THE IMPACT OF REAL-WORLD VIBRATION GAIT RETRAINING ON GAIT BIOMECHANICS IN PEOPLE WITH CHRONIC ANKLE INSTABILITY

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ABSTRACT

Kimmery G. Migel: The Impact of Real-World Vibration Gait Retraining on Gait Biomechanics in People with Chronic Ankle Instability
(Under the direction of Erik A. Wikstrom)

Background: Chronic ankle instability (CAI) is characterized by incomplete resolution of impairments and functional limitations after an ankle sprain. CAI stems from interactions between impairments including altered movement patterns. Real-world vibration feedback gait retraining (RW-VF) decreases lateral center of pressures (COP) and excessive inversion in people with CAI which are thought to lead to increased ankle sprain risk and early joint degeneration. However, it remains unknown how cumulative training impacts gait biomechanics.

Purpose: To determine how two-weeks of RW-VF impacts COP location and explore influences of feedback sensor location and modifiable/ non-modifiable factors on capacity for COP change in people with CAI.

Methods: In two separate studies, participants walked with a custom vibration feedback tool. In the first study, measures of modifiable and non-modifiable factors were obtained (Foot posture index (FPI), tibial varum, dorsiflexion range of motion (ROM), calcaneal eversion ROM, and postural control) before walking on a treadmill with feedback. Participants completed two sessions with the feedback sensor under either the 5th metatarsal head (5MH) or the lateral heel. In the second study, baseline biomechanics were measured while walking on a treadmill with no feedback followed by 6 real-world training sessions with feedback. Posttest biomechanics were collected after a single and 6 RW-VF sessions. Retention was measured after 1-week of no intervention.

Results: Sensor location did not impact COP location with either sensor location, but the heel location generated a mid-forefoot initial contact and a shortened step length. A pronated foot, decreased ROM, and worse postural control were associated with decreased capacity to change COP. Following a single training the COP changed during late stance and after multiple trainings the COP changed during early stance with moderate retention. However, at baseline, the CAI COP was not statistically different than controls during key gait events.

Conclusion: Cumulatively, these results suggest that RW-VF is a feasible intervention to make lasting gait changes in people with CAI, however, target variables should be individualized, and gait retraining should be combined with other interventions which may improve the capacity to change.

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TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

%FL	Percent of Maximal Foot Length
%FW	Percent of Maximal Foot Width
AJFAT	Ankle Joint Functional Assessment Tool
ANCOVA	Analysis of Covariance
AP-COP	Anterior-posterior Center of Pressure
B1	Baseline Assessment 1
B2	Baseline Assessment 2
CAI	Chronic Ankle Instability
CAIT	Cumberland Ankle Instability Tool
CI	Confidence Interval
COP	Center of Pressure
COPv	Center of Pressure Velocity
COPv-AP	Center of Pressure Velocity in the Anterior-Posterior Direction
COPv-ML	Center of Pressure Velocity in the Medial-Lateral Direction
EC	Eyes Closed
EMG	Electromyography
EO	Eyes Open
ES	Effect Size
FAAM	Foot and Ankle Ability Measure
FADI	Foot and Ankle Disability Index
FPI	Foot Posture Index
FSR	Force Sensing Resistor

IdFAI	Identification of Foot and Ankle Instability
KP	Knowledge of Performance
kPa	Kilopascals
KR	Knowledge of Results
LAS	Lateral Ankle Sprain
MD	Mean Difference
MDC	Minimal Detectable Change
MH	Metatarsal Head
ML-COP	Medial-lateral Center of Pressure
MRI	Magnetic Resonance Imaging
MWM	Mobilization with Movement
OA	Osteoarthritis
PL	Peroneus Longus
PRO	Patient Reported Outcome
PROMIS	Patient Reported Outcomes Measurement Information System
PTOA	Post Traumatic Osteoarthritis
QTM	Qualysis Track Manager
rmANCOVA	Repeated Measures Analysis of Covariance
RMS	Root Mean Square
ROM	Range of Motion
RQ	Research Question
RW	Real World
RW-VF	Real World Vibration Feedback

SEBT	Star Excursion Balance Test
SEM	Standard Error of the Mean
sEMG	Surface Electromyography
SF-36	Short Form-36
SLS	Single Leg Stance
TTB	Time to Boundary
vGRF	Vertical Ground Reaction Force
WBLT	Weight Bearing Lunge Test

CHAPTER 1: INTRODUCTION

Lateral ankle sprains (LAS) are a seemingly innocuous injury with the potential for long-term ramifications. Individuals experience two primary outcomes after a LAS: symptoms either resolve quickly or they persist causing persistent functional limitations. Those whose symptoms and functional limitations resolve are deemed “copers”. Copers typically return to preinjury levels of activity and do not experience long term impairments that impact function.[1] Individuals whose symptoms do not resolve within the first year are deemed to have chronic ankle instability (CAI). Symptoms of CAI persist many years past the initial injury. Up to 74% of people who have experienced an ankle sprain continue to have symptoms for 4 years,[2] and 49% continue to have symptoms for 10 years following injury.[3] Classic signs of CAI include multiple LAS, episodes of giving way, persistent pain, and self-reported functional limitations.[4] The presence of πmechanical and functional instability leads to early and abnormal cartilage composition changes,[5] excessive cartilage deformation in response to loading,[6] and early degenerative joint changes[7] causing an increased risk for post traumatic osteoarthritis (PTOA) of the ankle.[8]

A retrospective study has identified 5 prognostic risk factors for developing CAI after a first time LAS.[9] Researchers reported that a young age, a higher BMI, and MRI findings including posterior talofibular ligament injury, large bone marrow lesion, or swelling of the tibiotalar joint within a few days of injury could contribute to CAI development.[9] Additionally recurrent sprains are thought to be detrimental as each subsequent injury may decrease the likelihood of coping, and therefore recovery of function.[8] New insults likely cause further damage to ligamentous structures and require that the healing process restart. Additionally, extended healing time exposes individuals to increased opportunities for central compensatory neuroplastic changes[10-12] which persist following return to activity or sport and can leading to long term compensation patterns.[10,11,13] For example, individuals with CAI demonstrate significant changes in gait mechanics including increased inversion throughout stance,[14-20] a lateral center of pressure (COP) during stance phase,[17,21] and decreased dorsiflexion in swing[18,22-26] in both walking and functional tasks following return to activity. Specifically during walking, people with CAI show 6-7 degrees more inversion[27] and a lateral shift in the COP of up to 7.5 mm[17] compared to controls during stance. These gait maladaptations have been identified as risk factors for subsequent recurrent ankle sprains,[21] thus creating a feedforward loop between abnormal biomechanics and risk of reinjury.

Alterations in gait mechanics are likely influenced by other contributing factors such as ligamentous or joint laxity,[13,28-30] limited range of motion,[13,24] decreased strength,[13,31-34] and altered neuromuscular control.[4,13,25,35,36] Furthermore, while theoretical these structural and functional mechanics may lead to changes in the contact surfaces of the joint and therefore increase intraarticular contact stress leading to early joint degeneration. Effective interventions that can disrupt the cycle of dysfunction may decrease the risk of recurrent sprains, increase function, and slow early joint degeneration and therefore the rate of PTOA development following LAS.

Traditional, impairment-based treatments are an important component of rehabilitation, but do not resolve abnormal gait mechanics. For example balance training, improves static and dynamic postural control as well as scores on patient reported outcomes (PROs).[37-47] Strength training at the hip and the ankle improve isometric strength and dynamic postural control.[31,32,48-54] Joint mobilizations improve PROs, sensorimotor function and coordination, motor neuron excitability, and weight bearing range of motion (ROM).[55-65] Finally, bracing and taping techniques improve components of gait such as dorsiflexion in swing, plantar flexion in loading, inversion in stance, and foot-shank coordination, but only while the modality is in place with no significant aftereffects.[66-81] However, these interventions do not restore normal gait biomechanics[67,82,83] which leaves individuals at risk for future injury. Therefore, new treatment recommendations support the addition of gait retraining as a component of multimodal rehabilitation programs.[84]

Feedback strategies using knowledge of results techniques are emerging in gait retraining research for people with CAI. By providing feedback using externally focused knowledge of results strategies, the patient is allowed to explore various sensorimotor strategies within the confines of the feedback in order to successfully complete the intended task.[85] Knowledge of results has repeatedly shown superior outcomes for both short- and long-term motor learning.[85-87] For example, mechanical feedback strategies include the use of destabilizing shoes which place the ankle in a vulnerable position (30 – 45 degrees of combined plantar flexion and inversion).[88,89] Training with the shoes immediately increases the activity of the peroneus longus (PL) in people with CAI, a key muscle in modulating frontal plane foot position at initial contact during gait, compared to wearing normal shoes while completing various functional exercises such as a single leg stance and the star excursion balance test.[88] When the shoes were combined with a four week impairment based rehabilitation program and walking on the treadmill, similar changes were noted in the PL activity following program completion, however there were no changes in frontal plane kinematics or kinetics while walking.[89] Additionally, external weights have been applied to the dorsolateral foot to magnify inversion and plantar flexion errors while walking.[90] While people with CAI demonstrated and initial increase in eversion while walking with the load, participants accommodated to the load and returned to baseline biomechanics within one minute of walking on a treadmill.[90] Last, a mechanical resistance device placed over the treadmill with resistance bands attached to participants' lower legs was designed to produce a medially directed force on the leg.[91,92] Both single and multiple (n=5) training sessions improved PL activation up to 200 ms before heel strike and created medial shifts in the COP throughout the stance phase.[91,93]

Sensory based feedback has also been investigated in people with CAI. Textured insoles, for example, do not decrease ankle motion variability during overground walking,[94] likely as the modality does not provide feedback targeted at specific gait impairments but rather a general feedback strategy. However, targeted auditory[95] and visual[27,96] feedback have shown promising results. Auditory feedback delivered when pressure under the lateral foot exceeded a threshold decreased peak plantar pressure in the lateral foot and increased PL activity 200 ms before and after initial contact.[95] Visual feedback has been used in two different techniques. First, a crosshair laser was attached to the shoelaces of a shoe while walking and a vertical target was placed on the wall in front of a treadmill.[96] Participants were instructed to align the vertical laser beam with the vertical target on the wall, which was achieved by pronating the foot. While walking with the laser feedback, participants shifted the COP medially for the first 80% of stance and had decreased peak plantar pressure under the lateral foot.[96] Next, visual feedback was integrated into the impairment based rehabilitation and walking program.[27] When completing the walking intervention, half of the participants received real time visual feedback about their frontal plane ankle position at heel strike.[27] Those who received the visual feedback during walking had decreased ankle inversion at initial contact and decreased peak inversion ROM across the entire stride.[27]

While there are promising initial results using feedback to modify gait biomechanics in people with CAI, the mechanisms and requirements to deliver the feedback may limit long term motor learning and therefore the use of these interventions. Existing feedback tools require special equipment, such as a treadmill near a wall (resistance bands, kinematic and laser visual feedback), a motion capture system capable of real time analysis (kinematic feedback), or a quiet environment to hear the feedback (auditory). This restricts the modalities to a clinic or laboratory environment, which limits frequency of sessions and variety of surfaces encountered while training. However, haptic feedback improves the portability of feedback and therefore negates the need for controlled, quiet environments and stationary equipment. This means that training can occur away from the lab or clinic and in the real world. Real world (RW) training could enhance motor learning due to the inherent variability encountered through uneven surfaces and unexpected perturbations. Variable practice is suggested to improve long term learning in both simple tasks such as graded force production and head tracking movement accuracy to complex, sport specific tasks such as volleyball and tennis serving.[97-104] Additionally, RW training that can be incorporated into daily activities with a portable feedback tool allows for distributed practice, or smaller practice sessions spread out over time. Distributed practice is thought improve initial skill acquisition[105-107] and retention[106,107] by decreasing fatigue[108] and allowing time for mental practice.[109]

Vibration feedback is a form of haptic feedback that has been investigated in gait retraining to modify knee adduction moments in those with medial knee osteoarthritis.[110] In this study participants with knee osteoarthritis walked overground with and without vibration feedback. The feedback was delivered by a small tool attached to the shoe which gave a vibration stimulus when pressure under the lateral heel exceeded a threshold. In order to achieve a modified trajectory of the vertical ground reaction force, authors concluded that the vibration feedback facilitated a medial shift in the COP location during the first half of the stance phase.[110] The results of this study indicate that vibration feedback can be used to modify targeted biomechanics while walking. Due to the heterogeneity within people who have CAI, results from one population should not be generalized to those with CAI. Therefore, we completed a crossover pilot study using vibration feedback to modify the COP location in people with CAI while walking on a treadmill and in the RW. Participants completed a baseline assessment, followed by a 10-minute training on the treadmill or a 1 mile walk in the RW with feedback at their first session. They then returned at least 48 hours later to complete an identical collection session with training in the other environment. Our feedback tool consisted of a force sensing resistor (FSR) which detected pressure under the lateral foot, electronics which allowed a threshold for the FSR to be set, and a vibration motor placed under the lateral foot which provided a vibration stimulus when pressure on the FSR exceeded the threshold. Biomechanics were collected before, immediately after the intervention, and 5 minutes after the intervention. Our results indicated that immediately following lab training, the COP location was more medial for the first 90% of stance and that changes were retained from 20 to 90% of stance phase.[111] Similarly, following real world vibration feedback (RW-VF) training, the COP was immediately more medial for the first 80% of stance and changes were retained for the first 60% of stance.[111] Furthermore, participants demonstrated decreased propulsive vertical ground reaction force and decreased ankle joint contact force during lab training[112] and decreased ankle inversion following training.[113]

Individuals with CAI show abnormal ambulatory and functional biomechanics which increase the risk for recurrent sprains and persistent functional limitations. Preliminary evidence suggest that gait retraining is needed to modify gait biomechanics in those with CAI. However, techniques in the existing literature have limited real world application and minimal information about long-term retention. Therefore, further investigation into community-based gait retraining devices with longer follow up tine intervals is warranted. The overall goal of this study is to examine the immediate and delayed effects of real-world gait retraining devices on gait biomechanics in those with CAI. We will work towards this goal by 1) beginning to optimize feedback timing through modifying the FSR placement, 2) exploring relationships between non-modifiable structural factors, modifiable clinical outcomes of the leg and COP changes, and 3) examining multiday training. Overall, we hypothesize that community-based gait retraining interventions will improve gait mechanics in those with CAI. To achieve this goal, we will use the following specific aims:

Specific Aims

Aim 1: Understand the impact of FSR placement (lateral heel versus 5th metatarsal head) on COP location during gait following 10 minutes of training on a treadmill.

