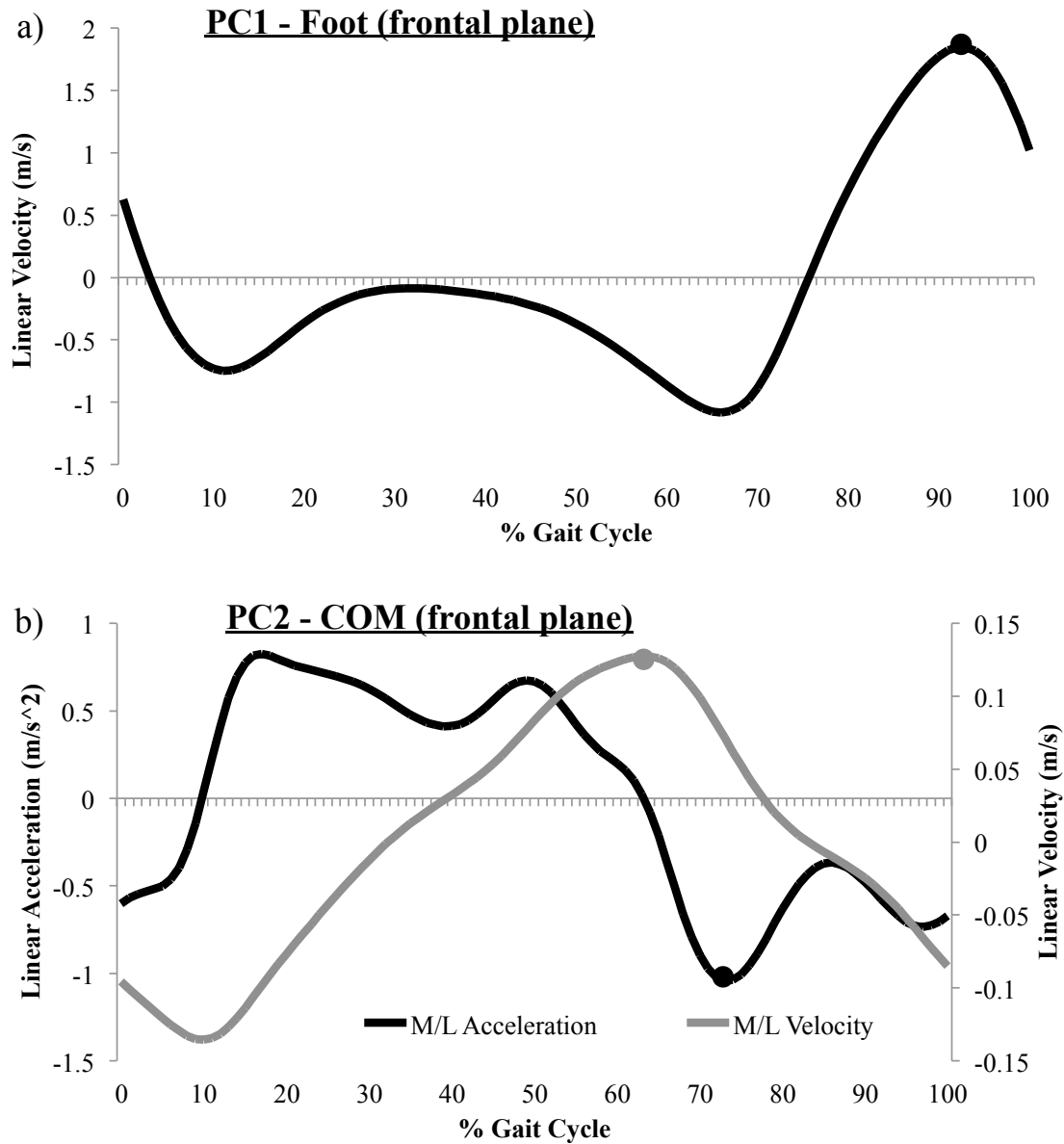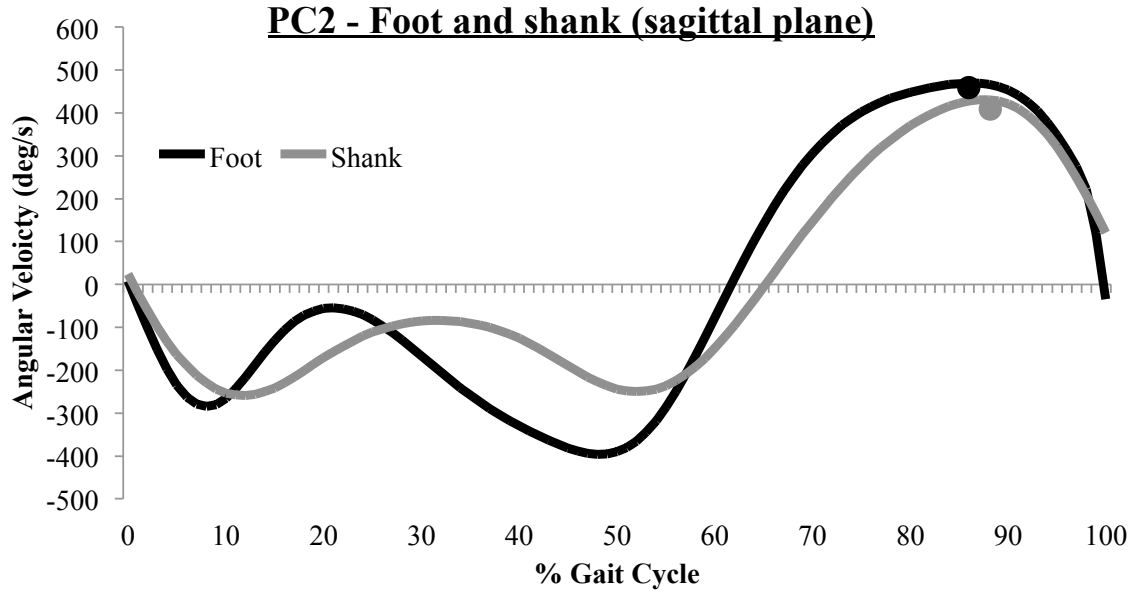**Fig 6.7.** Timing of peak values for variables with loading coefficients greater than 0.32 for PC2 during transfer. Peak values are denoted by large points. This was the only retained PC from transfer with variables with non-trivial loading. This PC was loaded by positive peak angular velocities of the variable limb foot and shank in the sagittal plane, which also occurred during swing phase.

