KINEMATIC EFFECTS OF MOTOR LEARNING MECHANISMS TO IMPROVE SYMMETRIC WALKING IN PEOPLE WITH STROKE

by

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Abstract

Gait asymmetry is a motor dysfunction commonly seen in stroke patients. Here, we proposed three training paradigms to improve step length symmetry: 1) Adaptation (split-belt treadmill walking followed by overground walking without reinforcement signals), 2) Reinforcement (tied-belt treadmill walking followed by overground walking with reinforcement signals), and 3) Adapt-Reinforcement (split-belt treadmill walking followed by overground walking with reinforcement signals). In addition to evaluating change in step length, a secondary analysis was performed to investigate the indirect effect on joint kinematics, which is the main focus of this thesis.

Our results showed that the paradigms implement different approaches to achieve gait symmetry. Adaptation was capable of shaping step lengths but its benefits did not sustain well. On the other hand, reinforcement learning led to longer-lasting changes in step length but its efficacy may be hampered by weakness of the paretic limb. Further analyses suggested that the paradigms can pose different kinematic influences on participants depending on whether their paretic leg takes a longer or shorter step, which correlates with distinctions in treadmill training and in muscle strength. Individual kinematic parameters of therapeutic interest were also evaluated: for the paretic-short group, a slight increase in paretic hip flexion was observed and for the paretic-long group, an even larger increase in paretic hip extension was seen. To connect analyses on step length and on kinematics, an in-depth investigation was done on joint angles at heel strike. We found that the Adaptation paradigm led to
distinct distributions of the change in hip spread between the long versus short steps. On the other hand, the Reinforcement and Adapt-Reinforcement paradigms promote exploring joint angle variations. Finally, a probability map of how likely certain kinematic strategies are implemented under designated conditions was built based on kinematics at heel strike.

Due to the limitation in sample size, very few of the results achieved statistical significance. However, this exploratory study can potentially drive future endeavors on providing direct feedback based on joint angles, as well as informing future rehabilitation therapy design tailored to individual patient conditions.

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Secondary readers: Amy J. Bastian, Ryan T. Roemmich
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Han Huang.
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Chapter 1

Introduction

Gait dysfunction is a common cause of mobility disability and restricted independence after stroke [1]. Recent rehabilitation research has developed innovative ways to improve gait patterns. For example, split-belt treadmill walking has shown considerable potential for improving step length symmetry in people with stroke via aftereffects of locomotor adaptation [2,3]. Unfortunately, improved walking patterns acquired through this adaptation learning-based therapy tend to decay rapidly, particularly if followed by overground walking [4,5]. Reinforcement is another mechanism through which new movement patterns can be learned. During reinforcement, a person learns by exploring the optimal movement in response to binary feedback about movement success or failure. While new movements are formed more slowly in reinforcement learning paradigms, they tend to be resistant to decay [6,7]. Here, three training paradigms: Adaptation (A), Reinforcement (R) and Adapt-Reinforcement (AR) were tested to evaluate whether combining adaptation and reinforcement learning paradigms leads to longer-lasting improvements in overground walking in people with stroke.

In addition to gait asymmetry, stroke patients also experience reduced ability to generate maximal force in the paretic limb, which has been verified through EMG recordings of major muscle segments involved in gait generation [8]. Such muscle weakness leads to kinematic differences such as decreased maximum hip extension, decreased hip flexion at initial contact and decreased knee flexion
during the swing phase [9]. One study showed that the average maximum hip extension of stroke patients was 14 degrees less than healthy controls walking at comparable speed [10]. Another study stated that the paretic knee flexion of stroke patients could be 15-20 degrees less compared to that of the non-parietic knee [11].

In light of such impairments, this thesis focuses on the indirect influence of the three proposed paradigms on gait kinematics. These paradigms were designed to solely improve step length asymmetry, and in two of the three paradigms, explicit feedback was given based on spatial parameters exclusively. However, it is unclear as to how a more symmetric gait pattern can be achieved through change in joint angles at the individual or group level. Understanding what kinematic benefits and losses are associated with each paradigm is critical to designing individualized rehabilitation therapy.
Chapter 2

Methods

2.1 Patient Selection

Fifteen participants with chronic stroke and mild-to-moderate lower extremity motor deficits were enrolled in the study (Table 2.1). This cohort of participants was further divided into two subgroups for detailed analyses. The paretic-long (PL) group consists of participants whose paretic leg takes the longer step during overground baseline (n=9), whereas the paretic-short (PS) group includes those whose paretic leg takes the shorter step during overground baseline (n=6).

2.2 Treadmill Training and Motion Capture

Treadmill walking portions of the experiment took place on a custom split-belt treadmill (Woodway USA, Waukesha, WI) which has separate treadmill belts under each leg, driven by independent motors. In the treadmill training period of Adapt and Adapt-Reinforcement conditions, participants walked with “split-belts”, where right and left belts moved at different speeds. All other treadmill walking periods occurred with “tied-belts”, where both belts moved at the same speed. Treadmill belt speeds were based on each individual’s overground walking speed during pretest, and were held constant throughout the experiment. During split-belt walking, the fast belt speed was set
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Table 2.1: **Demographics of participants**
to the participant’s fast overground walking speed and the slow belt was set to half of that speed. During tied-belt walking, both belts moved at the slow speed. The leg that took the shorter step during overground walking was placed on the fast belt during split-belt walking. For the PS group, this was the paretic leg and for the PL group, it was the non-paretic leg.

During treadmill walking, kinematic data were collected at 100 Hz using Optotrak (Northern Digital, Waterloo, ON, Canada). Bilateral infrared-emitting markers were placed over the fifth metatarsal head, lateral malleolus, lateral femoral epicondyle, greater trochanter, iliac crest, and acromion process. Heel strike events were approximated as the maximum (positive) angle of the limb, and toe-off events were approximated as the minimum (negative) limb angle.