> *Research Hypothesis 1:* The sensor at the 5th metatarsal will cause a superior shift in the COP compared to the sensor location at the lateral heel.

Outcomes: In this cross-over study, participants with CAI will complete two sessions separated by at least 72 hours during which they will walk on a treadmill with the FSR of the vibration feedback tool placed under the lateral heel or under the head of the 5th metatarsal which will alter the timing of the feedback. COP data relative to the midline of the foot will be compared before and immediately after training for each subphase of stance. The results of this study will provide the ideal sensor placement, which will be used for all subsequent interventions. Given that there are multiple subphases of gait and two sensor locations which can produce a variety of results, it is unlikely that we will be able to define superiority in a way that has a clear outcome until the data are analyzed. Therefore, decisions regarding superiority of one sensor location over the other will be made based results the data analysis. The superior sensor location along with the rationale behind the decision will be presented to the committee for approval following the analysis. If no significant differences between sensor placements are identified (i.e.: both sensors demonstrate the same significant differences among phases with similar effect sizes), the original sensor placement under the 5th metatarsal head will be used.

Aim 2: Understand how the COP location during gait changes after RW-VF training in those with CAI and how such changes compare to the COP location of healthy controls.

Research Question 1: Does the COP location in those with CAI change following a single session of RW-VF training?

> *Research Hypothesis 1:* A single session of RW-VF training will cause a medial shift in the COP in people with CAI and this change will exceed the calculated MDC.
>
> *Research Hypothesis 2:* The COP location after a single session of RW-VF will be similar to the COP location of healthy controls while walking.

Research Question 2: Does the COP location during gait in those with CAI change following two weeks of RW-VF training?

> *Research Hypothesis 3:* Two weeks of RW-VF training will cause a medial shift in the COP in people with CAI and this change will exceed the calculated MDC.
>
> *Research Hypotheses 4:* The COP location after two-weeks of RW-VF will be similar to the COP location of healthy controls while walking.

Research Question 3: After 2 weeks of RW-VF, is the COP location during gait retained in those with CAI after 1 week with no intervention?

> *Research Hypothesis 5:* Following a one-week period of no training, the COP location will be retained for at least 40% of the significant phases identified immediately after two-weeks of RW-VF.

Outcomes: In this cohort study, CAI participants will complete six supervised real world training sessions during which they walked for 1 mile with vibration feedback. Center of pressure data will be collected before initiation of the program, immediately after the first training sessions, within 72 hours of completing the training program, and after 1 week with no intervention. The COP data will be calculated as the distance from the midline of the foot and normalized to maximum foot width for each participant. The post-training v control comparisons will be made using preexisting healthy control data.

Aim 3: Determine the relationship between non-modifiable structural factors of the lower leg/foot, clinical outcomes, and COP location change during vibration feedback gait retraining.

Research Question 1: Do structural differences such as tibial varum, Foot Posture Index Score, and passive calcaneal eversion ROM associate with COP location change during vibration training in those with CAI?

> *Research Hypothesis 1:* Increased tibial varum, increased Foot Posture Index score (i.e., a supinated foot posture) will associate with lesser COP change. Lesser passive calcaneal eversion ROM will associate with lesser COP change.

Research Question 2: Do clinical outcomes such as the Weight Bearing Lunge Test (WBLT) and center of pressure velocity (COPv) during single leg stance (SLS) with eyes open and closed associate with the COP location change during vibration feedback training.

> *Research Hypothesis 2:* Decreased WBLT and decreased COPv will associate with lesser COP change.

Outcomes: A structural and clinical exam will be completed as part of the baseline session of aim 1. Standing tibial varum will be measured as the angle between the transverse plane and the bisection of the distal third of the lower leg with the participant in single limb stance.[114] Foot Posture Index score will be obtained in standing, and calcaneal eversion will be measured as degrees of passive ROM of the calcaneus in a non-weightbearing position. WBLT will be measured in standing with a knee-to-wall procedure[55,115] and SLS will be captured using a force plate with eyes open and eyes closed.

CHAPTER 2: LITERATURE REVIEW

Epidemiology of Lateral Ankle Sprains

Musculoskeletal injuries are extremely disabling and costly conditions in the US, affecting 54 out of every 100 people.[116] Approximately 13 million[3,116] injuries occur to the ankle joint per year, with 3.1 million[3] diagnosed as acute LAS. Studies report that 15-74%[2,117,118] of people who have sustained an ankle sprain continue to have symptoms at least four years later[2] and as many as 49% of people will have symptoms ten years after inury.[117] The most common, chronic, complaints of LAS are pain, perceived instability, weakness, and swelling.[2] Recurrent sprains and an inability to return to previous activity levels are also commonly reported.[2,29,117] Unfortunately, LAS are erroneously considered a minor injury with no lasting consequences. However, prospective data indicates that 40% of those who sustain a LAS will develop CAI. Other reports indicate that this number may be as high as 70%.[119] The International Ankle Consortium[4] recommends that CAI be defined as 1) at least one major sprain, 2) recurrent sprains or ankle "giving way", and 3) evidence of instability and limited functional capacity on self-reported outcomes.[4]

A recent retrospective study looking at demographics and acute (within 2 weeks of initial injury) MRI results to predict CAI development in a first-time lateral ankle sprain.[9] Authors concluded that a younger age and higher BMI at the time of injury were predictive of CAI development. MRI evidence of a posterior talofibular ligament injury, a large bone marrow lesion of the talus and tibiotalar effusion with at least 50% capsular distention also predicted CAI development.[8] Finally, no clinical examination techniques (i.e.: anterior or posterior talar drawer, talar tilt test, ankle figure 8, functional tests, or the Cumberland Ankle Instability Tool (CAIT)) predicted CAI development, however 1 positive finding on the 10-m walk test, anterior talar drawer, or inversion tilt had a 90% sensitivity and 77% specificity in detecting at least one prognostic factor on MRI.[9] Authors recommended that patients with these clinical results should get an acute MRI.[9]

While we now have predictive factors which may discern who may or may not develop CAI, the exact mechanism of CAI remains unclear and is hypothesized to be multifactorial in nature.[120] Following a LAS, individuals move through the acute, inflammatory phase of healing within a few days, but sub-acutely have deficits in sensorimotor function and neuromuscular control leading to aberrant movement patterns.[8] These deficits are associated with ROM deficits, balance deficits, and a lack of ascending afferent signals caused by ligamentous injury.[8] It is estimated that approximately 50% of individuals who sustain a LAS do not seek treatment.[8] Interestingly, a recent systematic review on the predictors of CAI following an index LAS found that people who sustained a grade 1 and 2, or mild to moderate ankle sprain had up to 2.6x higher odds of developing CAI.[121] These individuals are less likely to seek care as they may not experience significant functional limitations related to the initial injury. However, it is also hypothesized that CAI may develop due to an inappropriate level of care.[8] For example, passive care is based on the principles of early injury management including rest, ice, compression, elevation, and self-guided return to activity, which may leave impairments from the initial LAS unresolved in the long term. Additionally, treatment that is too active typically returns patient to full activity within a week which is before physiological healing has concluded.[8] Unresolved deficits, due to no, incomplete, or inappropriate treatment, continue in perpetuity and the effects are hypothesized to summate over time. The difficulty in treating individuals with CAI is that there is little known about the onset and latency of each stage of the cascade of impairments, which makes optimal timing of early interventions a challenge.

CAI is a known is a risk factor for PTOA of the ankle.[8] Arthroscopic investigations of people in their late teens and early 20s with CAI show that 21-50% of individuals have evidence of degenerative ankle joint changes, and 55-95% have cartilage lesions less than two years following the initial LAS.[8] These intraarticular changes are the beginning stages of PTOA of the ankle, which is known to develop earlier in life compared to arthritis in other lower extremity joints.[8] An estimated 70-80% of people who seek treatment for end stage PTOA have a history of a previous ankle sprain.[8] In fact, 50% of people who present for surgical management of PTOA indicate that they had one significant ankle sprain, while 50% report they experienced recurrent sprains.[8] Individuals with PTOA present with similar impairments to individuals with CAI including decreased isometric strength,[122] decreased ROM and altered muscle activation patterns in gait, [123-125] decreased static balance,[122,126] decreased self-reported function,[8,122,127,128] and physical activity limitations.[8] Finally, people with osteoarthritis report increased pain, decreased physical activity and decreased quality of life,[7] which can lead to further negative health and biopsychosocial outcomes.

Consequences of Lateral Ankle Sprain Sequela

The current model of CAI[120] attempts to describe the theoretical framework for how CAI develops from a LAS. Within the model, impairments related to CAI are grouped into three main categories: pathomechanical impairments, sensory-perceptual impairments, and motor behavioral impairments.

Pathomechanical Impairments

Structural Alterations

Individuals with CAI demonstrate structural and mechanical adaptations including ligamentous[4,13,28] and/ or joint laxity,[120,129] positional faults of both the talus[130,131] and fibular head,[132,133] altered orientation of the inferior talar facets,[134] and abnormalities of talar cartilage structure and posterior subtalar joint.[5,135,136] Clinically, ligament and joint laxity is measured by the anterior drawer test and the inversion stress test to assess the integrity of the anterior talofibular and the calcaneofibular ligaments respectively. In those with CAI, both tests indicate an increase in laxity of the involved ankle.[4,13,28] Objective measures that can quantify the degree of joint laxity measured with an arthrometer demonstrate increased inversion joint laxity in those with CAI compared to controls.[137] Furthermore, a recent systematic review indicates that those with CAI demonstrate increased joint laxity in all four directions (anterior, posterior, inversion, and eversion) as measured by a variety of techniques including clinical tests, arthrometers, and stress radiographs.[129] Authors noted that tests assessing inversion laxity demonstrated the greatest deficits in those with CAI (effect size (ES): 0.06-2.62) followed by anterior laxity (ES: 0.32-1.82), eversion laxity (ES: 0.03-0.69) and lastly, posterior laxity (ES: -0.06-0.68).[129] Laxity findings are consistent with what we would expect from the common inversion/ plantarflexion mechanism of the initial lateral ankle sprain.

In addition to laxity, individuals with CAI demonstrate boney malalignments, called positional faults, which may lead to additional impairments and possible changes in loading. Again, if we look at the inversion and plantarflexion mechanism of the initial sprain, it is logical that it might cause an anterior migration of the fibular head relative to its resting position as tension is applied to the anterior talofibular ligament. Non-weight bearing radiographic images were assessed in a population with subacute lateral ankle sprains and confirmed the presence of an anteriorly seated fibular head.[132,138] In those with CAI, both non-weight bearing and weight bearing radiographic images show an anteriorly positioned fibular head.[133,139] It has not been established whether an anteriorly positioned fibular head is a risk factor for CAI. The talus has also been assessed in CAI through radiographs, and, like the fibular head, was noted to be resting more anterior in the limb with CAI compared to the uninvolved limb and controls.[130] Furthermore, a systematic review of talar alignment using MRI images concluded that the talus was 3.85-5.7 degrees more anterior compared to healthy ankles.[131] Last, using dual lateral fluoroscopy and three dimensional bone position modeling, alterations in talocrural positioning have been identified during walking.[140] Fukano et al.[140] determined that the talocrural joint is more internally rotated for the first 60% of stance in people with CAI compared to healthy controls, though the cause of this adaptation remains unknown. Finally, on non-weight bearing CT images, people with CAI were found to have a more plantarly oriented (3.5 degrees) posteroinferior talar facet compared to healthy controls leading to a slight valgus position of the facet and therefore a valgus position the calcaneus relative to the talus. Authors theorized that people with CAI may overcompensate and offset the calcaneal valgus by generating varus directed moments during function, therefore increasing their risk of subsequent ankle sprains.[134]

There is new evidence emerging indicating those with CAI show early changes in talar cartilage quality. As mentioned previously, cartilage degeneration has been arthroscopically discovered as early as two years following the initial injury,[8] however using magnetic resonance imaging (MRI) we now have ways to investigate changes to the cartilage matrix in vivo. T2 mapping is an MRI technique that quantifies water content and the orientation of collagen fibers.[141] T2 relaxation time is characterized by the lapsed time for magnetized particles to return to their resting state following an introduction of a burst-like magnetic field.[142] An increase in relaxation time indicates a loss in collagen fiber structure, and therefore abnormal water content contained within the matrix.[141] T2 MRI studies indicate that those with CAI have increased relaxation times compared to controls in the medial compartment of their cartilage, indicating structural cartilage damage.[141] Similarly, a T1ρ MRI is another technique to measure cartilage damage in vivo. Increased T1ρ relaxation times indicate higher levels of cartilage degeneration.[5] Individuals with CAI also have higher T1ρ relaxations times in their talar cartilage.[5] Together, the MRI findings indicate that there is evidence of early cartilage degeneration in individuals with CAI.