Group strategies along these PCs are also visible through the individual projection scores for each PCA. During acquisition, serial practice resulted in a high distribution of variance along PC1, but fairly low along PC2 (Figure 3b). On the other hand, random practice had a lower distribution along PC1, and a higher distribution along PC2 (Figure 3b). Random blocked practice resulted in an approximately equal distribution of variance along both axes (Figure 3b). For retention, serial practice resulted in a wide distribution of variance along both axes, while random practice had a low distribution along PC1, and a higher distribution along PC2 (Figure 3d). Again, random blocked practice had an approximately equal distribution (Figure 3d). The transfer test results did not qualitatively reveal a group strategy, as there does not appear to be a clear pattern of variance organization for all groups (Figure 3f).

119

Discussion

PCA Extraction

Two PCs were extracted from each PCA (acquisition, retention, and transfer). A few factors were considered when making these decisions, based on previously established decision rules for extraction. One common rule, the Kaiser-Guttman criterion (Guttman 1954), states that any PC with an eigenvalue greater than 1 should be retained, as this PC represents more information than a single variable would. From the current results, according to the Kaiser-Guttman criterion, over 10 PCs would be retained. It has been demonstrated that this method consistently overestimates the number of PCs to retain (Jackson 1993). As this number of PCs would not serve the overall purpose of the present study in reducing this data set to a measurable number, we elected to not use this criterion. Another decision rule states that all components that comprise up to 95% of the total variance explained should be retained (Jackson 1993). This rule was also not followed in the present case because, like the Kaiser-Guttman criterion many PCs would also be retained from each PCA. Jackson (1993) has also not recommended this approach, as 95% also overestimates the number of PCs to retain. Instead, we elected to use the scree plot approach (see *Methods – Statistical Analysis)*. This method has been used in previous PCA approaches to gait analysis (Lord et al. 2010; Labbe et al. 2010; Olney et al. 1998). While a scree plot analysis is open to researcher bias, it also provides more flexibility for individual PC selection in cases like this where retaining many PCs would not help to reduce the data set to a small number of variables that can be used for measurement in future gait analyses. In the present data set, the scree plot approach resulted in only two PCs being retained for each PCA.