2.3 Overground Motion Capture

During overground walking, we collected kinematic data at 330 Hz using eight Vicon Vero 2.2 cameras (Vicon Motion Systems Ltd., Oxford, UK) positioned around a rectangular capture space. Participants continuously walked within this capture space, moving in the direction that placed their short-stepping leg on the outside during turns (e.g. participant with a shorter stepping left leg walked clockwise). Eight passive reflective markers were placed bilaterally on the foot (second metatarsal head), heel (midpoint of calcaneus), ankle (lateral malleolus), mid-shank, knee (lateral joint space), mid-thigh, and pelvis (anterior superior iliac crest and posterior superior iliac crest).
2.4 Overground Reinforcement Signal

Real-time reinforcement was given during overground training of the R and AR paradigms. Once a step event is detected, the algorithm calculates the step length and determines whether the step is symmetric based on individualized thresholds. If symmetric, a one-time auditory signal (1000Hz, 0.02 sec) is played through a standard speaker.

2.4.1 Step Event Detection

A step event was detected if both of the following criteria were met:

(a) Participant was in the stance phase of gait.
(b) Participant had recently completed the swing phase of gait.

To address the great variability in gait patterns across the stroke patient population and to minimize changing of parameters across participants, all thresholds were designed to be loose individually, but collectively their intersection accurately defines a step event.

**Criterion (a)** A participant was determined to be at stance if:

1. The vertical locations of the leading and trailing foot were within their respective thresholds,

and

2. The absolute difference between the left and right heel velocities was within a threshold.
The location of each foot was calculated as the average between toe and heel markers, and the same thresholds for the leading and trailing foot, respectively, were used across participants. Velocity was filtered to minimize influence from missing or drifting markers. A low-pass, second-order Butterworth filter with sampling frequency of 100Hz and cut-off frequency of 3Hz was applied at all times. The X and Y directions (coordinates within the walking space) were considered separately when calculating the absolute difference between left and right heel velocities to address both straight walking and turning conditions. In the overground setting, this hybrid measure of velocity and spatial parameters is more robust in determining stance than a single spatial threshold of vertical foot location, which is sensitive to environmental constraints in the walking space such as unleveled floors. The velocity threshold was manually fitted using pilot data and the same value was used across all participants unless there was significant circumduction.

**Criterion (b)** A participant was determined to have recently completed swing if:

1. The maximum heel velocity within a certain time window exceeded a threshold,

   and

2. Sufficient time had elapsed from the most recent step event,

   and

3. The average speed of the leading leg was greater than the trailing leg in the past 0.05-0.1 sec.
The same time window/threshold was used for criterion (b) 1&2, and was designed to be an estimate for swing time (approximately 60% of stride cycle) using the following equation:

\[
time \text{ window} = \text{round} \left( \frac{2 \cdot \text{average step length in Pretest}}{\text{average walking speed in Pretest}} \cdot 60\% \right)
\]

Under the assumption that an individual's cadence would be relatively constant, this estimate should be valid across sessions and was unique to each participant's preferred gait. The algorithm also accounts for sudden change in cadence, and a step could still be detected if the time difference exceeded a third of this window and the new step was led by an opposite leg. The maximum velocity threshold was determined using pilot data and the same value was used across all participants.

2.4.2 Step Length Calculation

Step Length was defined as follows:

\[
\text{Step Length} = \left| \frac{\vec{a} \cdot \vec{b}}{|\vec{b}|^2} \cdot \vec{b} \right|
\]

where \( \vec{a} = \) vector between leading and trailing heel markers

\( \vec{b} = \) direction of travel for the past 0.1 sec

The direction of travel was calculated by tracing the midpoint of the left and right ASIS or PSIS markers. In the event that direction of travel cannot be calculated due to missing markers
within any time frame of the past 0.1 sec, an alternative axis was defined as the direction which the trunk was facing at the current time point.

2.4.3 Turns

The walking space and motion capture system was set up so that all participants turn at approximately the same area:

![Figure 2.1: Walking space set-up rounded rectangular: track, blue arrows: direction of walking](image)

Therefore, if the direction of travel deviated from the Y-axis for more than 10 degrees and the participant was within a certain area in the walking space, the step would be marked as a turn.

2.4.4 Reinforcement Signaling

Reinforcement signaling consisted of real-time auditory feedback about step length difference during overground walking. Custom MATLAB (R2017a, The MathWorks, Inc., Natick, Massachusetts) software, that was synchronized with Vicon software (Nexus 2.7.1,
Vicon Motion Systems Ltd, Oxford, UK), was used to give a pleasant tone at heel strike if the participant achieved a step length difference that fell within their reinforcement window. During periods when reinforcement signaling was on, participants were told that they would hear a tone if the length of a step was equal to the length of the previous step and they were encouraged to earn as many tones as possible.

Figure 2.2: **Reinforcement signal determination** was based on whether the step length difference between the current and previous steps fell within the [-w, w] window, where w=customized threshold.

The reinforcement window was centered around equal length steps (SLD = 0) and its width was customized for each participant. During the first minute of overground training, steps that fell +/- 0.8 standard deviations (SD) of the participant’s Pretest step length difference were reinforced. After the first minute, a one-time adjustment of the reinforcement window width was applied based on how well the participant performed (i.e. frequency of being reinforced):

\[
\begin{align*}
&< 23\% \text{ steps reinforced} \rightarrow \text{window expanded to } \pm 1.75 \text{ SD} \\
&23 - 32\% \text{ steps reinforced} \rightarrow \text{window expanded to } \pm 1.5 \text{ SD} \\
&33 - 66\% \text{ steps reinforced} \rightarrow \text{window remained } \pm 0.8 \text{ SD} \\
&> 66\% \text{ of steps reinforced} \rightarrow \text{window reduced to } \pm 0.5 \text{ SD}
\end{align*}
\]
2.5 Training Paradigm

The paradigm for each experimental session consisted of five walking epochs: 1) overground baseline: 2 minutes of overground walking, 2) treadmill baseline: 2 minutes of treadmill walking with tied-belts, 3) treadmill training: 10 minutes of treadmill walking with either split-belts (Adapt, Adapt-Reinforcement conditions) or tied-belts (Reinforcement condition), 4) overground training: 10 minutes of overground walking with either reinforcement signaling on (Reinforcement, Adapt-Reinforcement conditions) or no reinforcement signaling (Adapt condition), and 5) overground retention: 10 minutes of overground walking with no reinforcement signaling. During retention epochs participants were told that auditory feedback was “off” and were encouraged to continue trying to take equal length steps. To mitigate fatigue, participants had 2-minute sitting rest breaks every 5 minutes during treadmill walking and every 2.5 minutes during overground walking.