New evidence continues to emerge about the total foot and ankle complex using these advanced imaging techniques. Most recently, similar increases in T2 relaxation times have been identified in the middle and posterior subtalar joints in people who had been clinically diagnosed with CAI who also have confirmed anterior tibiofibular ligament and/ or anterior tibiofibular ligament + calcaneofibular ligament injuries compared to healthy controls.[143] Additionally, analysis subtalar T1 ρ images identified higher relaxation times in the posterior joint facet in people with CAI relative to healthy controls.[136] Cumulatively, advanced imaging studies have identified early, subclinical changes to cartilage composition in both the subtalar and talar joints, which could be consistent with early development of PTOA. Furthermore, relationships have been established between T1 ρ outcomes of the foot and ankle complex and sensorimotor impairments that are common to people with CAI. Researchers discovered that greater T1 ρ relaxation times were positively associated with eyes open and eyes closed postural control variables including anterior-posterior and medial-lateral COP variability, anterior-posterior COPv, medial-lateral COPv (eyes closed only), and negatively associated anterior-posterior time to boundary (TTB) (eyes open only).[144] This suggests that people with CAI who have worse postural control also have worse cartilage composition. Additionally, those with worse subtalar cartilage composition on T1 ρ imaging also have lesser peak vGRF, lesser peak loading rate, and lesser vGRF loading rate.[144]

The literature supporting the use of T1 ρ is modeled after research looking into PTOA following an anterior cruciate ligament reconstruction. In that population, it has been shown that these same kinetic variables associate with biochemical markers of collagen turnover and cartilage matrix damage.[145,146] While these relationships have not yet been identified in people with CAI, given the established neuromechanical similarities between people post anterior cruciate ligament reconstruction and with CAI[112], it is not unreasonable to believe that people with CAI who have increased T1 ρ relaxation times may demonstrate similar cartilage biomarkers. If in fact true, this could improve the link between CAI and PTOA and the recent associations between sensorimotor impairments could provide therapeutic targets to slow the progression from CAI to PTOA.

Due to access barriers for advanced imaging using MRI, ultrasound images have been proposed as a method to assess cartilage health and the response of cartilage to loading protocols.[147] Cartilage measurements obtained through ultrasound images have been found to associate with MRI measures of cartilage thickness,[148] suggesting that this is an effective method to assess cartilage in people with CAI. Ultrasound images have also been used to quantify deformation after both static and dynamic loading protocols. For example, images were obtained from 30 participants with and without CAI before and after static loading (2 minutes of single-leg-stance) and dynamic loading (single-leg forward hops).[6] The CAI group demonstrated more deformation in the medial compartment following static loading and in the medial and lateral compartment of the talus after dynamic loading.[6] Similarly, people with CAI demonstrated more talar cartilage deformation following an exercised based loading protocol (single and double limb hop, 2-minute single leg stance, 10 single leg drops) compared to uninjured controls.[149] Cumulatively, this suggests that the talar cartilage in people with CAI is less resilient to both static and dynamic loading which could occur in both daily life and athletic activities. Further studies have identified that ultrasound cartilage deformation positively associates with inversion laxity,[150] poorer medial-lateral static balance,[150] greater plantar flexion angle at initial contact and greater peak vGRF while hopping,[151] a finally, a more lateral COP location from 5%-45%, and higher lateral forefoot plantar pressures during gait.[152] These results indicate that sensorimotor and pathomechanical factors identified in people with CAI could also be negatively impacting cartilage resiliency. Further causal work in this area could uncover a link between abnormal movement profiles and early onset of PTOA.

Range of Motion

Individuals with CAI are thought to have residual impairments from the initial LAS that go unresolved.[8] ROM is a deficit that persists in CAI, however only in a functional capacity.[13] A systematic review completed in 2011[153] identified five studies that measured dorsiflexion ROM using goniometry, electrogoniometry, and biodex dynamometry. All studies were completed before 2004, however there were no differences in ROM measurements between those with CAI and healthy controls.[153] More recently, studies have investigated functional measures of dorsiflexion range of motion including the WBLT,[23,115,154-156] the anterior reach of the Star Excursion Balance Test (SEBT),[115,155] and functional tasks including walking,[157] a step down,[24] and jogging.[158] Across all functional tests and activities, people with CAI had less dorsiflexion ROM than controls during the functional tasks.[23,115,154-158] Limited dorsiflexion in functional tasks may have an impact on the risk of recurrent sprains by preventing the ankle joint from achieving a stable, closed packed position, therefore increasing susceptibility to additional lateral ankle sprains in a closed kinetic chain position.

<u>Sensory-Perceptual Impairments</u>

Patient-Reported Outcomes

People with CAI report lifelong disability and decreased physical activity.[8] More specifically, those with CAI report decreased physical health on the Short Form -36 (SF-36) Physical Component Summary,[159-161] and increased disability on the Disablement in the Physical Active Scale.[159,161] Additionally, results from region-specific patient-reported outcomes, such as the Foot and Ankle Ability Measure (FAAM), the Foot and Ankle Disability Index (FADI), the Ankle Joint Functional Assessment Tool (AJFAT), and the Cumberland Ankle Instability Tool (CAIT) all show decreased self-reported function compared to both healthy controls and ankle sprain copers across all domains including activities of daily living and sport related tasks.[159,161,162] One study determined that FAAM Activities of Daily Living subscale was the most important factor associated with quality of life and explained 65.7% of the total variance in their regression model.[163] More recently, a new patient reported outcome has been developed called the Patient Reported Outcomes Measurement Information System (PROMIS). This measure encompasses physical, mental, and social domains which all interact to create what has been termed “Health Related Quality of Life”. Results of a recent study in middle-aged adults with CAI (age: 40-70) indicate that people with CAI have worse scores on physical function, pain, fatigue, depression, and social role subscales than both uninjured controls and ankle sprain copers.[161] Furthermore, a relationship has been established between generic physical function scores (SF-36 and PROMIS) and injury frequency and severity; as injury frequency and severity increases in this population, physical function declines.[162] Measures of kinesiophobia including the Fear Avoidance Belief Questionnaire and the Tampa Scale of Kinesiophobia-17 indicate that those with CAI have an increased fear of reinjury compared to both copers and controls.[159]

Pain is an often overlooked self-reported outcome, however is a defining characteristic of CAI.[8] As many as 60% of people with CAI have pain at any given point, however that number increases to 79.4% during moderate to vigorous physical activity.[164] Pain during daily activities is associated with instability, an increased age, and a unilateral ankle sprain.[164] Furthermore, people with a history of a unilateral ankle sprain who are over the age of 30 and have joint instability are 30.4 times more likely to have pain during daily activities than those without these characteristics.[164] Pain during daily activities can lead people to be less physically active, and therefore develop other chronic health conditions which negatively impact overall health and quality of life.

Sensory Alterations

People with CAI demonstrate disruptions in the sensory system, which has implications for broader function. First, people with CAI have decreased plantar cutaneous sensation.[165-167] Using vibrotactile cutaneous stimulation, Hoch et al.[165] determined that people who have CAI have increased sensory thresholds at the head of the first metatarsal, the base of the fifth metatarsal, and the calcaneus. As these points are the main boarders of the foot, these results indicate an overall decrease in plantar sensitivity. Similarly, using nylon monofilaments, authors have determined that, compared to controls, CAI have higher thresholds in the same locations along the border of the foot[166,167] and at the lateral ligaments in the region of the sinus tarsi.[167] The authors hypothesize that a lack of plantar sensation may alter foot position while in contact with the ground as the plantar surface of the foot is the only interface between the individual and the supporting surface.[165]

People with CAI have decreased proprioception in their ankle as measured by active and passive joint repositioning. In a systematic review and meta-analysis, authors determined that both active (10 studies) and passive (6 studies) joint repositioning accuracy (degrees of error from the target) in plantar flexion and inversion was worse (i.e.: more degrees of error) in people with CAI compared to healthy controls.[168] Passive joint repositioning had an absolute error of 0.7 degrees from the target range of motion and active repositioning showed an error of 0.6 degrees.[168] A second meta-analysis concluded that joint position sense errors were consistently replicated across studies, regardless of differences in study methodologies including between group versus between limb comparisons, starting foot position, active or passive repositioning methods, testing range of motion (neutral or end range), testing velocity, and data reduction methods.[169] A loss of joint position sense of the ankle, possibly due to repetitive ankle trauma and deafferentation of mechanoreceptors, is thought to have implications for injury risk due to abnormal walking mechanics.[120,170] In normal gait, the foot clears the ground by approximately 5 mm during swing.[170] Individuals with CAI may not be able to detect small errors in their foot position, such as increased inversion and plantarflexion during swing and therefore do not correct the errors to create an optimal heel strike position. This means that the foot may contact the ground in a position that is more susceptible to straining or tearing of the ligaments once the limb is loaded,[170,171] which increases the risk of recurrent ankle injury.

The loss of proprioception is thought to lead to a deficit in the dynamic reweighting of sensory information to maintain postural control during functional tasks in people with CAI.[172] In a healthy sensorimotor system, the temporary removal of one source of sensory information (somatosensory, visual, or vestibular) typically leads to increased reliance on the remaining two systems. However, if one system is permanently removed by an injury, the use of one or both remaining systems is also permanently increased. This phenomenon can be observed in people with CAI as they have poorer postural control when vision is removed during balance tasks compared to healthy individuals.[37,173-175] Therefore, to examine postural control in those with CAI the International Ankle Consortium recommends that individuals with known vestibular conditions be excluded from research involving people with CAI.[4] As a result, the significant decline in postural control stability noted in people with CAI is indicative of limited proprioceptive information when vision is removed. Authors hypothesized that the chronic lack of proprioceptive input may lead to an overreliance on the visual system to maintain postural control during all activities.[172]

Motor-Behavioral Impairments

Strength

People with CAI demonstrate decreased isometric strength in inversion, eversion, and plantarflexion,[33,34,176] and decreased eversion: inversion and increased dorsiflexion: plantarflexion strength ratios[177] compared to controls. Isokinetic strength measures indicate that those with CAI have lesser plantarflexion strength compared to dorsiflexion strength at the same speed.[178] These strength alterations have been hypothesized to limit the effectiveness of stabilizing co-contractions during functional tasks.[33] Proximally, ipsilateral hip abductor weakness has been identified in this population.[34,179,180] This could lead to an ineffective hip strategy to maintain postural control or improper gait mechanics and foot placement at heel strike.[179] In addition to static strength, functional tests are routinely used in clinical practice to measure dynamic or functional strength which aim to quantify ability to complete activities of daily living, muscle endurance, isokinetic strength, and muscle power.[181,182] In individuals with CAI, functional tasks such as a SLS for time, single leg heel rise, single leg squat, single leg hop, double leg forward jump for distance, and a side to side jump for repetitions in a set amount of time have been studied.[182] Results indicate that scores were lower in the involved limb of people with CAI compared to the contralateral limb. Additionally, the SLS, single leg heel rise, and the side to side jump tests all demonstrated small to moderate correlations ($r = 0.229$-0.514) with isokinetic inversion ankle strength.[182]

Balance

Balance or postural control deficits have been identified in those with CAI. Postural control is the ability to maintain the center of mass inside the base of support. Static balance can be assessed with eyes open and eyes closed using clinical tests, such as the Balance Error Scoring System, time in balance test, and the foot lift test, all of which quantify the amount of errors or time that a participant takes to complete the task.[183] Objectively, static postural control can be measured while standing on a force plate in single limb or double limb stance,[184] from which spatiotemporal variables such as center of pressure location and velocity and time to boundary can be calculated. The COP location is measured by dividing the foot into regions and determining the percentage of COP datapoints in each region. People with CAI spend more time with the COP in the anterolateral section of the foot, compared to controls, who balance on the posteromedial compartment of the foot in a SLS.[175,185] The center of pressure velocity (COPv) indicates how quickly the COP location is moving within the confines of the foot.[186] Faster COPv values, such as those seen in CAI,[8,174,187,188] indicate either an increase in total excursion or a decrease in the amount of time of the activity, both of which are indicators of poorer postural control. Time to boundary (TTB) combines the COPv and the location of the COP within the foot; it measures how quickly the COP will reach the edge of the foot should the trajectory continue on the current path.[188] Lower TTB scores commonly seen in those with CAI,[8,188] indicate that the subject has less time to make postural corrections and therefore has decreased postural control. Dynamic postural control is measured through clinical tests, such as the SEBT,[183] or through functional tasks such as a step down,[189] a unilateral jump landing,[190-192] and lateral leaping[193] onto force plates to assess time to stabilization. Across all measures of static and dynamic postural control, individuals with CAI perform worse than controls.[8,154,174,175,187-194] Recent evidence has exposed that these individuals not only have deficits on the involved limb, but show similar deficits on the uninvolved limb, indicating that postural control deficits might be centrally mediated.[11,13,195]

Biomechanical Adaptations

Individuals with CAI have demonstrated a broad range of sensorimotor adaptations including limited range of motion,[13,24] decreased strength,[13,31-33] impaired postural control,[11,156,174,176,185,188,190,195-208] diminished plantar cutaneous sensation and proprioception, and altered neuromuscular control[4,13,25,35,36] that interact to create altered movement patterns.[14,16,18,24-26,70,191,192,209] Cumulatively, the pathomechanical, sensory-perceptual, and motor-behavioral impairments are thought to constrain how an individual can complete a task which manifests as either compensations, maladaptations, or avoidance of typical movement patterns. This is problematic because poor biomechanics, or movement quality is thought to facilitate abnormal loading of the talar articular cartilage and subsequently talar cartilage degeneration.

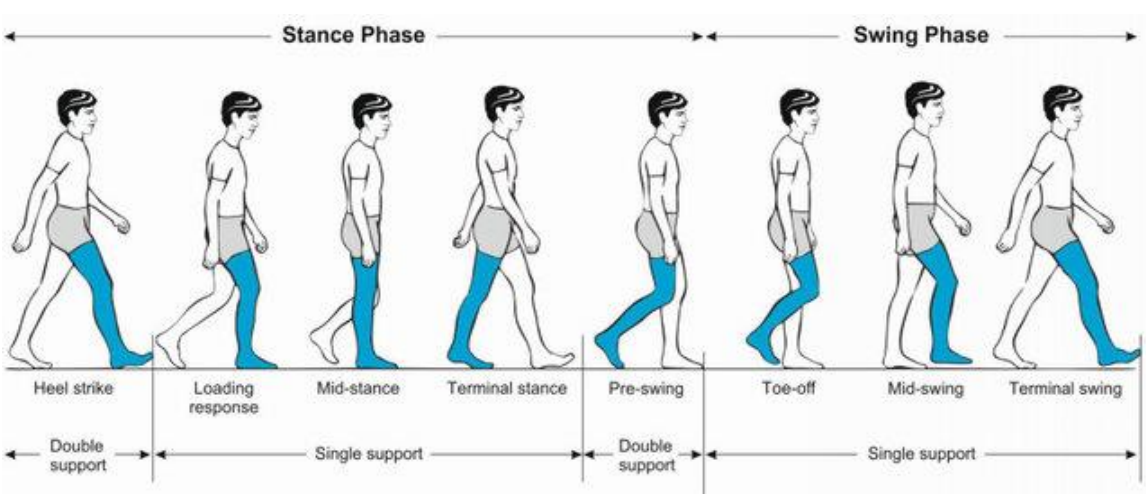


Figure 1: Subphases of the gait cycle

Pirker W, Katzenschlager R. Gait disorders in adults and the elderly: A clinical guide. Wien Klin Wochenschr. 2017 Feb;129(3-4):81-95.