The high number of PCs with eigenvalues greater than 1 suggests that a complex structure of lower-limb segmental and joint coordination exists during gait adaptation. This finding is in contrast to studies that have used PCA to describe asymmetric gait kinematics in clinical populations (Deluzio and Astephen 2007; Olney et al. 1998), where a large percentage of the total variance was explained by only a few PCs. As those studies described populations with chronic gait deficiencies, those individuals may have found the most optimal organization of degrees of freedom long before being studied. Other studies have used PCA in more acute learning situations to identify "synergies", or combinations of variables that describe motor behavior (Latash et al. 2007; Tresch et al. 2006). It is possible in the present study that the acquisition process involved exploration of many different synergies to find the appropriate solution, resulting in a large number of relevant PCs.

Variable coefficient loadings and practice group adaptation strategies

The loadings of each variable on a given PC represent the absolute value of that variable's correlation coefficient with the PC. Since the sum of squared correlation coefficients for each PC is equal to 1, a higher loading represents a greater contribution of variance by that variable to the calculated PC (Abdi and Williams 2010). Hence, multiple variables that load highly on a PC vary together, and researchers can interpret the relationship between variables that highly load a single PC as a specific coordinative structure. The question of which threshold to set for the variables to retain for analysis is up to the interpretation of the researcher, although it has been suggested that any variable with a coefficient below 0.32 can be considered trivial in terms of its explanatory power

121

(Brown 2009; Comrey and Lee 1992). Using these criteria, each PC extracted from the data set from this study with the exception of PC1 from transfer was found to be loaded by a small set of non-trivial variables.

For acquisition, PC1 was loaded by two non-trivial variables; positive thigh angular velocity in the sagittal plane for the variable limb (0.5421) and constant limb (0.3403). Temporally, both of these values occur during the swing phase of the gait cycle, potentially indicating that PC1 is related to control of hip swing velocity in the sagittal plane. These findings are consistent with previous reports (Hinkel-Lipsker and Hahn 2016b) of changes in hip work over the course of adaptation to a novel asymmetric gait pattern. As the most proximal joint of the leg, the hip contributes greatly to the trajectory of the foot during swing phase (Winter 1992). Alterations in swing velocity may reflect an exploration of sagittal plane foot placement in response to the novel asymmetries experienced during acquisition.

Three variables made non-trivial contributions to PC2 during acquisition, positive frontal plane linear acceleration of the thigh on the constant limb (0.5023) , negative frontal plane linear acceleration of the thigh on the constant limb (-0.4602), and positive frontal plane linear velocity of the thigh on the constant limb (0.4040). Given these variables, it is evident that this PC is related to frontal plane control of the constant limb thigh segment during late stance to early swing phase, since these variables occur between 50-70% of the gait cycle. Research has demonstrated that temporally, the ankle musculature during this phase of the gait cycle is largely under passive feedback control (Ogawa et al. 2014) and responsible for the majority of power generation to propel the limb into swing phase (Neptune et al. 2001). Thus, since the velocity of the constant limb

treadmill belt did not change during acquisition, the CNS may be providing predictive adjustments to frontal plane hip motion on the constant limb. On the other hand, since body weight is shifted onto the variable limb during this phase of gait, it is also possible that frontal plane hip adjustments are under passive feedback control, and simply a response to the imbalance created by the unpredictable variable limb velocity. Regardless of the reason, it is of interest that frontal plane variance occurs on the constant limb and not the variable limb during acquisition, even when the variable limb is the one being driven at different velocities.