Figure 2.3: Training paradigm for the Adaptation (top), Reinforcement (middle) and Adapt-Reinforcement (bottom) conditions.
2.6 Step Length Analysis

Step length was calculated again during post-processing, after the motion capture system combined information from two different cameras to reconstruct more accurate marker data. The detection and calculation algorithms were the same as those in real-time, and only in very few cases did the real-time and post-processing step length values differ. In those cases, the post-processing values were selected for analyses. The average and standard error of step length difference across all participant means for each paradigm were calculated at the following epochs of interest:

(a) Baseline (BL): the first two minutes of overground walking before any intervention
(b) Early Training (ET): the first minute of overground walking right after treadmill walking
(c) Mid Training (MT): 4-6.5 minute of the 10-minute overground training
(d) Late Training (LT): the last 2.5 minute of overground training
(e) Early Retention (ER): the first 2.5 minute of overground retention
(f) Late Retention (LR): the last 2.5 minute of overground retention

The average lengths of the long and short step were calculated for each epoch respectively for comparison. A paired t-test was performed to evaluate statistically significant difference between baseline and specific epochs. In addition, the first 15 steps of ER were used to determine which of the three paradigms was able to achieve maximum change in step length difference from BL, and which paradigm led to the most symmetric gait.

2.7 Kinematics Analysis

2.7.1 Defining Stride Cycle
Heel strike by the leg which takes the longer step at BL marks the beginning and end of each stride cycle, where gait events occur in the order of: heel strike (long) - toe off (short) - heel strike (short) - toe off (long) - heel strike (long). If a toe-off event failed to be detected for the current heel strike, that heel strike event would be deleted before starting the next iteration.

**Heel Strike** This algorithm was modified from step event detection to pinpoint a heel strike event. Ankle velocity was used instead of heel velocity for its signal reliability. In addition, in order to capture the first point of contact, the absolute difference between the filtered left and right ankle velocity has to not only fall under an upper bound threshold, but also exceed a lower bound threshold. These parameters were manually fitted for each participant by verifying randomly selected heel strike timings calculated by the algorithm against Vicon video recordings of each trial.

**Toe Off** After a heel strike event is detected, the algorithm searches for a peak of the same angle velocity profile in the next 1.5 sec. It then evaluates all points within a 0.2 sec window (± 0.1 sec) around that peak. If the Z-location, as well as the X- and Y-velocity of the toe are all under their respective thresholds, this time point would qualify as a toe-off candidate. The average of these candidate time points was recorded as the timing of toe-off.

2.7.2 Angle Calculation

Due to frequent gaps in marker data for some trials, joint angles were calculated directly from marker data instead of employing a standardized Vicon pipeline to collect segment information.
Two joint angles of interest are the hip and knee angles, each calculated using one of three potential vectors (one default and two alternatives for gaps in marker data). The vector was then projected onto the sagittal plane parallel to the direction of travel, and compared to a reference axis (for hip angle) or the hip vector (for knee angle).

Figure 2.4: **Hip and knee angle definition** red arrows point in the direction of positive angle.

(a) **Hip Angle**

1. Default vector: from midpoint of ASIS and PSIS to knee
2. Alternatives: from midpoint of ASIS and PSIS to thigh, from thigh to knee

(b) **Knee Angle**

1. Default vector: from knee to ankle
2. Alternatives: from knee to tibia, from tibia to ankle

These calculated angles were then passed through the same butterworth filter used previously, followed by interpolation to fill in gaps due to missing or drifting markers. Finally, each angle profile was visually inspected to eliminate inappropriate interpolation due to exceedingly large gaps. The entire stride cycle where such interpolation occurred was cropped out. In order to average
across strides of varying duration within an epoch, the angle vector within each stride cycle was resampled to match the single stride with most time points.

2.7.3 Kinematic Benefit and Loss

The change in flexion (defined as the maximum of joint angle within a stride cycle; positive change indicates increased flexion), extension (defined as the minimum of joint angle within a stride cycle; positive change indicates increased extension via negation of the difference) and range of motion (ROM; defined as the maximum subtracted by minimum; positive change indicates increased extension) across all participants were calculated for the hip and the knee respectively. The two legs were labeled based on whether it was on the paretic side. Based on statistical results from a one-way ANOVA across paradigms during the ER epoch, kinematics data from the PL and PS groups were further investigated separately.

Among all kinematic parameters, the paretic hip extension of the PL participant group and the paretic hip flexion of the PS participant group were given specific attention, since they align with the desired therapeutic outcomes in gait kinematics.

2.7.4 Kinematics at Heel Strike

Joint angles at each heel strike were calculated in order to understand how kinematic change can influence step length outcome. Based on whether the leg which took the longer (shorter) step
during Pretest was leading, each heel strike was labeled as long (short). To examine the net influence of the hip and knee, spread angles were calculated based on how each angle contributes to inward (negative) or outward (positive) spread at each joint:

\[
\text{hip spread angle} = \text{leading hip angle} - \text{trailing hip angle}
\]

\[
\text{knee spread angle} = -(\text{leading knee angle}) + \text{trailing knee angle}
\]

For comparison at the group level, all data were considered separately within their respective paradigm and were averaged per participant per epoch. A principal component analysis (PCA) was conducted to explore potential patterns. To further connect kinematics with change in step length, spread angles at the long and short heel strike were plotted as two separate distributions, with a bin width of 2 degrees.