People with CAI have demonstrated differences in gait mechanics. Gait is divided into two phases, swing phase and stance phase. Each of the two main phases can be further divided into subphases. See Figure 1 for the specific subphases. In the sagittal plane of *normal gait*, the ankle is in a roughly neutral position during initial contact (also known as heel strike).[210] Loading response creates a small amount of plantarflexion (approximately 8 deg) and which quickly returns towards a dorsiflexed ankle as the gait cycle moves towards midstance.[210] In midswing and terminal stance, the ankle moves into as much as 10-12 degrees of dorsiflexion.[210] During preswing, the last subphase of stance, the ankle moves from a dorsiflexed position to a plantarflexed position.[210] Throughout swing phase, the ankle in the sagittal plane, moves gradually from a plantarflexed position to a neutral position in preparation for the subsequent heel strike.[210] In the frontal plane, the foot strikes the ground in a slightly inverted position and quickly becomes everted just after initial contact and lasting through the first 5% of midstance.[211] At that point, the foot begins to invert, reaching maximal inversion at preswing prior to returning to neutral as the toe leaves the ground.[211]

Compared to normal gait, people with CAI exhibit greater ankle inversion up to 200 milliseconds prior to heel strike, and up to 200 milliseconds following heel strike,[15,17,24,19] regardless of walking speed compared to healthy controls.[20] They also demonstrate an increase in eversion moment and are more plantarflexed at heel strike compared to controls.[15,18,19,25,26,67,157,212] Additionally, there is an larger plantar flexion moment during loading response[26] and lesser mean dorsiflexion noted specifically at midstance for both shod and barefoot walking conditions.[17,26,33,67,157,188,212,213] Throughout stance phase, CAI individuals are more inverted by up to 7 degrees, and have a lateral displacement in the COP location by anywhere between 2.9-7.5 mm compared to healthy controls.[17,19,26,67] In fact, a prospective study identified lateral COP displacement at initial contact as a risk factor for future sprains.[21] Furthermore, the position of the COP location at heel strike and loading response is more variable among those with CAI compared to healthy controls when measured by the standard deviation, coefficient of variability, and the range of COP locations across subsequent steps.[214] Increased variation in movement patterns is thought to be related to a more constrained sensorimotor system which is unable to respond efficiently and effectively to functional demands.[215-217] These individuals also show higher peak pressures and larger pressure time integral under the lateral part of the foot indicating overloading of the lateral foot.[17] from a kinetics perspective, people with CAI demonstrate higher normalized ground reaction force loading rates and less time to peak vGRF[218], changes in joint contact forces[219] (i.e.: decreased compressive peak and impulse, higher anterioposterior shearing), and decreased dynamic joint stiffness[220] compared to controls. This suggests that people with CAI are loading unstable (i.e.: less stiff) joints faster which could theoretically lead to changes in joint contact forces and the eventual development of PTOA.

During the swing phase of walking, individuals with CAI demonstrate less dorsiflexion[18,26] less knee flexion, [221] less hip flexion,[221] and higher peak hip adduction range of motion compared to healthy controls.[20] Excessive plantarflexion in swing has also been identified as a risk factor for subsequent lateral ankle sprains.[22] Biomechanical adaptations at the ankle during both swing and stance phases are present in shod and barefoot running conditions over level ground at a predetermined and self-selected speeds.[15,18,21,25,67,157] For example, individuals with CAI demonstrate the same pattern of more inversion at heel strike, lateralization of COP at toe off, and less dorsiflexion in swing while running and jogging.[15,18,21,25,67,157]

When looking proximally during shod walking, there is contradictory information regarding biomechanical changes throughout the stance phase of gait. Some studies report increased mean hip flexion angle at self-selected and predetermined walking speed,[26,212,222,223] while others find decreased mean hip flexion compared to controls.[221] Similarly, studies have demonstrated both more[222] and less[212] mean hip extension ROM at toe off compared to controls. Interestingly, in a large scale cohort study which included 100 participants with CAI and 100 healthy participants, researchers determined that people with CAI walk with a more hip dominant strategy due to decreased plantar flexor power.[224] In this hip dominant strategy, people with CAI either categorized in a higher hip flexion group or a higher hip extension group.[224] Regarding the knee, some studies report higher knee flexion angles during stance related to lower ankle dorsiflexion range of motion noted in loading response.[212] However, other authors have reported both no change in knee kinematics[15,25,157] or less knee flexion[224] during shod walking. There is little consensus on proximal biomechanics, indicating that there is high variability of proximal motor control strategies[10] among individuals with CAI.

Biomechanical adaptations are also present in those with CAI during a variety of other functional tasks. A study by Donovan et al[14] examined foot position at initial contact across level ground walking, a step down task, and jump landing using video recorded sessions.[14] They found that approximately 50% of a mixed population with a history of LAS and no history of LAS show excessive inversion across all three tasks at initial contact.[14,213] Step down and jump landing, both of which have a flight phase, showed higher inversion during the flight phase prior to initial contact.[14,213] Additionally, foot position in flight phase was correlated with foot position in the stance phase of walking.[213] While the step down task has not been kinematically assessed in individuals with CAI, in jump landing tasks, there is clear consensus that individuals with

CAI, regardless of athletic level, have a more inverted ankle prior to initial contact[14,16,35,213,225] and up to 200 milliseconds following initial contact.[70] Additionally, in jump landing, there is increased variability in joint coupling patterns between the hip and ankle and the knee and ankle using vector coding.[226] Authors suggest this indicates a lack of a coordinated sensorimotor system.[226]

Individuals with CAI also demonstrate increased, or longer time to stabilization during landing[192] and a greater variety of stabilization techniques used to maintain stability compared to healthy controls, including excessive trunk motion, self-bracing with contralateral limb, and deviations in base of support strategies.[191] Proximally, studies have found decreased knee flexion ROM following initial contact, but no change in knee moment during jump landing compared to healthy controls.[70] While landing from a jump, individuals with CAI have more hip flexion prior to initial contact, but less hip flexion moment following initial contact compared to controls. The authors concluded that there is increased stiffness at the hip joint during a jump landing task in individuals with CAI.[209] An overall greater excursion of the ipsilateral limb in the sagittal plane has also been noted compared to controls.[23] Similar to assessments of walking, there is conflicting evidence when looking at proximal joint angles in a jump landing task.[70,192]

Muscle activity measured by EMG also has contradictory results throughout the literature in individuals with CAI. Prior to initial contact, the PL muscle has been shown to have both a decreased integral electromyography (EMG) amplitude of contaction[16] as well as increased root mean squared (RMS) activation[17,157,227] under shod treadmill walking conditions compared to controls. A systematic review found that those looking at barefoot walking have noted an more PL activity when assessing peak RMS amplitude, but no change in the magnitude of PL activation when looking at total area under the RMS curve compared to controls.[157] Immediately following initial contact, there is also contradictory information stating both an higher[25,157], lower,[26,224] and no change in PL activity compared to controls.[17,93] Some authors conclude that there is evidence of early and prolonged peroneal longus activation surrounding initial contact while walking and performing functional tasks.[17,26,33,36,93,157,212] The literature regarding the remaining subphases of stance phase appear to have more consensus. During midstance, less EMG activity for tibialis anterior, PL, medial gastroc, as well as more activity proximally in the gluteus medius and maximus during mid stance were noted compared to controls.[26,224] Terminal stance and toe off appear to have evidence for increased PL activity.[26,93,157] Most EMG studies to date have not investigated EMG activity of the foot and ankle in swing, however, Koldenhoven et al[17] did note higher gluteus medius activity compared to controls during the swing phase of the gait cycle.

Alterations in muscle activity are also present in other functional tasks. For example, during a step down task, an increase in preparatory activity of the tibialis anterior 200 milliseconds before and after touch down has been noted in individuals with CAI compared to healthy controls.[36] Finally, jump landing tasks have shown higher preparatory activity in tibialis anterior of the contralateral limb prior to take off,[35] and lesser PL amplitude in the ipsilateral limb 200 milliseconds before landing, [228] followed by an increase in PL amplitude after initial contact compared.[70] The current literature regarding muscle activation in individuals with CAI also supports the notion that individuals with CAI demonstrate a significant amount of variability to complete a task following ankle sprains.

Common Therapeutic Interventions

A variety of interventions to address the impairments associated with CAI have been investigated, such as balance training,[37-44] exercise and strength training,[31,32,48-52] taping techniques,[67,69,71,73-77,80] and joint mobilizations.[55-61] (Table 1) For example, a four to six week balance training program consisting of 8-12 sessions on a variety of compliant surfaces improves self-reported outcomes,[37-39] measures of static and dynamic balance,[37,39,45] and improved ankle joint proprioception.[37,45] Balance training when coupled with sensory-targeted interventions, such as tactile stimulation from stochastic resonance or the application of tape to the lateral and plantar surface of the foot, may result in larger dynamic postural stability improvements relative to balance training alone.[40,41] The combination of balance training and tactile input also increases the rate of postural stability gains in individuals with CAI.[42] A balance training program was implemented in a group of 22 individuals with CAI, half of whom trained with two strips of tape over the lateral ankle and half trained without.[42] During baseline testing, an additional group of 21 healthy individuals were assessed to determine the normal range of values for postural sway.[42] The training program was considered complete when the postural sway score of a CAI individual was statistically similar to the group of healthy individuals.[42] The CAI subjects who trained with the tape completed the program in 6 weeks, whereas those who trained without the tape completed the program in 8 weeks.[42] The authors concluded that the addition of a tactile stimulus decreased the required training time.[42]

A tactile stimulus has also been implemented as a textured surface on which the training occurs. In this study, participants completed a 6 week training program consisting of single and double leg activities on a variety of unstable surfaces.[46] One group completed the exercises on a smooth surface, a second group completed the program on a textured surface, and a final, control group received no training. Though training did not impact COP characteristics while in SLS, plantar cutaneous threshold, or PROs, there were improvements in isometric inversion strength testing in the textured training group.[46]

Finally, researchers have begun to investigate balance training with obstructed vision in people with CAI.[229] In this study, 26 participants completed a multimodal balance training program 26 participants completed the same program with stroboscopic glasses to occlude vision, and 26 participants were in the control group who received no intervention. The supervised balance training program was a combination of static and dynamic exercises and progressed to compliant surfaces. Training was provided 3 x per week for 6 weeks. Those who trained with the stroboscopic glasses wore them for the whole training session. The level of visual occlusion was set individually for each participant based on performance and was progressed as able. At the end of training, both intervention groups demonstrated improved DFROM with the WBLT, improvements on the SEBT, the CAIT, and the FAAM.[229] However, the stroboscopic glasses group had larger improvements on the anterior direction of the SEBT and the CAIT compared to balance training alone.[229] Authors concluded that training with visual occlusion may improve rehabilitation strategies by forcing participants to use sensory information rather than visual information in balance strategies.[229]

Studies have begun to investigate the impact of training the contralateral limb as there is evidence that postural control may be, in part, centrally mediated.[11,13,195] A randomized controlled trial enrolled participants with CAI into one of three groups, a control group, a contralateral training group where training was completed on the unaffected limb, and an ipsilateral training group where training was completed on the affected limb.[47] Participants in both training groups completed the same progressive loading program consisting of four single limb tasks for six weeks while participants in the control group received no intervention. At the conclusion of the training program, participants in both training groups showed improved stability in the medial-lateral direction, the anterior-posterior direction, and in overall stability during a single limb task.[47] Stability was measured as the mean distance around a zero point which was established at baseline with the participant standing in a SLS on a stable surface.[47] There were no differences between the training groups[47] indicating that training the contralateral limb is at least as effective as training the affected limb. This may allow training to begin sooner after an index LAS by initiating balance training on the contralateral limb while the affected limb remains protected in the acute phase of healing. Despite improvements across a range of impairments, balance training does not change frontal[43] or sagittal plane biomechanics during gait,[44] or walking gait velocity.[44]

Strength training has also been examined in those with CAI. For example, multiplanar ankle strengthening programs using resistance bands (12-18 sessions in 4-6 weeks) have shown improvements in self-reported outcomes[31,32,49] and inversion and eversion strength.[31,32,48,50,52,54] However, resistance band interventions do not influence average torque or isometric peak torque inversion to eversion ratios.[50] Hip abduction and external rotation strengthening (one exercise per plane) consisting of three sessions per week for four weeks resulted in improved hip abduction and external rotation strength and balance improvements as measured by the Balance Error Score System test and SEBT in people with CAI.[51] In a recent systematic review, training the intrinsic foot muscles has also demonstrated improvements in foot position, measured by the navicular drop and FPI score, static and dynamic balance, toe flexion strength, and PROs compared to no foot training in people with CAI.[230] Most recently, a randomized controlled clinical trial aimed to determine if strength training or neuromuscular control training were more effective over no treatment in improving dorsiflexion ROM, dynamic balance on the SEBT, or functional outcomes including the CAIT and the FAAM.[231] Authors concluded that 8-weeks of either intervention improved each outcome, however, no intervention proved to be superior over the other.[231] This suggests that there may be more than one intervention strategy to address various domains of CAI impairments. However, there have been no studies to date on the effects of strength training on biomechanics of gait.