Taken together, these two PCs describe two major strategies adopted during the acquisition trial: sagittal plane thigh swing velocity for both limbs and frontal plane thigh peak linear velocities and accelerations for the constant limb. From the perspective of coordinative structures, it is not surprising that PC1 is sagittal plane related. This plane of motion has larger ranges of motion at each joint compared to the frontal plane, and a greater number of muscles controlling that motion. This leads to greater motor redundancy in this plane, or a larger combination of muscle activation and joint kinematic patterns that can be utilized in order to successfully ambulate (Todorov and Jordan 2002). It is also of interest to note that each practice group explores these coordination solutions in different ways, helping to explain previously noted observations in Chapter 3. In that Chapter, it was demonstrated that serial practice had the least amount of balance control variability during acquisition, and that random practice had the most. The projected scores for each subject show a low amount of variance along the PC2 axis for the serial practice group, and a high variance along the PC1 axis. It seems that the small amount of variance along the PC2 axis, representing frontal plane thigh motion for the serial

practice group allowed them to explore different combinations of joint and segmental coordination along PC1, representing sagittal plane thigh motion. Conversely, the high level of variance along PC2 for the random practice group indicates that they were restricted from exploring different coordinative structures along PC1. Finally, since random blocked practice seems to be focused around the centroid with a small spread in all directions, it is possible that this group was able to find an optimal coordinative balance between frontal and sagittal plane motion.

During the retention test, all major coordinative solutions seem to be related to the frontal plane. The PC1 was loaded by only one non-trivial variable, constant limb positive linear velocity of the foot in the frontal plane (0.3358). Temporally this peak occurs late in swing phase, and could be representative of swing phase control of the dynamic base of support (BOS) on the constant limb, a major factor affecting mediolateral gait stability (Rosenblatt and Grabiner 2010). For the retention test, PC2 has two non-trivial loading variables, center of mass mediolateral linear acceleration towards the constant limb (0.3400) and mediolateral linear velocity towards the variable limb (0.3204). Both of these measures represent whole-body center of mass motion during single-limb stance on the variable limb (or swing on the constant limb). Combined, these PCs appear to describe the interaction between two strategies utilized to control frontal plane balance. Previous research has demonstrated that control of the BOS and COM is a dynamic way to regulate frontal plane balance (Chou et al. 2003; Lugade et al 2011). Findings from the present study indicate that frontal plane motion was retained after acquisition of asymmetric SBW, but not sagittal plane motion. This observation may indicate that individuals were able to find an optimal coordination solution in the sagittal

plane, allowing them to explore the frontal plane during retention through adjustment of either the BOS or COM.

Like the acquisition phase, it appears that the type of practice experienced altered the coordinative structures utilized. However, the practice effect seems to change what is actually retained from acquisition. The serial practice group, which was able to limit frontal plane variance during acquisition, exhibited a high level of variance along both PCs during retention. It appears that most individuals in this group utilized a strategy of either BOS variance or COM variance (but not both), as the projections for each individual show large scores along one axis and low scores along another for most subjects in this group. The random group appeared to maximize variance along PC2 (related to COM control), and minimize variance along PC1. Since this group explored frontal plane limb placement during acquisition, it is possible that they found a more optimal solution to BOS control and retained it. Again, the random blocked group had a small spread of projected scores in all directions relative to the other two practice groups. This group previously demonstrated very low variability in mediolateral balance control (Chapter 3) on both limbs during this test. Based on these results, that low variability can be partially explained by low variance in control of both the COM and BOS.

The two PCs from the transfer test reveal almost wholly different coordination strategies compared to acquisition and retention. The PC1 did not have any non-trivial variables that met the 0.32 threshold. Analysis of PC loadings occurred following a varimax rotation, which should maximize variable loadings. Thus it is likely that this PC is described by a complex or noisy relationship between a large number of variables (Abdi and Williams 2010). On the other hand, the PC2 had two non-trivial loading