2.7.5 Probability for Adopting Certain Kinematic Strategy

After evaluating the kinematic effects of each training paradigm, one potentially interesting question is whether predictions can be made on what specific kinematic strategy is more likely implemented in different conditions. In other words, before an individual is exposed to any training, can the change in his/her gait pattern using the Adapt/R/AR paradigm be predicted based on the current data at hand? In order to estimate a more detailed kinematic strategy, the hip and knee of the leading and trailing legs were considered separately as opposed to being generalized as net hip and knee spread. The probability \( P \) of adopting a specific kinematic strategy \( S_i \) given a certain paradigm \( P_j \) was calculated as:
\[ P(S_i \mid P_j) = \frac{P(P_j|S_i) \cdot P(S_i)}{P(P_j)} \]

where \( S_i = \begin{cases} 
\text{hip outward, knee inward} \\
\text{hip outward, knee outward} \\
\text{hip inward, knee outward} \\
\text{hip inward, knee outward} 
\end{cases} \), \( P_j = A, R, AR \)

If the leg is leading, an outward hip movement corresponds to more flexion, and an outward knee movement suggests more extension. Whereas if the leg is trailing, an outward hip movement corresponds to more extension, and an outward knee movement suggests more flexion.

For the simplicity of data visualization, the hip and knee strategies were presented separately and the probability associated with the two outward and two inward strategies were combined. For example, the probability of moving the hip outward is the sum of \( S_1 \) (hip outward, knee inward) and \( S_2 \) (hip outward, knee outward). In order to further inform personalized therapy and make pattern predictions based on patient conditions, the PL and PS groups were considered distinctively.
Chapter 3

Results

3.1 Step Length

3.1.1 Group Step Length Difference (SLD)

Critically, baseline measures, training methods, and questionnaire responses were similar across conditions and there was no order effect. Before introducing participants to the experimental conditions, their voluntary correction of gait was tested and validated as insufficient for improving step length difference during overground walking. A paired samples t-test showed that during pretest, step length difference during a period of voluntary correction was not different from baseline (difference: 0.710 ± 2.20cm, p = 0.248). Changes in SLD were comparable across all three conditions. A 3-by-4 repeated measures ANOVA of step length differences found a main effect epoch (F(3, 126) = 5.452, p = 0.001) and a condition-by-epoch interaction effect (F(6,126) = 2.994, p = 0.009), but no main effect of condition (p = 0.137).

Adapt Participants presented with a significant step length difference at overground baseline, which persisted to a lesser degree during treadmill baseline. Exposure to the split-belts caused
an immediate perturbation, decreasing SLD significantly from treadmill baseline. The group adapted their walking pattern to account for the perturbation such that step length difference returned to near-baseline levels by the end of treadmill training. Following the transition to overground walking, participants demonstrated an initial motor aftereffect of improved step length difference, compared with baseline values. Over the course of overground training and retention, in the absence of reinforcement signaling, this aftereffect decayed and participants resumed walking with their baseline gait pattern. Repeated-measures ANOVA demonstrated a significant effect of epoch on change in step length difference (F(1.975, 27.647 = 16.045, p < 0.001). Post-hoc tests showed that early training was significantly different from baseline (6.470 ± 4.27cm, p < 0.001), but these changes were not maintained (late training: 1.352 ± 2.80cm, p = 0.082).

Reinforcement During the Reinforcement condition, only modest changes in step length difference was observed during overground walking. Participants demonstrated step length differences during overground baseline which were reduced at treadmill baseline. This SLD persisted throughout tied-belt treadmill training. During subsequent overground training, which included reinforcement signaling, participants made slow, incremental improvements in step length difference. Upon the removal of feedback during overground retention, participants lost these small gains. Repeated-measures ANOVA did not show a significant effect of epoch for change in step length difference (p = 0.711).
**Adapt-Reinforcement** Participants showed significant step length differences at overground and treadmill baselines. Initial exposure to split-belt walking exaggerated this SLD but over the course of treadmill training, participants adapted their walking pattern, ultimately returning to their baseline SLD. Upon transitioning to overground walking, participants initially exhibited a motor aftereffect of improved SLD. Reinforcement signaling during overground training helped the group maintain a portion of these improvements into late overground training and early retention. Over the course of retention, SLD decayed back toward baseline. Repeated-measures ANOVA did not show a significant effect of epoch (p = 0.422).

### 3.1.2 Change in Long and Short Steps

The step lengths of long and short steps are plotted separately for each paradigm across *all participants, the paretic long group* and *the paretic short group*. Due to the large variance and small sample size, none of the epoch data demonstrated statistically significant change from baseline using a paired t-test. Some notable observations based on the change in average step length include:

*All participants* By using the Adapt paradigm, the long step was shortened and the short step was lengthened. For the long step, the magnitude of change was greatest during ET, after which the step lengths began to approach baseline value; on the other hand, the effect on the short step sustained longer until late retention. In the Reinforcement paradigm, while the short step remained fairly consistent compared to baseline, the long step was shortened and such
negative change was still observed during late retention. The AR condition exhibited a similar trend to Adapt, but the short step length continued to increase over training and sustained well at late retention.

_Paretic long_ For Adapt, the overall trend was similar compared to the entire cohort, except that the positive change in short step length was even more prominent. In the R condition, the negative change in long step length at ET was even greater compared to the entire cohort, and lengthening of the short steps occurred during training. In the AR condition, the positive change in short step length was more prominent compared to the entire cohort, but the long steps also got more extended during retention.

_Paretic short_ For Adapt, a fast washout after ET was observed in the positive change of short step length. In the R condition, both long and short step lengths decreased during MT, but were otherwise similar to baseline. For the AR condition, there was a faster increase in short step length (during ET) and a more prominent decrease in long step lengths compared to the entire cohort and the PL group using the same paradigm.
Figure 3.1: **Change in long and short steps over time** average step length change in the long (blue) and short (red) step at baseline, early training, mid-training, late training, early retention and late retention. Error bars indicate standard error across participant means, and dotted lines mark baseline average values. (a) all participants, (b) PL group, (c) PS group.