Manual therapies have also been investigated. A single session of anterior to posterior joint mobilizations, applied for two – two minute bouts to the talocrural and distal tibiofemoral joint immediately increased dorsiflexion ROM,[55,62,115] improved self-reported outcomes,[56] improved dynamic balance,[55,58] and increased soleus H-reflex activity for up to 30 minutes in those with CAI.[58] Similarly, up to three repetitions of high velocity low amplitude thrust distraction manipulation in a single session to the talocrural joint increased dorsiflexion ROM for up to 48 hours following application.[59] These outcomes can lead to an optimization of performance immediately following applications which may increase the effects of rehabilitation.[58] However, it appears that treatment dosage is important. After a single session, mobilizations applied for 120 seconds created greater improvements in weight bearing dorsiflexion ROM than those applied for 30 seconds.[63] After 2 and 3 sessions, mobilizations applied for 120 seconds created larger improvements in ROM than those applied for either 60 or 30 seconds.[63] While improvements in weight bearing dorsiflexion ROM and SEBT due to talar joint mobilizations are retained for up to one week following the single session intervention,[56] two- two minute applications of clinician applied anterior to posterior joint mobilizations over 2-

3 weeks result in a more profound improvements relative to a single session.[56,62] Finally, joint mobilizations demonstrate superior improvements in ROM when combined with impairment based rehabilitation compared to rehabilitation alone or sham mobilizations with rehabilitation.[232] The results of these cumulative studies indicate that longer within session treatments and multiple sessions of manual anterior to posterior talar joint mobs combined with impairment based rehabilitation programs generate better outcomes in people with CAI. Furthermore, a recent systematic review and meta-analysis pooled data from nine joint mobilization studies and concluded that joint mobilizations improve dorsiflexion ROM and dynamic balance in people with CAI.[65]

Weight bearing mobilization with movement (MWM) treatments are also commonly used in clinical practice and increase dorsiflexion ROM for up to 48 hours in isolation.[59] A combination of non-weight bearing MWM for dorsiflexion, grade III anterior to posterior distal tibiofibular joint mobilizations, and grade III anterior to posterior talar joint mobilization have been shown to increase dorsiflexion in jump landing at initial contact in those with CAI.[60] Interestingly, the results of a single randomized controlled trial may suggest that supervised self-mobilizations may be slightly superior to clinician applied mobs in this population.[64] Participants in the clinical mobs group of this study sustained four 2-minute sets of grade III anterior to posterior talocrural joints, while those in the self-mobilization group completed four 2 minute sets of a weight bearing lung self-mobilization with a strap across the anterior talus for additional counterpressure.[64] At the conclusion of the 6 sessions, participants in the self-mobilization group showed improvements in the weight bearing lunge test (WBLT), the posteromedial reach direction of the SEBT, increased eversion strength, and improvements on the FAAM, Fear Avoidance Beliefs Questionnaires, and the Tampa Scale of Kineophobia-11.[64] Participants in the clinician mobilization group showed improvements in the posteromedial and posterolateral reach directions of the SEBT and increased inversion strength.[64] While the effect of joint mobilizations has not been investigated with regard to gait mechanics in the CAI population, it has been assessed in acute ankle sprains. More specifically, four sessions of anterior to posterior joint mobilizations applied every other day for three rounds of 60 seconds significantly increase dorsiflexion ROM within two sessions and resulted in a faster recovery of stride speed and step length in gait when added to conventional "rest-ice-compression-elevation" treatment.[61]

Taping and bracing have both been examined in the population with CAI. [66-78,233] Common taping techniques for the management of CAI are kinesiotaping, Mulligan fibular stabilization, and the basketweave technique employed by athletic trainers. While Mulligan fibular stabilization taping has been shown to increase reflexive excitability[78] and prevent subsequent lateral ankle sprains,[79]and patient reported outcomes on the FAAM,[233] it does not aid significantly in static or dynamic postural control.[71,80] Some might argue that the improved sense of reassurance, stability, and control noted following the application of taping[74] may be the result of an improved perception of stability, but overall the body of literature refutes its use as a recent systematic review found low quality evidence and inconsistent outcomes.[80] Similar to the Mulligan taping, the basketweave technique does not alter balance,[69] but does have an effect on gait mechanics by decreasing plantar flexion at loading response,[75] decreasing inversion in terminal stance,[77] and decreasing plantar flexion throughout swing phase.[67,73] While the basketweave tape does mitigate some abnormal biomechanics, namely excess inversion in terminal stance[77] and excess plantarflexion in swing,[67,73] the rigid tape provides only a passive biomechanical correction while the tape is applied, but not after removal. Similarly, the application of kinesiotape, decreases inversion ROM during the loading response of gait while applied,[77] which might decrease the risk for recurrent sprains, however, it is also passive in nature. Bracing has also been employed and investigated in the CAI population; flexible and semirigid bracing increased dorsiflexion at heel strike, and at toe off, the semirigid brace limits excess plantar flexion.[76] Additionally, a semirigid brace increased coordination and coordination variability of the foot-shank in early stance.[81] In more sport related activities, external bracing has also been shown to decrease frontal and sagittal plane excursion and plantar flexion angle at initial contact, but not inversion angle at contact during landing.[234] Taping and bracing have been the only interventions in this review to make any changes in gait biomechanics, however, these modalities continue to lack the benefit of carryover to the non-supported condition. Passive modalities might decrease the risk for recurrent sprains by facilitating biomechanical changes towards a more typical gait while applied, however, the lack of motor learning for lasting biomechanical change leaves individuals with CAI at risk in untapped and unbraced exposures. It is important to train the body to be self-reliant and function without external supports as it is unlikely that individuals with CAI will always be wearing tape or a brace.

Recent literature has aimed to assess current rehabilitation practices and has identified areas of weakness. For example, two recent systematic reviews[235,236] have assessed therapeutic exercise interventions reported in the literature. Authors concluded that while rehabilitation does decrease the risk of subsequent injury compared to usual care,[235] most active rehabilitation interventions targets sagittal plane range of motion, strength, and plyometrics.[236] Furthermore, authors concluded that the majority of therapeutic exercises are uniplanar and directed at the sagittal plane, which does not mimic the typical method of reinjury.[236] Finally, authors make no mention of movement retraining, suggesting that these interventions are not part of current clinical practice. Uniplanar sagittal based activities could leave those with a first time LAS

Table 1: The impact of common interventions on gait.

Interventions on Gait Mechanics			
Intervention Domain	**Improves Gait Mechanics?**	**Intervention Summary**	**Outcomes Modified**
Balance[37-44,47,229]	No	• Various single and double leg, static and dynamic tasks • 4-6 weeks, 3 sessions per week	• Improves static and dynamic postural control
Strength[31,32,48-52,54,230,231]	Not Studied	• Local and proximal training • 4–6 weeks, 3 sessions per week	• Improves strength and dynamic postural control
Joint Mobilization[55-65,232]	No	• Anterior to posterior and distal tibiofemoral mobilizations • Single session and 2-3 week intervention	• Improves PROs, sensorimotor function, motor neuron excitability/ reflex testing and ROM
Taping/Bracing[66-81,233,234]	Yes (while applied)	• Basketweave • Kinesiotaping • Fibular Stabilization	• Improves swing dorsiflexion, plantarflexion in loading, inversion in stance • Prevents LAS • No After Effects
Gait Retraining[27,88-92,95,96,111-113]	Yes	• Muscular Facilitation • Visual Feedback • Auditory Feedback • Vibration Feedback	• COP Medialization • Decreased lateral peak plantar pressure and time pressure integral • Decreased inversion at initial contact • Improved PL activity • Decreased propulsive vGRF, ankle joint contact force

vulnerable to recurrent recent sprains. Therefore, it has been recommended that gait training be incorporated in conservative management of lateral ankle sprains and CAI as an active, multiplanar movement retraining strategy.[84]

Feedback for Motor Learning

Gait retraining can be accomplished using biofeedback aimed at providing information about task performance to encourage motor adaptation. Motor adaptation occurs over time in response to error driven motor calibration.[237-239] In other words, as a person identifies error in their movement pattern, small adjustments, or adaptations, of the movement are created to minimize the errors and improve performance. The purpose of feedback is to help the user identify errors and facilitate motor plasticity[240] in order to increase the rate of adaptation.[238]

Feedback can be provided in a variety of ways, however all modalities identify errors by one of two neurocognitive techniques: by directing a subject's attentional focus internally or externally.[87] Internal feedback refers to cues about body structures (i.e.: body segments, joints, alignments).[87] An example of internal focus is a verbal cue such as, "Bend your knee more when you squat." Internal feedback draws the participants focus to his or her body and is detrimental to long term motor learning.[87,241] It is hypothesized that conscious control of movement through internal feedback, places constraints on reflexive movement, therefore limiting the number of strategies an individual can access to facilitate motor adaptation.[87,241] Conversely, external feedback draws the learner's attention to interactions between their body and the environment.[87] An example of external feedback for squatting is a verbal cue similar to, "try to touch the chair with your hips." This facilitates the same outcome as the previous internal feedback example and will produce increased knee flexion, but the learner is not focused on a single joint but rather their body in the environment. External feedback allows automatic control of afferent processing and leads to greater learning and retention.[87]

Two forms of external feedback are knowledge of results (KR) and knowledge of performance (KP). KR is defined as information regarding the successful outcome of a task, while KP provides information about the technique with which a person uses to complete the task.[241,242] KR feedback can be a dichotomous outcome such as "successful completion/ unsuccessful completion" after each trial or given as summary feedback such as how many times a player hit a target with a ball,[108] whereas a KP form of feedback could be about the height or trajectory of the ball as it approaches the target. KR has repeatedly shown superior outcomes for both short and long term motor learning[85-87] as well as across a variety of healthy[86,242] and pathological populations.[241] KR is theorized to allow the learner the independence to explore different strategies to complete the task and therefore promotes more active task involvement and deeper information processing.[85] In other words, it places less constraints on the techniques used to complete the task.

Sensory Feedback

In an uninjured system, inherent sensory feedback is used to facilitate smooth, gait characteristics while in motion. From animal models, we know that muscle spindles, golgi tendon organs, and joint receptors provides sensory input that contributes to the rhythm and timing of key gait events which assists in the progression from one phase of walking to the next.[108] Furthermore, cutaneous receptors play an important role in postural control and reactive balance during motion,[108] as the skin is the only interface between the individual and the environment.[165] In decerebrate cats, a moving treadmill underfoot stimulated proprioceptive organs and initiated reflexive movements that mimic consciously controlled gait, and when the treadmill speed was changed, so did the elicited movement pattern.[108] This indicates that movement can be both initiated, but more importantly modified in response to peripheral feedback without input from the higher cognitive levels.

Vision is another feedback source used to modulate gait. Visual cues help alter walking speed and stride length, visual orientation to vertical, and navigate obstacles and terrain.[108] However, as the function of vision is shared with other tasks during locomotion, the environment is sampled for less than 10% of total time while walking over stable surfaces and approximately 30% of total time when walking over uneven surfaces.[243,244]

Finally, vestibular feedback is a source of gait control. The role of this system is to detect and correct head movement independent of the trunk, therefore stabilizing the head and gaze to allow for intake of accurate visual information.[108] Additionally, the vestibular system detects head orientation relative to gravity and assists with fast postural corrections in response to unexpected external perturbations during movement through the vestibulo-spinal reflex.[245]

The visual, vestibular, and somatosensory systems work together in a healthy individual, to create a steady, consistent gait pattern during locomotion. Damage to a single system can cause a shift in sensory reweighting towards the remaining two systems and disrupt gait.[108] While an altered reweighting of sensory information has not been established during dynamic tasks in those with CAI, we know it exists in static tasks.[172] Furthermore, as the need to reweight the use of sensory in CAI, (i.e.: damage to mechanoreceptors and cutaneous receptors) is due to a permanent pathology, and not temporary one such as performing a task with the eyes closed.

Therefore, we can assume that reweighting is consistent across all tasks. In CAI, the use of feedback during training may help replace or supplement missing or decreased sensory input.

In the literature, external, KR feedback has been provided through augmented sensory feedback, most commonly in the form of visual modalities, auditory modalities, and haptic modalities. Visual feedback, the most studied modality, has demonstrated positive effects for both simple (visuomotor aiming) and complex tasks, such as learning complex motor skills like stepping patterns, however shows limitations in long term (greater than 1 week) retention.[246] Auditory feedback improves retention over visual feedback with complex tasks, such as hip position during the gymnastics pommel horse, showing retention as long as two weeks after the feedback was removed.[246] Haptic feedback is, to date, the least researched form of feedback, however, it is suggested to mediate motor learning in both early, or new learning and improve error detection and correction mechanisms in late learning by allowing the individual freedom within the confines of the feedback.[246] For example, a common use of haptic feedback is to set a path or time constraint during an activity and provide feedback when performance is not within the constraint. However, the acceptable paths and speed ranges are wide, which allows the participant to explore multiple paths and speeds within the constraints mediated by the feedback.[246] Therefore, haptic feedback has been suggested to be the best suited feedback modality for skill acquisition of spatiotemporal movement.[242]

Early studies using haptic feedback relied mainly on robotic limbs to facilitate or resist movement.[246] For example, in a study using error based feedback to modulate step height, haptic feedback supplied through movement resistance was compared to visual feedback.[247] Subjects were asked to walk on a treadmill with a robotic arm attached to their leg and screen in front of them. All participants had a marker placed on the outside of their ankle. Then, a virtually created avatar of the person's limbs was projected on the screen. The subjects were instructed mimic the avatar's walking to align the marker on their ankle (viewed through a live video feed overlain on the avatar) with a marker on the avatar's ankle. During the trial, the avatar was programmed to walk with an asymmetrical step height between limbs.[247] Subjects walked under three conditions; no feedback, haptic error modulation, or visual error modulation.[247] Haptic error modulations were produced by a force generated by the robotic limb which resisted the target movement. Participants also completed a visual error modulation trial in which the avatar walked with exaggerated movements that subjects were trying to mimic.[247] Subjects showed no negative learning effects during the haptic error modulation condition and had improved transfer of the new gait pattern to over ground gait compared to the visual modulation condition.[247] Furthermore, under the visual error modulation, subjects made more mistakes during training, negatively impacting learning and task transfer.[247]

As technology has advanced, researchers moved away from robotic feedback and started to use vibration stimuli. These tools are more portable and can be used in a variety of settings. For example, vibrotactile feedback has been applied to training in the field of sport performance and was found to be more effective than auditory[248] and visual[249] feedback mechanisms at improving skill acquisition such as learning to control heart rate during exercise,[248] learning simple snowboarding skills and gymnastics techniques,[248] as well as skill refinement (i.e.: wrist position while playing the violin, larger and faster strokes while rowing).[249] Vibrotactile feedback has also been used during gait training to alter foot progression angle in healthy subjects.[250] In one study, participants walked on a treadmill and received a vibration stimulus when their foot progression angle was above or below the targeted position.[250] Participants were able to correct the foot placement on the subsequent step, and only required feedback from 7-25% of the training session.[250]

Gait Retraining Interventions in CAI

Early gait retraining interventions for individuals with CAI focused on adding external forces with adapted shoes, weights on the foot, and resistance bands attached to the lower leg. First, researchers used two types of shoes which put the foot in a position of 30-45 degrees of combined plantarflexion and inversion.[88,89] Participants completed a series of functional exercises while wearing each of the destabilizing shoes and in standard lab shoes (shod) including a SLS, the SEBT anterior posteromedial and posterolateral direction, lateral hops, and walking on the treadmill. Results indicate that there was increased surface electromyography (sEMG) amplitude (normalized to quiet standing) of the PL, gastrocnemius, biceps femoris, and gluteus medius muscles in both destabilizing shoe conditions compared to the shod condition during the SLS, SEBT, lateral hops, and increased PL activity during walking compared to the shod condition.[88] Next, researchers studied a 4-week progressive loading rehabilitation program in people with CAI consisting of dynamic neuromuscular control exercises on varied surfaced and treadmill walking, which was completed either with or without the destabilization shoes.[89] Following completion of the program, results showed that the device group had decreased sEMG amplitude and decreased joint coupling, or variability during walking compared to the shod group.[89] However, neither group had any changes to ankle, hip, or knee kinematics after treatment.[89] While there were changes to dorsiflexion ROM when walking was included in the program, there were no significant frontal plane or kinetic changes following rehabilitation with destabilizing shoes.