variables, positive sagittal plane angular velocity of the variable limb foot (0.4280) and shank (0.3313). The combination of these two variables indicates that individuals explored different coordinative control strategies using positive angular velocity of the more distal segments of the leg. Because these two peak values occurred during mid-to-late swing phase, it is further possible that PC2 represents fine-tuning of foot placement in the sagittal plane. Researchers have demonstrated that during a reaching task, the more proximal shoulder and elbow joints have a relatively invariant kinematic pattern compared to the more distal wrist joint (Lacquaniti and Soechting 1982). These results may help to explain PC2 during transfer in the current study, where the goal was to measure how well subjects generalized their learned pattern to a new context. One possibility is that these individuals were able to generalize sagittal plane limb motion in the proximal system (PC1 during acquisition), and then used the distal segments to explore a smaller area in search of an optimal foot placement. However, the results of the transfer PCA do not present as clear an understanding of the coordination strategies used. An examination of individual projections by group further confounds this analysis, as there seems to be no clear organization or clustering of groups along either the PC1 or PC2 axes. Hence, outside of the transfer-related PC2 (related to distal variable limb control in the sagittal plane), no further conclusions regarding the effect of variable practice on transfer of a novel gait can be drawn.

The outcomes of this study help to further elucidate the role of error variance in gait adaptation. The group with the highest amount of contextual interference, random practice, had a challenging experience during acquisition. Behaviorally, this manifested as a large amount of variance in the frontal plane and relatively less in the sagittal plane.

126

Unlike the serial group, which had a high amount of sagittal plane variance, this group may have been unable to make that exploration while being unbalanced in the frontal plane by the random practice paradigm. Error variance during acquisition seemed to affect retention, where the random practice group had a high level of variance with regards to COM motion, but not BOS motion. A possible explanation for this is that the error variance experienced during acquisition led to this group's ability to control BOS motion during retention, giving them more space to explore COM positioning during re-adaptation. Random blocked practice did not seem to result in a strategy of favoring any of the analyzed PCs for any test, and seems to represent an optimal middle ground in terms of contextual interference. This finding supports our findings from previous analyses, where random blocked practice had performed well in terms of retention and transfer of balance control (Chapter IV), and retention and transfer of gait biomechanics (Chapter V).

Future Work

One goal of this study was to determine if use of PCA might serve as a way to translate fundamental findings about human gait adaptation to a more focused, clinical context through use of a reduced data set using IMU measurement. The results of this study, however, indicate that more fundamental work needs to be done in order to gain a more thorough understanding of the kinematic coordinative structures that can be measured and describe how an individual is adapting his or her gait. The results of this study did not investigate changes in PC eigenvalues over time during the acquisition, retention or transfer processes. It is likely that as an individual explores coordinative

structures, some may be used early in adaptation and their role might diminish as adaptation continues, while others may be used more dominantly over time. Thus, a dynamic PCA which helps to describe stride-by-stride changes in individual PCs over the course of acquisition, retention, and transfer may facilitate a more detailed understanding of the gait adaptation process. If knowledge of lower-limb gait adaptation can be reduced to a description of a small number of variables and their change over time, then there is great potential for using IMUs to test the efficacy of different rehabilitative paradigms outside of a research laboratory.

Limitations

A few study limitations may have affected the results of this study. First, all groups during acquisition experienced a maximum walking velocity of SSWS+0.5 m/s on the variable limb, while the retention test utilized a 1.5*SSWS velocity. Thus, if a subject had a SSWS greater than 1.0 m/s, then he or she would have a variable limb belt velocity during retention faster than the fastest velocity experienced during acquisition. As such, all individuals may not have truly been given a previously experienced environmental condition during retention. However, the individuals with the fastest SSWS in this cohort would have had their variable limb only driven at ~0.3 m/s faster during retention compared to the maximum belt velocity during acquisition, and all groups had a similar mean SSWS. Further, if recall was not tested for given the discrepancy in belt velocities, then subjects would have had to generalize their learned gait pattern, but a clear difference is apparent in the results of this study between the coordinative strategies utilized during the retention and transfer test. Second, the exploratory nature of a PCA

leaves some decision making up to the researcher. For example, in the present study, the decision rule used to decide which PCs to retain for each test was based on a scree plot, a more biased decision rule than some other algorithms. However, as described previously the scree plot resulted in a more conservative approach compared to some others. A second decision that may have affected these results is the use of 0.32 as a threshold to determine non-trivial factor loading. While other groups have used a higher factor loading threshold (Ho 2006; Labbe et al. 2010), use of the 0.32 threshold in this study still proved to be very conservative, as few loading variables were retained. Still, it is unknown whether the variables that loaded poorly (above 0.32 but below 0.45) truly have practical significance. Finally, the results do not provide temporal resolution with regards to the time during adaptation when coordinative structures were being utilized. However, these results provide an initial exploration into the overall use of coordinative structures during a bout of novel gait adaptation.