### 3.2 Kinematic Benefit and Loss

#### 3.2.1 Change from Baseline

**(a) All participants**

Each kinematic parameter (flexion, extension, ROM) demonstrates a different change from baseline across epochs and among paradigms at the *paretic hip, non-paretic hip, paretic knee* and *non-paretic knee*. Due to the large variance and small sample size, a one-way ANOVA did not show a significant effect of paradigm during early retention, which is the epoch of optimal interest (all numerical values reported in Section 3.2.1 are means and standard deviations of ER unless otherwise specified). Even the parameter closest to achieving significance (*paretic knee, p=0.1716*) requires a total sample size of 129 to reach 80% power when employing $\alpha=0.05$. During straight walk (Fig. 3.2):

**Paretic Hip** A slight positive change in flexion was observed in the AR condition, and all paradigms exhibited positive change in average extension. However, the magnitude of increase in extension reduced across epochs using the Adapt paradigm. The average range of motion increased using all paradigms, especially with AR ($2.12 \pm 2.41^\circ$). A slight reduction in the magnitude of such increase was observed in the A and R conditions.
Non-paretic Hip All paradigms exhibited positive change in average flexion, especially with AR (1.50 ± 1.90°). The average range of motion increased using all paradigms, especially with A (1.29 ± 1.98°) and AR (1.70 ± 2.59°). A slight reduction in the magnitude of such increase was observed in the R condition during retention compared to the training epochs.

Paretic Knee Both the A and R conditions exhibited negative change in average flexion right after treadmill walking during ET, but only the R condition showed a sustaining effect of such decrease (-1.33 ± 4.05°). As for extension, the AR condition showed negative change across all epochs while the A and R conditions exhibited slight positive change. The average range of motion decreased using the R and AR conditions, especially during early training (-1.79 ± 5.01° and -2.29 ± 3.80°, respectively).

Non-paretic Knee Positive change was observed in average flexion using the R and AR paradigms, especially during the training epochs of R (2.03 ± 3.69° for ET). All paradigms exhibited no or slightly negative change in extension. Only during training of the R condition did the ROM show an increased average from baseline.

In general, similar trends in average change from baseline joint angles were observed during turns (Appendix 5.1), with two notable exceptions: the R paradigm led to a more sustained and larger positive change in average paretic hip extension compared to others during late retention (2.65 ± 3.29°), and less negative change in average paretic knee ROM was observed in R and AR during training.
Figure 3.2: Change in kinematic parameters from baseline during straight walk group average change (n=15) in paradigms A (blue), R (red) or AR (yellow). Positive value indicates increased kinematic parameter. Error bars indicate standard error.
(b) Paretic-long group

A one-way ANOVA on paretic knee flexion data showed significant effect of paradigm during ER (F(2,24)=3.9244, p=0.0335). In comparison with data of the entire group, some notable observations on other kinematic parameters include:

**Paretic Hip** There was a larger positive change in flexion using the AR paradigm (1.54 ± 2.76°), whereas the Adapt paradigm exhibited a more prominent negative change in flexion (-1.73 ± 3.33°). A larger increase in average extension was observed in the Adapt condition, especially during early training (4.09 ± 3.90°). There was also a greater positive change in the average range of motion using the Adapt and AR paradigms, especially during early training (2.86 ± 3.24° and 3.40 ± 2.26°, respectively).

**Non-paretic Hip** The AR paradigm exhibited greater positive change in flexion, especially during early training (2.91 ± 3.38°) and a more prominent increase in ROM, especially during late retention (2.88 ± 2.80°).

**Paretic Knee** The trend in change of flexion among paradigms was similar to the entire cohort, and such discrepancy was statistically significant (-2.07 ± 5.02°, -2.50 ± 2.84°, 2.59 ± 4.66° for Adapt, R, AR). A greater positive change in extension was observed in the Adapt condition (2.22 ± 2.71°), whereas the R paradigm exhibited a more prominent negative change in ROM, which sustained until late retention (-2.40 ± 5.59°).
**Non-paretic Knee** For extension, a slightly greater positive change was observed in the Adapt condition, whereas the R paradigm exhibited more prominent negative change (-1.64 ± 3.03°).

(c) **Paretic-short group**

A one-way ANOVA on paretic knee ROM showed significant effect of paradigm during ER (F(2,15)=4.7500, p=0.0252). In comparison with data of the entire group, some notable observations on other kinematic parameters include:

**Paretic Hip** The Adapt paradigm exhibited greater positive change in flexion (1.56 ± 1.87°), but showed a negative change in extension (-1.06 ± 1.53°) as opposed to the positive change observed in the entire cohort and in the PL group. The positive influence of the Adapt and AR paradigms on ROM was also less prominent in the PS group, whereas the increase in ROM achieved through the R paradigm remained comparable.

**Non-paretic Hip** Less positive change in flexion was observed using the R and AR paradigms, especially during ET. The R paradigm exhibited greater positive change in extension (0.98 ± 2.42°), whereas the AR paradigm showed less positive change in ROM.
**Paretic Knee** Flexion across paradigms in the PS group exhibited distinct trends compared to the entire cohort and the PL group: a prominent increase was observed in the Adapt condition (3.63 ± 2.61°), the negative change in the R condition was diminished, and moderate reduction occurred using the AR paradigm (-1.81 ± 5.11°). The Adapt paradigm also exhibited negative change in extension (-1.59 ± 3.45), but obtained a greater positive change in ROM (2.04 ± 1.65°). In contrast, a more prominent negative change in ROM was observed in the AR condition (-2.77 ± 1.97°).

**Non-paretic Knee** A faster washout of the increase in flexion was observed in the R condition, while the Adapt paradigm exhibited a larger increase across epochs (1.94 ± 1.57° during ER). On the other hand, extension was further decreased in the Adapt and AR conditions (-2.66 ± 3.07° and -1.51 ± 2.34°, respectively). Compared to training data of the entire cohort and of the PL group, the positive influence of the R paradigm on ROM was diminished, whereas the AR paradigm led to greater reduction (-1.70 ± 1.39° during ET).