Another treatment modality explored was an external load, which was applied to the dorsal anterolateral surface of the foot with a 1 pound sand bag (0.45 kg) in an attempt to magnify inversion and plantarflexion errors while walking.[251] Healthy participants walked on a treadmill for a 1 minute baseline assessment prior to the application of the weight. Next, participants walked for 5 minutes with the weight (adaptation phase) followed by one additional minute without the weight (post adaptation phase). A progressive increase in average eversion per step was noted in the adaptation phase (up to 1.1 ± 4.1º of eversion) at heel strike.[251] In the post adaptation phase for healthy individuals, their foot position has moved back into inversion (0.06 ± 4.1º of inversion), however, their foot remained less inverted than at baseline (1.4 ± 3.6º of inversion).[251] The subsequent study in this line of research used the same protocol to compare between a group of 12 individuals with CAI and 12 healthy control subjects.[90] As expected, the healthy controls exhibited the same pattern of increased eversion throughout the duration of walking with the load.[90] However, the group with CAI showed an initial increase in eversion at heel strike during the first minute of the adaptation phase, but had returned to the baseline position shortly after the first minute.[90] Authors hypothesized that the CAI participants either accommodated more rapidly to the initial sensory change associated with loading or they did not have the endurance to maintain the everted position.[90]

Last, Feger et al[91,92] created a device which is placed over the center of a treadmill to that the participant has a foot on each side of a track. Resistance bands were attached to from the center track to the participants legs and provided a medially directed force at the lower leg throughout the entire gait cycle. In the first study using this feedback device, participants completed a single session in which they walked on the treadmill at a self-selected pace until they reported achieving their normal walking, at which point data were collected for 30 seconds.[91] The main outcome variables were plantar pressure measures in different regions of the foot, sEMG normalized to quiet standing, and COP location. To determine the COP location, the stance phase was divided into 10 subphases and data within each phase was averaged to obtain a single representative point.[91] After the single session intervention, results indicated that peak plantar pressure had decreased in the lateral midfoot from 129.66 ± 25.74 kilopascals (kPa) at baseline to 99.82 ± 11 kPa at posttest and in the lateral forefoot from 157.60 ± 28.00 kPa at baseline to 130.20 ± 30.72 kPa at posttest, sEMG RMS area has increased 200 ms before and after heel strike, and the COP location had shifted medially across all 10 subphases of stance with effect sizes ranging from 0.88 to 1.63.[91] Authors then went on to use the device in a training protocol. Participants with CAI completed 5 sessions of 7-10 minutes of walking with progressive resistance across training sessions.[92] A posttest assessment session was completed 23-72 hours following completion of the last training session. Training improved scores on the FAAM-Sport, increased PL activity in mid and terminal stance, and created medial shifts in the COP location from 10% through 100% of stance with effect sizes from 0.5 to 1.83.[92]

After investigating external forces, newer feedback tools have focused on sensory stimuli rather than mechanical interventions. A low-tech feedback option is textured insoles. Twenty-one participants completed 5 overground walking trial with and without textured insoles in their shoes.[94] Researchers examined between trial variability of the ankle position from 200 ms before to 200 ms after initial contact and from heel strike to toe off. Variability was evaluated using the coefficient of multiple correlations and intraclass correlation.[94] Authors indicated that results showed a trend towards increased coefficient of multiple correlation values in the frontal plane, or less movement variability, while using the textured insoles, however neither of the phases of interest reached statistical significance ($p \geq 0.681$). It appears that this low-tech option may not have been effective as the feedback was not targeted to a specific action or foot segment, and therefore does not effectively target aberrant biomechanics. Similarly, feedback provided to the entire foot does not provide any suggestion as to how to correct the abnormal biomechanics. Finally, as those with CAI have decreased plantar cutaneous sensation,[165-167] it is questionable as to whether participants were able to perceive the full magnitude of the feedback.

An auditory appliance which provides active feedback was developed and tested during gait.[95] The tool is made of a pressure sensor placed under the 5th metatarsal and an auditory buzzer that can be calibrated to so that an auditory signal sounds when excess pressure is put on the lateral border of the foot.[95] In this study, subjects with CAI walked on a treadmill with and without the feedback at a self-selected speed. Data were collected at baseline (no feedback) and while the feedback was being given. Researchers examined peak plantar pressure and sEMG normalized to quiet standing as done by Feger et al.[91,92] During the experimental condition, subjects with CAI demonstrated decreased peak pressure in the lateral foot and an increase in PL activity as measured by sEMG compared to baseline.[95] These authors did not report COP data during this study.

Next, a visual feedback tool was developed and tested in people with CAI. The visual feedback tool consists of a crosshair laser mounted to the shoelaces of each participant.[96] Participants are instructed to align the vertical beam of the laser with a piece of tape placed vertically on the wall in front of a treadmill. The laser is positioned such that the person needs to pronate their foot to achieve the goal described in the instructions. Prior to walking with the feedback, participants completed a baseline assessment while walking without feedback on the treadmill. Then, they were fitted with the visual feedback tool and walked on the treadmill a second time. Following a short acclimation period, data were collected for 30 seconds. The main outcome variables were peak pressure and COP location as described by Feger et al.[91,92] While walking with the visual feedback, subjects showed a significant medial shift in COP location across the first 80% of stance (ES: 0.27-0.62) and a decrease in peak plantar pressure values under the lateral side of the foot (Baseline: 161.7±31.2 kPa, Feedback:142.6±37.7 kPa).[96]

The concept of visual feedback for gait retraining has been integrated into a comprehensive rehabilitation program.[27] In this study, 27 participants with CAI were randomized into either a feedback or a no feedback group. All participants completed the same, 8-session impairment-based rehabilitation program as the protocol used in the destabilization shoe study, which consisted of progressive neuromuscular control exercises on a variety of surfaces.[89] The program ended with walking on the treadmill for both groups, however the feedback group received visual feedback while walking whereas the no feedback group did not. Rather than a laser pointed at the wall, the visual feedback in this project was the real time position of the ankle at heel strike projected as an green oval on a screen in front of the treadmill.[27] A maximum inversion threshold was set for each gait retraining session and was made more difficult based on performance during the sessions. If participants exceeded the threshold, the oval turned red indicating a misstep. Feedback was faded after the first four gait retraining sessions. Baseline assessments were completed prior to the initiation of treatments and posttests occurred within 72 hours of the final session. Results identified significant differences in frontal plane ankle biomechanics with the feedback group showing decreased ankle inversion at initial contact (pre: 4.2 ± 4.6º, post: -3.1 ± 4.1º) and decreased peak inversion across the entire stride (pre: 6.7 ± 5.0º, post: 08 ± 4.3º).[27]

Sensory feedback tools are starting to be applied to areas outside of gait to determine their utility in other intervention strategies. For example, the auditory feedback tool and laser visual feedback tool have been used to address lateral COP deviations and altered plantar pressures during functional tasks in people with CAI.[252] Participants completed a SLS, a step down, lateral hops, and forward lunges under baseline (no feedback), auditory feedback, and visual feedback condition.[252] During a SLS with eyes open, both the auditory and visual feedback reduced the number of data points in the anterolateral quadrant and increased the number of data points in the posteromedial quadrant of the foot compared to baseline indicating a medial shift in the COP[252] making them more similar to controls.[175,185] When the SLS was performed with eyes closed, the results were similar for the auditory feedback condition, however, there were no differences between the visual feedback condition and baseline.[252] These results are logical because, despite the visual feedback being available, the person could not use it given the "eyes closed" constraint of the task. For the step down task, the auditory feedback condition increased peak pressure in the lateral heel, and pressure time integral in the lateral forefoot compared to baseline, while no changes were noted between the baseline and the visual feedback conditions.[252] The results of the auditory condition may be due to a change in strategy where participants tried to land with a more flat foot while stepping down as opposed to a forefoot contact which would normally be expected.[252] Similarly, the visual feedback was likely not useful in this task as midflight, there is no place to project the feedback until after heel strike and your foot is on the ground, in which case you have missed the opportunity to set up a good foot position by modifying heel strike. During the lateral hop, peak pressure in the lateral heel was increased with visual feedback compared to baseline, but auditory feedback did not alter any variables compared to baseline.[252] Authors indicated that during the lateral hop, participants kept their foot more dorsiflexed when using the visual feedback to keep the feedback projecting on the wall.[252] However, this would cause them to land in a more flat footed position, similar to that during the step down, which would cause an increase in pressure at the lateral heel. Regarding the auditory feedback, authors indicated that participants were unable to complete the task appropriately and respond to the feedback.[252] Finally, during forward lunges, the visual feedback did not change plantar pressure, however the auditory feedback condition significantly decreased the pressure-time integral in the lateral forefoot. Cumulatively, these results indicate that, while auditory and visual feedback had similar results in in gait, neither modality is appropriate for all functional tasks. It appears that the mechanism and requirements to successfully give and receive the feedback has a significant impact on the type of task with which it can be employed.

Despite promising results using feedback for gait retraining to date, the mechanisms and requirements to deliver feedback may limit long term motor learning. First, many of the modalities require either a treadmill (visual and resistance bands) either with or without a motion capture system to collect and analyze real time kinematics, or it requires a quiet environment where the feedback can be heard (auditory). This restricts use of the modalities to a clinic or laboratory environment which limits 1) the frequency of training, and 2) limits the variety of surfaces over which training can occur. However, haptic, vibration-based feedback provides a solution to overcome these limitations. First, vibration feedback creates the same external focus of attention as visual and auditory feedback, which we know are effective at changing gait biomechanics.[95,96] Second, using vibration feedback is portable and does not require a controlled, quiet environment, as the stimuli is tactile in nature. This makes the modality suitable for training an any environment, even in the real world.

RW training could enhance motor learning due to the inherent variability encountered through uneven surfaces and unexpected perturbations, and variability in practice is suggested to improve long term learning.[97-104] Shea and Kohl[97,98] completed a series of novel studies in which participants were asked to match a target force by pushing on a force transducer. Participants were assigned to a constant force group, a variable force group, or a constant + variable group. In the constant group the target was equal to the testing force for each trial, whereas in the variable group, the target fluctuated within 50N above and below the testing force. At a 24 hour retention test, in which the participants were asked to generate a force equal to the criterion force, participants in the variable force group demonstrated less absolute error,[97] or more accurate force generation, compared to the constant force group. Additionally, participants in the constant + variable group had smaller retention errors compared to the constant force group.[98]

Early motor learning results were then applied to a variety of other functional tasks. For example, improvements in mechanical efficiency, i.e.: an optimized movement strategy, was retained for 1 week following 7 sessions of wheelchair propulsion training in a variable training group versus a control group.[99] Additionally, in a study looking at movement accuracy,[100] participants moved their head to follow a target on a screen. Participants who trained with variable movement of the target showed less absolute errors (i.e.: less over- or undershooting of the head) than those who practiced with the same target movement over a 10 minute retention period.[100] More recently, these results have been replicated in tasks requiring larger movements, such as volleyball and tennis. Two different studies[101,102] investigated the impact of serving a tennis ball or volleyball with the goal to hit a target. Participants were randomized into in a variable practice group, where the distance of the target changed, or a constant group, where the target was fixed. In both studies, those in the variable group showed superior accuracy over the constant group after a 72 hour retention test.[101,102] These cumulative results indicate that variable training produces greater motor learning as measured by decreases in movement errors and an increase in efficiency over time. Variable practice is also suggested to create a motor program that transfers to other skills, indicating a more flexible, stable motor program. With both head tracking training,[100] tennis forearm training,[102] and volley ball training,[103] those in the variable practice groups generated more accurate movements when targets were moved to a novel distance compared to the constant training groups. This means that the learned skills can be used in new tasks, which promotes an improvement in overall function following training.