Conclusions

The results presented from this study provide fundamental information about the nature of gait adaptation, and the effects of error variance on lower-limb coordination. During acquisition of a novel gait pattern, two PCs explained a large amount of variance in the total data set compared. These were related to 1) control of thigh angular velocity in the sagittal plane, and 2) control of linear velocity and acceleration of the thigh in the frontal plane. Serial practice, with the least amount of error variance during acquisition, was able to tightly control frontal plane motion and explore sagittal plane lower-limb coordination. Random practice, with the most error variance, was unable to explore the

sagittal plane due to the need to control frontal plane motion. A retention test highlighted the interaction between control of the BOS and COM, as these two factors compose PC1 and PC2, respectively. Group effects indicated that the low error variance experienced by the serial practice group during acquisition resulted in preference for either variance in BOS or COM control. However, the high error variance experienced during acquisition by the random group possibly allowed them to retain control of frontal plane foot placement (BOS), allowing for higher variance only along the axis representing COM control. A transfer test indicated that the coordinative structures adopted during acquisition were not very generalizable outside of sagittal plane limb control. No observable group effects were present from the results of this test. Taken together, these results show that control of sagittal plane motion and frontal plane motion are perhaps a trade-off during acquisition of a novel asymmetric gait pattern. Finally, in more general terms, error variance during novel gait acquisition ultimately affects exploration of coordinative solutions to those errors, lending further credence to the role of contextual interference in locomotor adaptation and learning.

CHAPTER VII

CONCLUSION

Summary of Results and Findings

This dissertation sought to determine if a variable practice paradigm would influence locomotor adaptation during and following a novel bout of asymmetric SBW. First, the feasibility of implementing this paradigm was tested in Chapter III, where an automated controller was developed. Next, the effect of variable practice on acquisition, retention and transfer on a task-specific locomotor outcome, mediolateral balance control variability, was examined in Chapter IV. Using the same data set, this work then delved deeper and investigated the biomechanical strategies adopted by each group as a result of the variable practice paradigm in Chapter V. Finally, Chapter VI reduced the kinematic data set from this study to make recommendations about what should be measured if such a paradigm is implemented in a clinical setting.

Results from Chapter III indicated that a variable practice paradigm could be automated on an instrumented split-belt treadmill. For the present study, this made use of the designed paradigm in the succeeding Chapters achievable. Most importantly, it removed the need for the researcher to control the treadmill manually. Since many speed changes occurred rapidly throughout the variable practice paradigm, manual control would have required extremely fast and accurate adjustments of treadmill belt velocity. This would have left room for additional factors that may have confounded the results of the remainder of this dissertation. In a more general sense, this control loop provides proof of concept that treadmill belt velocities can be automated for other types of studies or rehabilitation protocols.

131

Chapter IV demonstrated the connection between variable practice and locomotor adaptation. During the acquisition phase, it was noted that random practice had a significantly higher amount of variability in mediolateral balance control. This indicated that this group experienced more challenge during practice. On a retention test, random blocked practice performed best, with a significantly lower amount of balance control variability compared to the other two groups. Additionally, this group had less variability compared to symmetric walking, which is potentially indicative of a careful or guarded gait pattern. Finally, serial practice had significantly more mediolateral balance control variability on a transfer test.

Chapter V provided a description of the strategies implemented by each practice group. It was found that the random practice group adopted a strategy of limiting propulsion onto the variable limb during late stance phase of the constant limb. This strategy may have been a means to avoid the variable limb as much as possible, further describing the high level of challenge that the random practice group experienced during acquisition. It was also found that during a retention test, random blocked practice resulted in an increase in knee joint stiffness on the variable limb. This group may have used this strategy to maximize economy of motion during retention, further highlighting the high level of performance on retention by the random blocked group. Finally, serial practice resulted in a very conservative gait pattern during transfer, in terms of sagittal plane balance. These results help to further explain conclusions from Chapter IV, as well as lend additional insight into the connection between error variance during acquisition and retention and transfer of gait biomechanics.