Comprehensive kinematic data of each sub-group (described above in Section 3.2.1 b&c) are presented in the following two figures (Fig. 3.3 and Fig. 3.4) using the same format and notation as in Fig. 3.2:
Figure 3.3: Change in kinematic parameters from baseline during straight walk for the paretic-long group.
Figure 3.4: Change in kinematic parameters from baseline during straight walk for the paretic short group.
3.2.2 Joint Angles of Interest

Two particular joint angles of interest are the *paretic hip extension of the PL group*, and the *paretic hip flexion of the PS group*.

**Paretic hip extension of the Paretic Long group** All paradigms exhibited positive change. With the Adapt paradigm, the initial increase in paretic hip extension was around 4 degrees, followed by a slight decrease over the training period to around 3 degrees during retention. With the R paradigm, the initial increase reached about 2 degrees, around which subsequent extension values steadily oscillated. The AR paradigm showed the least positive change among the three (<2 degrees).
Figure 3.5: **Change in kinematic parameters of interest over time** average change (black) in a) paretic hip extension for the PL group, and b) paretic hip flexion for the PS group using the A (left panel), R (right panel) or AR (right panel) paradigm. Shading indicates standard error across participants. The first and second vertical red dotted lines indicate start of overground training and start of retention, respectively. Horizontal red dotted line marks no change from baseline.

**Paretic hip flexion of the Paretic Short group** Less change was observed in paretic hip flexion of the PS group compared to the previous parameter. The maximum change was again observed in the A paradigm (~2 degrees). The R and AR paradigms showed barely no change and their values oscillated around zero. There was even a slight negative change at the beginning of training in the AR condition.

3.2.3 Individual Examples
One sample participant was selected from each of the PL and PS groups to demonstrate how hip kinematic parameters varied across epochs and among paradigms. These examples serve as a more straightforward visualization of how varying or invariant flexion and extension could result in either shrinkage, expansion or merely shifting of ROM.

**Paretic long participant** The participant exhibited similar kinematic change using the Adapt and AR paradigms. In spite of the slight decrease in flexion, a wider kinematic range was observed during training for the paretic leg due to an even larger increase in extension. However, during retention, the kinematic range seemed to have decreased and was merely a downward shift from baseline due to further decrease in flexion. The non-paretic leg exhibited barely no change, except during ET when there was a slight decrease in hip extension. With the R paradigm, the kinematic range of both the paretic and non-paretic legs shrunk due to a decrease in hip flexion and extension, respectively.
Figure 3.6: Individual hip angle profile over time for the paretic (red) and non-paretic (blue) legs using the A (left panel), R (middle panel) or AR (right panel) paradigm. Black diamonds, which are connected through vertical blue or red lines, indicate the average flexion (top) and extension (bottom) at epochs baseline, early training, late retention, early retention and late retention. Circle dots represent individual data points within each epoch. The horizontal blue and red dotted lines mark the average between flexion and extension at baseline for the non-paretic and paretic leg, respectively. a) sample participant from the PL group, b) sample participant from the PS group.

Paretic short participant With the Adapt paradigm, the kinematic profile of the paretic leg seemed to have shifted upwards and was held through retention. An increase in flexion of the non-paretic leg contributed to an extended kinematic range across epochs. Whereas in the R condition, both legs experienced a slightly wider kinematic range due to increase in hip flexion. With the AR paradigm, both flexion and extension of the paretic leg decreased during ET, leading to a smaller kinematic range. However, they recovered after ET and there was even an increase in flexion during LT and ER. For the non-paretic leg, flexion seemed to have increased during LT and ER, leading to a greater kinematic range. However, such effect diminished in LR and the profile was merely an upward shift from baseline.
3.3 Kinematics at Heel Strike

3.3.1 Hip versus Knee Spread

Most data points for both the long and short heel strikes fell into the second and fourth quadrant of the hip spread versus knee spread plane. In the R and AR paradigms, more instances were spotted in the first and third quadrant. In particular, there was a higher chance of experiencing simultaneous positive and negative change in both the hip and knee spread using the R and AR paradigms. Most participants achieved maximum change in step length in the AR condition, whereas the chances of obtaining symmetric walking was more evenly distributed between the R and AR paradigms.

(a)
Figure 3.7: **Knee versus hip spread at early retention** at the long (blue) and short (red) heel strike. Circle dots represent the average change in spread angle during ER compared to baseline for individual participants. Positive value indicates that the net effect of both hips/knees had contributed to an outward motion at the hip/knee level compared to baseline. Filled markers indicate data points which achieved a) maximum change in step length difference from baseline, or b) most symmetric walking using the A, R or AR paradigm during ER.

The difference in the shape of spread among paradigms could be visually inspected in Fig. 3.6, and was also confirmed by the PCA results (Fig. 3.8). For the long heel strike, the coefficients of the first component were [-0.5, 0.9] (corresponding to variable order of [hip spread, knee spread]) for the Adapt paradigm, and [-0.6, 0.8] for the R and AR paradigms. For the short heel strike, the coefficients of the first component were [-0.6, 0.8] for the Adapt paradigm, [-0.4, 0.9] for the R paradigm and [-0.3, 0.9] for AR. The variance represented by each component was also different; for example, the first component in the long step captured nearly all (97%) variance in the Adapt dataset.
3.3.2 Hip Spread of Long and Short Steps

A clear separation between the peaks of hip spread angle distribution for the long and short steps was observed. The long step distribution appeared to be right-tailed, with more distribution mass on the negative end, while the short step distribution seemed left-tailed, with more data concentrated to the positive end. Such trend either persisted throughout training and ER (for the Adapt paradigm), or emerged during mid- to late training and sustained in ER (for the R and AR paradigms).
Figure 3.9: **Distribution of hip spread angle change from baseline** at the long (blue) and short (red) heel strike during a) t=0~1, b) t=1~2.5, c) t=2.5~5, d) t=5~7.5 and e) t=7.5~10 minutes of overground training, as well as during f) early retention using the A (top panel), R (middle panel) or AR (bottom panel) paradigm.
3.3.3 Knee Spread of Long and Short Steps

There was less prominent separation in knee spread distribution compared to the hip,
Figure 3.10: **Distribution of knee spread angle change from baseline** at the long (blue) and short (red) heel strike during a) $t=0\sim1$, b) $t=1\sim2.5$, c) $t=2.5\sim5$, d) $t=5\sim7.5$ and e) $t=7.5\sim10$ minutes of overground training, as well as during f) early retention using the A, R or AR paradigm.

except during mid- to late training (Fig 3.10d). In that epoch, the characteristics of skewness remained the same for the AR paradigm compared to those observed in the hip (right-leaning for short, left-leaning for long), but was flipped for the A and R paradigms (right-leaning for long, left-leaning for short).