RW training that can be incorporated into daily activities, such as vibration feedback, allows for distributed practices, or small practice sessions spread out of over time. This is thought to limit fatigue[108] and allow time for mental practice[109] leading to better motor learning outcomes. First, distributed practice improves initial skill acquision.[105-107] For example, in a study looking at postural control training, measured by movement of an unstable platform, authors discovered that participants who trained with a distributed practice schedule (16 trials of 30s training: 30s rest) showed greater improvement in stability (i.e.: less platform movement) compared to those who trained with a massed practice session of 8 mins of training.[105] Interestingly, when authors provided an additional rest break to the massed group prior to a second massed practice episode, participants performed more similarly to the distributed group[105] indicating the benefit of rest. Distributed practice also leads to improved retention.[106,107] A study used a tapping task where participants had to quickly and accurately tap a series of 2 targets for 20 repetitions per trial with a stylus.[106] Results indicated that those who completed the task with 25 seconds of rest between each trial had higher accuracy at a 1-week follow up compared to the group who had 0.5 seconds between each trial.[106] These results were replicated in a golf putting task. When learning to putt in golf, researchers learned that distributing practice trials over four consecutive days, compared to a single mass practice session, led to more putting accuracy during the acquisition phase of learning and at 1- and 7-day retention tests.[107] The cumulative results surrounding varied and distributed practice indicate that these two practice schedules may lead to better long term changes in gait following RW training.

Currently there have been a handful of studies investigating the use of vibration feedback to modify gait biomechanics. The first study used a feedback device, similar to that of the auditory device, with a plantar pressure sensor attached to a vibration motor which was attached to the lateral lower leg in healthy participants.[253] The purpose of the device was to decrease the first peak knee adduction moment while walking and was calibrated to each individual so they received a vibration stimulus if the pressure under the lateral foot exceeded a set threshold. Results showed that during overground walking, vibration feedback reduced the first peak knee adduction moment compared to a control condition with no feedback.[253] From there, this study was repeated in a sample with medial compartment knee osteoarthritis.[110] Participants walked over level ground under a vibration feedback condition and a sham feedback condition where a similar, but unpowered device was attached to the shoe. The results of this study showed that the first peak knee adduction moment was reduced by as much as 9.2% and the peak varus knee angle decreased from 0.99 ± 4.90º during the sham condition to 0.29 ± 4.65º while walking with vibration feedback.[110] Interestingly, authors noted a medial shift in the COP location over the first half of stance (distance from lateral border of the foot - control: 43.1 ±5.6 mm, vibration feedback: 49.0 ± 7.6 mm).[110] The results of these preliminary studies in healthy subjects and those with medial knee osteoarthritis demonstrated that vibration feedback could be used to modify the COP location under the foot.

As CAI is a condition which can lead to a variety of impairments between people, results from one population should not be generalized to those with CAI. Therefore, we completed a pilot study using vibration feedback to modify COP location in people with CAI with the intervention applied while walking in a laboratory on the treadmill and overground in the real world.[111] In alignment with the International Ankle Consortium's recommendations,[4] participants were between 18 and 45 years of age, had at least one significant ankle sprain more than 1 year prior to enrollment, repeated episodes of the ankle "giving way", and self-reported functional limitations including a score ≥11 on the Identification of Functional Ankle Instability (IdFAI) questionnaire, ≤90% on the Foot and Ankle Ability Measure (FAAM) activities of daily living subscale and ≤80% on the sport subscale.[4] Exclusion criteria included a history of previous lower extremity surgery, a lower extremity fracture requiring realignment, or acute injuries within the past 3 months.[4] A custom made vibration feedback tool was secured to each participant's personal shoe and lower leg (Figure 2). A small force sensing resistor (FSR) (Model 402, Interlink Electronics, Inc, Camarillo, CA) was placed in the shoe under the fifth metatarsal head, the electronics were secured to the shoelaces, and the vibration motor was placed on the lateral malleolus. The feedback tool was calibrated to each participant such that they received a vibration stimulus when pressure under the lateral foot exceeded an individualized threshold. The threshold was manually set to that participants

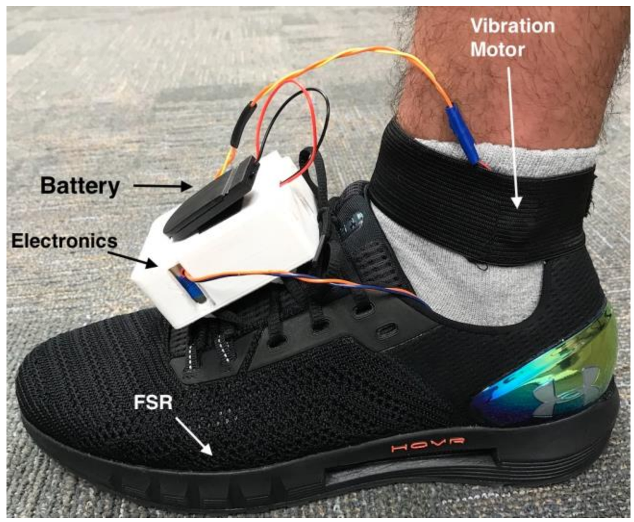


Figure 2: Vibration feedback tool in situ

received continuous feedback while in single limb stance with a fingertip touch for balance but not feedback in double limb support.

All participants completed a baseline assessment with the feedback tool attached to the shoe but turned off so they did not receive any feedback. During the assessment, participants walked on a split belt treadmill for 2 minutes with data collected during the second minute to allow participants time to accommodate to the weight of the feedback tool.[90] Next, participants completed a training in either the lab or the real world. For the lab training, the feedback tool was turned on while participants walked on the treadmill for 10 minutes. In the real-world training, participants walked a supervised 1-mile loop outside with feedback. After both sessions, participants completed an immediate posttest and 5-minute retention tests without feedback which were identical to the baseline assessment. Sessions for each participant were separated by at least 48 hours.

The stance phases of each step were averaged and divided into 10 subphases as previously done in the literature.[91,96,214] Due to a COVID-19 related research suspension or corrupted files, our final analysis included

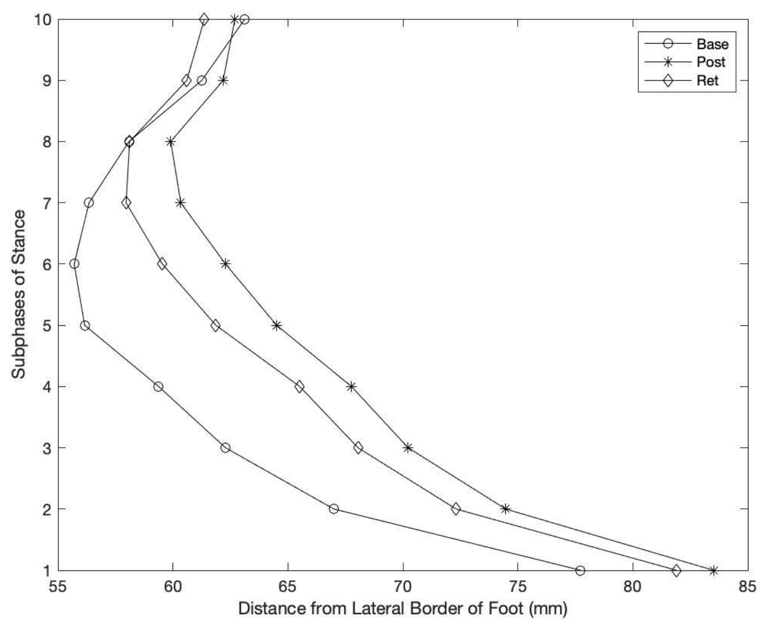


Figure 3: Group mean center of pressure change.

Migel KG, Wikstrom EA. The effect of laboratory and real world gait training with vibration feedback on center of pressure during gait in people with chronic ankle instability. Gait Posture. Mar 2021;85(1879-2219 (Electronic):238-243.

16 participants in the lab setting and 18 participants in the RW environment. Separate one-way repeated measures ANOVAs were completed among baseline, posttest, and retention tests for each subphase. Our results indicated that after laboratory training, the COP location for phases 1 through 9 differed among baseline, posttest, and retention timepoints (p<0.03).[111] Post hoc testing indicated that the phase 1 COP position was more medial (i.e.: larger) at the posttest (mean difference (MD): 3.63mm, p = 0.023) compared to baseline.[111] In phases 2-9, the COP was more medial at both posttest (MD: 0.57-5.12 mm, p ≤ 0.004) and retention (MD: 1.69-4.40 mm, p ≤ 0.049) compared to baseline.[111] All significantly different phases were associated with moderate to large effect sizes with 95% CIs that did not cross zero.[111] For RW training, there were statistically significant differences in the COP location among the three time points for phases 1 through 7 (p ≤ 0.016).[111] Post hoc testing revealed that**,** relative to baseline, posttest measures were more medial for phases 1-7 (MD: 2.26-8.27 mm, p ≤ 0.008) while retention measures were more medial in phases 1-6 (MD: 4.14-6.42 mm, p ≤ 0.049).[111] All significant time points were accompanied by moderate to large effect sizes with 95% CIs that did not cross zero.[111] (Figure 3) Secondary analyses of the data revealed that after

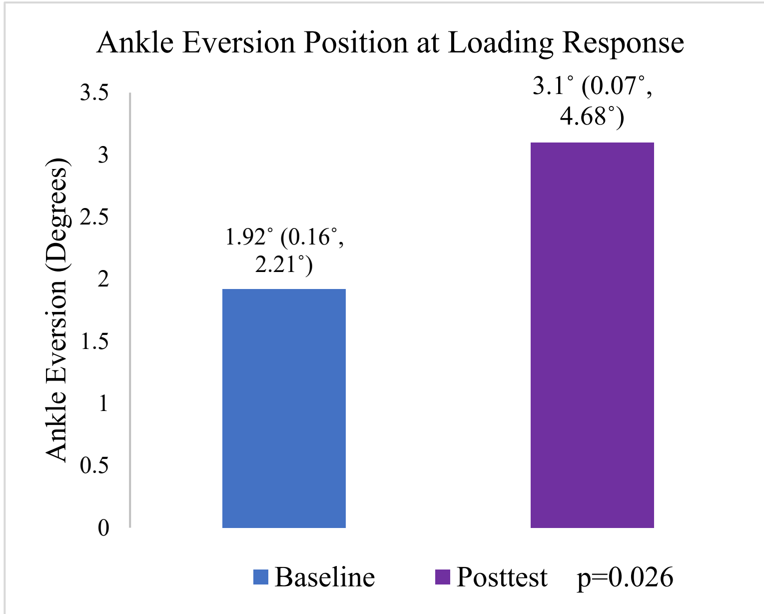


Figure 4: Ankle eversion position at loading response after a single real-world vibration training session.

Adapted from Migel KG, Wikstrom EA. Immediate effects of vibration biofeedback on ankle kinematics in people with chronic ankle instability. Clin Biomech (Bristol, Avon). Sep 25 2021;90(1879-1271 (Electronic)):105495.

real-world training, the ankle was more everted at initial contact than at baseline (mean difference:-1.19±2.12º, effect size:0.54, Figure 4).[113] Furthermore, during laboratory training participants experienced decreased propulsive vertical ground reaction forces (vGRF) and ankle joint contact forces during push off (Figure 5).[112] Cumulatively, the results of this pilot study demonstrate that vibration feedback gait retraining can mitigate abnormal gait biomechanics in CAI which may be able to slow the progression to PTOA. Real-world vibration feedback training is a plausible solution to creating long term lasting change in people with CAI.

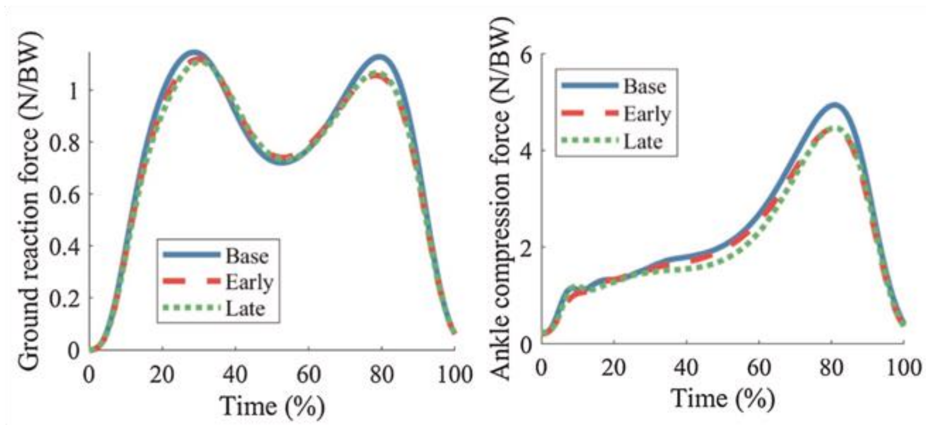


Figure 5: Vertical ground reaction force and ankle joint contact forces during vibration feedback gait retraining.

Jang J, Migel KG, Kim H, Wikstrom EA. Acute Vibration Feedback During Gait Reduces Mechanical Ankle Joint Loading in Chronic Ankle Instability Patients. Gait Posture. 2021;90:261-266. doi:10.1016/j.gaitpost.2021.09.171

In people with CAI, altered biomechanics are present during both daily activities (e.g., step-down, walking gait) and more sport specific tasks (e.g., jump landing). Altered biomechanics are also thought to contribute to recurrent sprains[21] and talar cartilage degeneration[5] leading to PTOA. The recent evidence to support gait re-training represents a promising opportunity to meaningfully impact movement biomechanics in those with a history of ankle sprains. However, the current evidence is preliminary at best and further research is needed to optimize modes and treatment parameters to create large and permanent biomechanical changes that can improve patient reported outcomes and potentially slow the progression of ankle post-traumatic osteoarthritis.

CHAPTER 3: EXPERIMENTAL DESIGN AND METHODS

Overview: Aims 1-3

The goal of Aims 1-3 were to understand factors related to RW-VF gait retraining delivery and possible outcomes of training. The purpose of Aim 1 was to begin optimizing feedback parameters to provide a data driven training schedule. The purpose of Aim 2 was to understand the immediate and cumulative effects of RW-VF training on gait biomechanics in people with CAI. The purpose of Aim 3 was to explore the role that non-modifiable structural factors and modifiable neuromuscular control factors have in RW-VF efficacy. Altered gait biomechanics are a known risk factor for subsequent injury[21,22] and may lead to altered cartilage loading and PTOA development. Current gait retraining interventions are not ideal for creating maximal motor learning and retention. Therefore, the studies included in this dissertation sought to begin developing a new, real world gait retraining protocol using vibration feedback which could be integrated into clinical practice to slow the progression of joint degeneration.