Finally, the results of Chapter VI indicate that certain coordination patterns are adopted during acquisition, but they are not necessarily recalled or generalized. During acquisition, two principal components were found to be representative of two general coordinative structures: thigh control in the sagittal plane and in the frontal plane. However, the two main coordinative structures noted from retention were control of the dynamic base of support and whole-body center of mass. Therefore, the adopted structures during acquisition were not recalled during a retention test. They were not generalizable either, as during transfer only one interpretable principal component was found: distal leg control in the sagittal plane. Noted use of these structures seemed to differ among practice groups during acquisition and retention, but there was no observable group effect during transfer.

As a whole, these studies help to further clarify the connection between error variance experienced during practice and locomotor learning. Very broadly, this work can serve as a reference to any future studies or rehabilitative paradigms that use contextual interference, since small changes in the amount of error variance experienced (such as random vs. random blocked practice) can have large impacts on how well a new gait pattern is retained or transferred. As such, future work should take care to consider how a contextual interference paradigm is designed. More specifically, random blocked practice appears to be most effective for retention and transfer of a novel asymmetric gait pattern. This was observed in Chapter IV, where this group performed best during a retention test and equally as well as random practice on a transfer test. Further, the positive effect of random blocked practice was noted in Chapter V, where they exhibited a gait pattern indicative of good walking performance during a retention test, and one not

much different from that of symmetric gait during transfer. Finally, qualitative observations from Chapter VI indicate that this group did not minimize or maximize kinematic variance with regards to any given coordinative structure. This may be demonstrative of low kinematic variability of all coordinative structures extracted for analysis. As noted in the introduction, the efficacy of a variable practice paradigm is partially dependent on the task being learned and the skill level of the learner. In the case of gait adaptation, it seems that random blocked practice meets the optimal level of error variance required to drive motor learning, while not being too challenging to prevent individuals from finding optimal gait solutions to those errors. Overall, this work demonstrates the potential of use of a random blocked protocol in a rehabilitative setting geared towards an individual adopting a new gait pattern. However, some limitations may have affected the results of this study and therefore more work is needed prior to clinical implementation.

Limitations

One major limitation affecting the ability to apply the findings of this study to a more clinical setting is the sample of subjects recruited. These individuals represented a young, able-bodied population that may not have the same behavioral response to sensory prediction errors during walking as an older population with gait deficiencies. Still, this cohort provided the statistical power needed for this work to be able to make recommendations for future studies focused on a disabled population. Additionally, this cohort allowed for general observations to be made about the fundamental nature of gait adaptation when variable sensory prediction errors are experienced.

Second, as discussed in previous chapters, the retention test implemented for this set of studies may have not have been truly representative of motor recall. This limitation was a function of the study design being based on individuals' SSWS. The retention test was set to be a 1.5:1 asymmetry prior to any information being collected on subject SSWS. Following data collection, results showed that the average SSWS for the entire cohort was around 1.3 m/s. This means that, with the designed velocity boundaries set, the maximum variable limb belt velocity experienced during acquisition for a person with a SSWS of 1.3 m/s was 1.8 m/s. On the other hand, the 1.5:1 retention test would set the variable limb belt velocity to be 1.95 m/s. Since the purpose of a retention test is to test performance in a previously experienced practice environment, it is possible that the discrepancy in belt speeds between acquisition and retention may not be reflective of that situation. Conversely, it was shown that all practice groups had approximately the same SSWS (Table 2.1), and therefore all group comparisons during retention are valid, even if the retention test was not exclusively testing for recall. Moreover, the results presented in Chapters IV, V and VI demonstrate entirely different behavioral outcomes between retention and transfer performance. If the retention test was not testing for recall, then it would be a case where subjects were generalizing their learned gait pattern. If that was the case, then their results would likely be similar to that of transfer. Since there is a large difference between retention and transfer results, it is likely that the discrepancy between acquisition and retention belt velocities was not enough to force subjects to generalize their learned gait pattern on the retention test.