3.3.4 Probability of Adopting Certain Strategy

The probability distribution varied for different patient groups (PL, PS), epochs (ET, ER) and for long or short steps. In some cases, the distribution was similar regardless of patient group and epoch; for example, the hip leading the short step in AR and the knee trailing in the short step in R had a tendency to swing outward and inward, respectively, between both groups and epochs. In other cases, the distribution was different between patient groups; for example, the hip leading the long step using the Adapt paradigm exhibited inward tendency for the PL group, and outward tendency for the PS group. There were also cases in which the distribution changed over epochs; for example, the knee trailing in the short step of AR became even more likely to swing outwards after training for the PS group, but for the PL group, the tendency to move inward versus outward became more similar after training. Such change could be drastic and lead to a flipped probability distribution; for example, within the PS group, the hip trailing the long step in Adapt paradigm had a 100% tendency for inward motion during ET, but was 33% more likely to swing outwards than inwards during ER.
Figure 3.1: Probability of implementing specific hip kinematic strategy at the leading (Le) or trailing (Tr) leg during long (L) or short (S) heel strike using the three training paradigms (A - left section, R - middle section, AR - right section). Blue bar represents probability of outward strategy, i.e., moving the leg further away from the trunk compared to baseline, and orange represents inward strategy, i.e., moving the leg closer to the trunk compared to baseline. Blue bar represents probability of outward strategy, i.e., moving the leg further away from the trunk compared to baseline, and orange represents inward strategy, i.e., moving the leg closer to the trunk compared to baseline.
Figure 3.12: Probability of implementing specific knee kinematic strategies.
The step length results showed that different paradigms employed different approaches for improving gait symmetry. Split-belt treadmill walking seemed to have brought the long and short steps together to their middle ground, but how well such effect was able to sustain could have been determined by the participant’s physical condition (PL or PS) and the presence of reinforcement signaling. For the PS-A (paretic short-adapt) condition, the lengthening effect washed out soon after treadmill walking. However, if there had been strength (or lack of weakness) in the leading leg (PL-A), or if reinforcement signaling had been available (PS-AR), the positive change in the short step length was able last longer. Following the same logic, the combination of strength and reinforcement (PL-AR) exhibited the most positive change across epochs.

The involvement of adaptation seemed to be essential for the PS group. For the PS-R condition, the short step length even experienced negative change during mid-training. Between Adapt-only and AR, AR seemed to be the better paradigm for the PS group due to its long-lasting effect in both long and short steps. Interestingly, reduction in the long step length was not observed for the PL group. One possible reason could be that the leg leading the short step had enough strength to achieve greater step length early on during training, which caused the long step to “follow along”
and thus the average in long step length was even larger at retention compared to baseline. The question of why the long step chose to follow the increase in short step length instead of continuing to decrease could potentially be interesting for further explorations.

In terms of kinematic benefits, at the group level (considering all participants), AR seemed to excel in all hip categories for its magnitude of positive change and its sustaining effect. The Adapt paradigm was exceptionally good in paretic hip extension, but the effect had slowly decayed after the end of treadmill training. On the other hand, R and AR seemed to have adopted the strategy of reducing the ROM of the paretic knee and compensating with increased non-paretic knee flexion. Interestingly, this sacrifice of the paretic knee was less prominent during turns compared to straight walking. This result suggests that the decreased paretic knee ROM might be related to an artificial strategy which required cognitive effort to execute. Therefore, during turns, it became more difficult to plan ahead and thus the kinematic effect was not present. Alternatively, the reason could also be that the use of paretic knee was required for turning motion in certain circumstances.

Further analysis at the sub-group level (paretic-long versus paretic-short) was initially motivated by the statistical insignificance observed in the larger group data, but was ultimately driven by the hypothesis that placing the paretic limb on the fast versus slow belt of the treadmill should lead to different kinematic effects. Following such assumption, when comparing between the PL and PS groups, the Adapt paradigm exhibited nearly opposite trends of kinematic change in the paretic hip, paretic knee and non-paretic knee. On the other hand, the R and AR paradigms exhibited less drastic
difference in hip kinematics upon sub-group comparison—the direction of average change was similar and the distinction between PL and PS lied mostly in the magnitude of average change. The discrepancy in the knee was more prominent for these paradigms involving reinforcement signaling.

When looking specifically at the continuous trace of paretic hip extension for the PL group, the Adapt paradigm appeared to be the most effective. There was still a decay over time, but overall the increased extension stayed above the R and AR conditions even during retention. One possible explanation, based on the comparison between A and AR, may be that the addition of reinforcement signaling was detrimental to increased hip extension because it shifted cognitive attention towards hip flexion, which was likely more intuitive as a gait changing strategy. On the other hand, paretic hip flexion for the PS group had a much smaller positive change. In particular, the R and AR paradigms exhibited nearly no change, possibly due to inherent muscle weakness for executing forward motion.

Plotting the hip versus knee spread at heel strike demonstrated the constraint of conjugation between the hip and the knee. Based on Fig. 3.7, the R and AR paradigms seemed to have encouraged exploration in the first and third quadrants, which are against the rule of conjugation. This result corresponds to how the maximum change in step length concentrated in the R and AR conditions. The PCA results showed that similar strategies were employed in the R and AR paradigms, since their loading coefficients were more similar for both long and short steps compared to those of the Adapt paradigm. Across all three conditions, the knee always carried a larger loading in the first principal component. This could suggest that changing knee motion was a more intuitive strategy, but could
also imply that the “correct direction” was hard to predict for the knee, or that the knee motion was merely balancing the hip so could vary under different circumstances.