Third, Chapter IV showed that the random blocked practice group experienced more variable limb belt velocities during acquisition that were closer to the retention

variable limb belt velocity compared to the other groups (Figure 4.1b). This may help to explain why this group performed better during retention, as indicated by the results from Chapters IV-VI. This was an outcome of the randomization of belt velocities prior to acquisition, where the random blocked group had only 32 possible belt velocities to be randomized, while the other two groups had 720. This group still did experience approximately the same range of belt velocities as the other two groups (Figure 4.1a).

Recommendations for Future Work

It is apparent that some additional work is needed prior to implementation of contextual interference into a gait rehabilitation protocol. For one, the studies in this present work represented an acute bout of asymmetric SBW. While the results helped to clarify gaps in fundamental knowledge about gait adaptation, it is unknown whether the noted effects change or are consistent during a long-term prospective study, where subjects are given multiple bouts of acquisition. It is entirely possible that, given enough time, subjects can find optimal solutions to error variance regardless of practice. On the other hand, effects could diverge further as motor output becomes more consistent. Therefore, the long-term effects of variable practice on gait adaptation should be studied.

Also, it is still largely unknown what the best way is to measure gait adaptation outside of a research laboratory. While the results of Chapter VI represent a step towards real-world implementation of variable practice in gait adaptation, there was not enough temporal resolution or clarity of results to make firm recommendations about the segment location to best measure gait adaptation. As mentioned in Chapter VI, a dynamic PCA that tracks the predominant usage of certain coordinative structures over the course of

adaptation (or multiple bouts, in the case of a long-term intervention) would further clarify results.

Once firmer conclusions can be drawn using the recommendations above, a rehabilitative variable practice paradigm could be introduced to a population with a gait deficiency. Asymmetric SBW bouts have been previously examined in different groups with varying results. For example, one group has primarily studied the use of asymmetric SBW in those with hemiparetic stroke (e.g. Reisman et al. 2007) and noted a transient effect of overground gait symmetry after adaptation. Some early work from other groups has demonstrated the possible use of an SBW paradigm to further understand gait adaptation in those with unilateral trans-tibial amputation using a passive-elastic prosthesis (Selgrade et al. 2017). However, it is still unknown whether the introduction of variable sensory prediction errors would alter the results of what was observed in these studies. Such work would establish the potential role of variable practice in such populations as a rehabilitative tool. This would require study for each gait deficiency and age group, since a specific cohort's walking skill may require a different level of contextual interference compared to able-bodied individuals.

The most potential for use of a variable practice paradigm in a gait rehabilitation setting may depend on future technological breakthroughs. Through the development of powered ankle-foot prostheses, individuals with unilateral lower-limb amputation can walk with near biomimetic gait symmetry (Herr and Grabowski 2011). Still, due to the very recent development of these devices, very little is known about how individuals adapt their gait when they transition from very little ankle power generation (with a passive-elastic prosthesis) to much greater power generation (with the powered

prosthesis. Since previous studies that have used SBW to correct for overground gait asymmetries have shown a very transient aftereffect following a practice session (Reisman et al. 2007), it is possible that the difference between treadmill and overground walking mechanics are different enough where asymmetric SBW may not be wholly effective. The difference between treadmill and overground walking has been demonstrated in other recent work (Selgrade et al. 2017). However, gait rehabilitation through powered ankle-foot prostheses would not require a split-belt treadmill, but could potentially be programmed to deliver a dose of variable practice during overground prosthesis acclimation sessions. This would require understanding of the role of variable sensory prediction errors, as shown in this work, and bypass the need to further understand treadmill to overground transfer of an adapted gait. Prior to this occurring though, much more work needs to be done to further understand the fundamental nature of gait adaptation, whether on the treadmill or overground. Additionally, technological developments need to occur to be able to program such a paradigm into an onboard prosthesis controller. Assuming these hurdles will be crossed at some stage, the future is bright for such an intervention.

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