The separation of hip distribution for the long and short steps was most prominent in the Adapt paradigm. This result suggests that split-belt training imposed different influence on the long and short steps as desired, and such effect was fairly long-lasting. On the other hand, the knee distribution results seemed less straightforward to comprehend. A possible explanation could be that the knee was an aid in improving gait symmetry for the AR paradigm, but was more of a conjugation of the hip in the A and R conditions. This result could be tied back to how the maximum changes tended to be achieved through AR.

Finally, the probability calculations further demonstrate that different strategies were favored across paradigms and between PL & PS groups. Each strategy can be sustained or polarized after training. For ease of understanding, stick figures like Fig. 4.1 could be drawn based on the information presented in Fig. 3.11 and Fig 3.12. For example, a PL participant trained by the Adapt paradigm would likely swing her leading hip inward, leading knee outward, trailing hip inward and trailing knee inward at the long heel strike during ET; however, after training, her trailing hip would tend to move outward. This pattern which is predicted based on probability matches data shown in Fig. 3.1b, where the decrease in long step length was more prominent at ET than ER for the PL-A condition.

Similar diagrams can be made and related back to step length results, keeping in mind that the
The hip is a larger effector than the knee. These probability results can help patients who wish to gain certain kinematic benefits or avoid certain kinematic losses in choosing the most suitable motor learning paradigm prior to starting a therapy program. For example, when the paretic hip is trailing for the PL group (A/R/AR-S-Tr), it is much more likely to swing outwards and sustain well using any

![Figure 4.1: Visualization of strategy probability](image)

**Figure 4.1: Visualization of strategy probability** at the leading and trailing hip & knee during (a) early training and (b) early retention of the PL-A condition. The two diagrams on the left with blue arrows represent kinematics at the long heel strike, and the two diagrams on the right with red arrows represent the short heel strike. Direction of arrow indicates direction of motion compared to baseline. Both the thickness and the shade of these arrows positively correlate with the absolute difference in probability (divided into three levels: >50%, 25-50%, <25%) between the outward versus inward strategy at each segment. For example, the thickest and darkest blue arrow pointing inwards at the femur of the leading leg in Fig. 4.1a indicates that at the long heel strike during early training, the probability of the leading hip moving inwards is >50% more than the probability of moving outwards. The grey dashed boxes highlight the difference in b) compared to a).
of the three paradigms. However, for the PS group, when the paretic hip is leading, the R paradigm is likely promoting inward motion (R-S-Le) or imposing no effect, and hence may not be an ideal training paradigm. This observation also corresponds to the data shown in Fig. 3.1c, where there was a decrease in short step length during training.

This thesis is an exploratory study on the indirect kinematic outcome of motor learning interventions which were originally designed to improve spatial aspects of walking after stroke. The results presented can provide insights about balancing kinematic benefits and losses versus gait symmetry. Furthermore, it can inform further studies that wish to explore direct feedback based on kinematics and help design a reasonable and yet challenging training scheme. Some limitations of this study include the large variance due to individual patient conditions and the small sample size. Future studies may be conducted on a larger patient population to achieve statistically significant results in both the PL and the PS group.
Chapter 5

Appendix

This chapter provides the figures for kinematic benefits and losses during turns (discussed in Section 3.2) for all participants, the paretic-long group and the paretic-short group.
Figure 5.1: Change in kinematic parameters from baseline during turns group average change (n=15) in flexion (flex; top row), extension (ext; middle row) and range of motion (rom; bottom row) for the paretic hip (PHip; first column), non-paretic hip (NHip; second column), paretic knee (PKnee; third column) and non-paretic knee (NKnee; fourth column) at epochs of early training (ET), late training (LT), early retention (ER) and late retention (LR) using paradigms A (blue), R (red) or AR (yellow). Positive value indicates increased kinematic parameter. Error bars indicate standard error.
Figure 5.2: Change in kinematic parameters from baseline during turns for the paretic long group (n=9)
Figure 5.3: Change in kinematic parameters from baseline during turns for the paretic short group (n=6).


Bibliography


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EDUCATION

Johns Hopkins University
Masters of Science and Engineering (Thesis-Track), Biomedical Engineering
Sep 2016 – May 2019 (expected)
Cumulative GPA: 3.90

Johns Hopkins University
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May 2016
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HONORS

Provost Undergraduate Research Award

RESEARCH

Kennedy Krieger Institute and Johns Hopkins Hospital, Motion Analysis Lab
Graduate Research Assistant
Aug 2017 - Present
- Designing user-centric algorithms & interface for stroke rehab research and participating in clinical experiments

JHU Institute for Computational Medicine, Neuromedical Control Systems Lab
Undergraduate & Graduate Research Assistant
May 2015 - Jul 2017
- Computationally designed an energy-efficient and personalized Deep Brain Stimulation paradigm for Parkinson’s

Johns Hopkins University Institute of NanoBioTechnology, Wirtz Lab
Undergraduate Research Assistant
Feb 2014 - May 2015
- Conducted wet lab work along with cell imaging to study in vitro 2.5D system, cancer cell metastasis and division

PUBLICATIONS


GROUP PROJECTS

Rehabilitation Engineering Design Team
Sep 2015 - May 2016
- Managed a year-long project on a sensor device for postural control and presented prototype at Design Day

MedHacks (Medical Hackathon), Health Alliance Award
Oct 2015
- Developed a webapp that gives grocery shopping advice for low-income families based on public databases

Computational Medicine Modeling Projects
Sep 2015 - May 2016
- Implemented machine learning and dynamic modeling methods to improve medical diagnostic processes

Pharmacokinetics and Pharmacodynamics Modeling Project
Apr 2016 - May 2016
- Computationally simulated drug effect on virtual patient populations to accelerate clinical trials and R&D efforts

SKILLS

- Computer: Matlab, Java, Python, R, C, Creo (CAD), Vicon, NDS Elements, LabVIEW
- Laboratory: cell culture (stem/cancer cell), microscopy, immunofluorescence staining, collagen gel making, PCR