Participants

Chronic Ankle Instability (Aims 1, 2, and 3)

CAI participants in these studies qualified based on the recommended selection criteria for CAI in research as published by the International Ankle Consortium.[4] Participants 1) were between the ages of 18 – 35 years, 2) had a history of at least 1 significant lateral ankle sprain which occurred at least 12 months prior to enrollment and defined as a sprain which caused at least 1 day of interrupted physical activity, 3) had a history of recurrent sprains and/or episodes of “giving way”, 4) had a sense of ankle instability measured by a score of ≥ 11 on the IdFAI, and 5) had self-reported functional limitations measured by a score of < 90% of the FAAM-Activities of Daily Living subscale and < 80% on the FAAM-Sport subscale.[4] Exclusion criteria included 1) evidence of bilateral CAI using the criteria above, 2) a history of previous surgery in either lower extremity, 3) a history of a fracture requiring realignment in either lower extremity, 4) an acute (< 12 weeks from enrollment) injury to either lower extremity, 4) any condition known to affect gait such as peripheral neuropathy, diabetes, neurological disorders, or neurodegenerative diseases, and 5) knowingly pregnant.

Enrolling participants who were between the ages of 18-35 targeted legal adults who were less likely to have age-related joint degeneration and less likely to have PTOA.[8] Participants were enrolled regardless of sex at birth as there is no evidence that CAI is more prevalent in either males or females and were not required to have a medical diagnosis to participate as at least 50% of individuals who sustain a lateral ankle sprain do not seek medical attention.[8] Participants had a history of recurrent sprains, defined as two or more ankle sprains to the same ankle, and/or episodes of “giving way” which are events of uncontrolled excessive inversion during activity that does not cause an acute lateral ankle sprain.[4] The IdFAI is a self-reported patient outcome directed at identifying those with CAI based on a sense of instability in the ankle. The questions included in the assessment encompass any care received, ankle behaviors such as rolling or giving way, function, and symptoms during activity. This test has a high accuracy for identifying individuals with CAI (89.6%) with low burden on both the participant and the test administrator.[254] Additionally, this test possesses high reliability (0.92) and validity (ρ=-0.38, p<0.01).[255] The FAAM is a non-disease specific, self-reported outcome that has been validated in the CAI population.[256] These two measures were used to capture instability and functional limitations. Demographics were collected for all CAI participants immediately after enrollment and included age in years, height in cm, weight in kg, number of ankle sprains.

CAI participants who enrolled in the study to complete Aim 1 and 3 were eligible to participate in the study for Aim 2 as the minimal wash out period was 10 days between studies. CAI participants complete an online screening survey prior to enrollment in both study 1 (Aim 1 & 3) and study 2 (Aim 2) which determined their eligibility based on the inclusion and exclusion criteria.

Healthy Controls (Aim 2 only)

Data from a healthy control cohort was collected as part of an unrelated project and acted as a reference group for the COP location in uninjured walking. The purpose was to aid in determining whether RW-VF created a large enough change in the COP location to be similar to that of healthy controls. Inclusion criteria for healthy control participants were as follows: 1) between the ages of 18-35 years, 2) no previous history of lower extremity surgery, 3) no lower extremity injury history in the past 6 months, 4) no history of neurological disorders (i.e.: stroke, cerebral palsy, multiple sclerosis, etc.), and 5) not knowingly pregnant. Patient reported outcome measures were not collected for healthy participants as this is a secondary analysis. Patient reported outcomes were not collected in the original investigation.

Feedback Tool

A custom-made vibration feedback tool weighing 56.67 grams was used to complete Aims 1-3. The tool was secured to each participant's personal shoe and lower leg (Figure 2). A small FSR (Model 402, Interlink Electronics, Inc, Camarillo, CA, Appendix A) was placed in the shoe under the lateral aspect of the foot. For Aim 1 the sensor was placed under the fifth metatarsal head and under the lateral heel, defined as the most lateral portion of the heel, for each participant. Based on the outcome of study 1/ Aim 1, the sensor was placed under the fifth metatarsal head for all subsequent studies (Aim 2 & 3).

The FSR was secured to the shoe insole with adhesive tape and the electronics and battery were secured to the shoelaces with a custom enclosure. The 200 Hz vibration motor (displacement of <1 millimeter) was placed on the lateral malleolus with a custom elastic strap. The lateral malleolus was chosen because placing the stimulus on a boney prominence reduces vibration attenuation due to soft tissue, therefore maximizing perception. A lateral location inside the shoe was not selected as people with CAI have decreased cutaneous sensitivity on the plantar surface of the foot,[165-167] which could lead to decreased vibration perception and subsequently decreased effectiveness of the feedback.

The feedback tool was calibrated for each participant prior to data collection or training by manually adjusting the threshold (i.e.: the electrical resistance) that the FSR must overcome to initiate a signal. The threshold was set as the lowest level such that participants received no feedback in a double limb support position but did receive feedback in a single limb support position while lightly touching down with their contralateral limb. The single limb position is adapted from McPoil and Cornwall[257] and was selected as it is known to mimic the single leg stance position during midstance. Active feedback in the single limb position ensured that the feedback was present during every step. This calibration technique was adapted from our pilot study investigating vibration feedback gait retraining in lab and RW environments which allowed a finger touch stabilization, however, using the contralateral limb to stabilize balance during calibration ensured that participants used a lateral weight shift at the pelvis similar to gait. When successfully calibrated the vibration motor turned on when the pressure on the FSR exceeded the threshold. To test the calibration, participants walked on level ground with standard instructions, "walk so you do not get the vibration," which was also modified from Donovan et al.[95] The device was considered successfully calibrated when participants were able to complete the task with reports of minimal vibration stimuli. In our pilot study as in the studies used to complete these Aims, no participant required more than two calibration attempts.

Biomechanical Gait Assessment Procedures

Throughout the two studies, multiple gait biomechanics assessments were completed on an instrumented treadmill. Treadmill walking speeds were based on a participant's self-selected walking speed. This was measured by completing 5 over ground walking trials between two timing gates approximately 1 meter apart (Dashr 2.0, Dashr Motion Performance Systems, Lincoln, NE). The average speed was converted to meters per second and used as the treadmill speed for all assessments.

At each assessment, participants donned a spandex top and shorts. Retroreflective markers were secured to the participant on the following boney landmarks and the shoes over the boney landmarks: bilateral 1st metatarsal head (MH), 2nd MH, 5th MH, anterolateral/medial calcaneus just distal to the malleoli, posterior calcaneus, and posterolateral/medial calcaneus half way between the anterolateral/medial calcaneus markers and the posterior heel, medial/lateral malleoli, tibial tuberosities, medial and lateral epicondyles of the femur, anterior thigh, greater

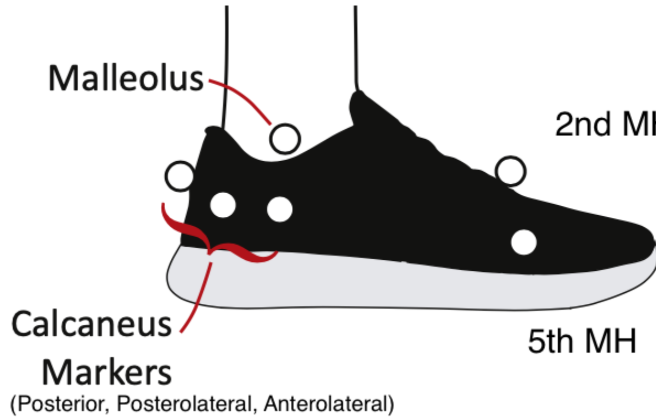


Figure 6: Foot marker arrangement, Adapted from Zelik & Honert

trochanters, and anterior superior iliac spines. Additionally, a sacral cluster was used which contained bilateral posterior superior iliac spine markers and a coccyx marker. The markers on the foot were adapted from Zelik and Honert[258] (Figure 6). These markers allowed us to model the foot as a single rigid segment as well as create a hindfoot and forefoot section of the foot. For this analysis, the foot was defined as a rigid segment based on results from our pilot data which suggested the segmented foot showed consistent results as a single foot model. Inversion was calculated as the angle between the foot and the shank in the frontal plane. Multi-segment foot analyses as well as calculations of other kinetic variables (i.e.: contact time of the lateral foot) will be used for exploratory analyses in the future. A static calibration trial was captured at the initiation of each assessment session.

For each assessment, participants walked on an instrumented, split belt treadmill (Bertec, Columbus, OH) with 1.75 x 0.5 m force plates embedded under each belt for two minutes. Data were collected during the second minute of each assessment to allow the participant to achieve their normal walking gait and to accommodate to the weight of the feedback tool[90]. Kinetic data were collected at a sampling rate of 1200 Hz and filtered using a 4th order lowpass Butterworth filter with a cut off frequency of 10 Hz. Synchronized marker trajectories were captured by an 8-

camera motion capture system (QTM, Qualisys, Gothenburg, Sweden) sampled at 120 Hz and filtered with a 4^{th} order lowpass Butterworth filter with a cut off frequency of 10 Hz. These procedures were used for all collection sessions.

General Data Reduction Techniques

Data were reduced by isolating all stance phases of the involved limb with a heel strike (vertical ground reaction force (vGRF) > 20 Newtons) followed by a toe off (vGRF < 20 Newtons) during the collection period. COP location relative to the laboratory coordinate system were extracted from the motion capture software. To determine the location of the COP within the foot, we subtracted the perpendicular distance between the COP location and the midline of the foot (COP – midline) such that positive values indicated that the COP was lateral to the midline and negative values indicated that the COP was medial to the midline. The midline of the foot was defined as the line between a point half the distance between the medial and lateral malleoli and a second point half of the distance between the 1^{st} and 5^{th} metatarsal heads during each frame. All COP data were normalized to maximum foot width and expressed as a percent of maximal foot width. (%FW) The maximal foot width was calculated as the distance in millimeters between the 1^{st} and 5^{th} metatarsal heads which were obtained from the static calibration file.

Next, the COP distance for each stance phase was divided into 10 subphases each representing 10% of stance.[17,91,96] Data within each subphase were averaged to obtain a single point representing the average COP distance during that subphase. The 10 discrete points were then averaged across each step obtained during the collection period.

Aim 1:

Understand the impact of FSR placement (lateral heel versus 5th metatarsal head) on COP location during gait following 10 minutes of training on a treadmill.

Rationale

Given that this intervention is still in the development phase, optimal feedback parameters to create the ideal COP changes in people with CAI remain unknown. This aim helps us understand how the timing of vibration feedback impacts the COP shift. With this feedback tool, feedback timing was altered by changing the location of the FSR within the shoe so that was loaded during different phases of gait. The sensor location at the 5th metatarsal head has been investigated within people with CAI. In this location, feedback was delivered during midstance. However, research in other population has placed the sensor under the lateral heel.[110,253] Using a lateral heel placement caused the feedback to be given earlier in the stance phase during loading response. This aim helped us understand which feedback location was more effective in people with CAI.

Experimental Procedures

This study used a two-session cross over design to determine the optimal sensor location using a between-within repeated measures factorial design. The order of sensor placement (lateral heel or 5th metatarsal head (MH)) was randomly assigned to each CAI participant using a random number generator (1 = heel, 2 = 5th MH) upon enrollment. After the feedback tool was in place, calibrated, and the participant was prepared for motion capture, a baseline session was collected as described above with the feedback device in place but not powered. After the baseline assessment, the feedback tool was turned on and participants completed a 10-minute training session while walking on the treadmill. Participants were given the instruction to walk so that there is no vibration. During training, the second minute of walking was captured as an early adaptation phase and was used in Aim 3. Immediately following completion of training, power to the feedback tool was turned off and participants completed a posttest assessment with the instructions to “walk normally” to determine if a medial COP shift occurred following the training session. Participants returned at least 72 hours after the first session to complete a second, identical session with the sensor in the second location.

Data Reduction

Baseline and posttest data were reduced as described above to determine a single representative point for each 10-percentile of stance for each sensor location.

Sample Size Analysis

Previous research using sensory feedback tools in the lab,[95,96] including our pilot study, have reported effect sizes ranging between 0.1 and 3.04 when comparing the intervention to a control condition[95,96] or pre-to-post intervention (pilot) analyses. More than 67% of the reported effect sizes (27/40) reported large effect sizes[259] ($g \geq 0.8$). Based on these results, we chose a conservative effect size estimate of 0.5 as we compared two active interventions (i.e.: feedback with the sensor at the lateral heel and feedback with the sensor at the 5th MH). However, as there is currently no evidence comparing active interventions and therefore no good estimates of correlations between intervention outcomes as required to calculate a sample size for a two-way repeated measures ANCOVA with baseline data as a covariate (see Statistical Analysis section below), our power analysis was based on an ultra-conservative estimate with a correlation of 0 between baseline and posttest measures and a correlation of 1 between the two posttest conditions, which transforms the calculation into an analysis based on a two way t-test as recommended by Morgan and Case.[260] This technique overestimates the sample size because using the most conservative correlations does not account for the variance ratio as an ANCOVA would.[260] The variance ratio and therefore the required sample size decreases by at least 43% as the number of repeated measures increases.[260] Our power analysis, with alpha = 0.05 and 80% power indicates that a maximum of 34 participants are required to determine statistical significance (G*Power v. 3.1.9.4). Given that this is an overestimation, our plan was to complete the first analysis when 50% of the data were collected (n=17). Significant results in the preliminary analysis suggested the sample size was sufficient for this pilot study. If the results were not significant, we were going to complete another analysis when 75% of the data (n=26) were collected. Similarly, a significant result would indicate an adequate sample size and a non-significant result would indicate the entire sample size (n=34) was to be collected. However, given unanticipated biomechanical changes involving foot position at initial contact as well as other deleterious kinetic chain and spatiotemporal gait variables, this committee chose to accept 10 participants as a sufficient number of participants and concluded the study early.

Statistical Analysis

Primary Analysis

Prior to statistical analyses, the data were assessed for normality and outliers, which were defined as any value greater or less than the product of 1.5 times the interquartile range. While the data were not normally distributed using the Kolmogorov-Smirnov Test for Normality, values of skew (-1.515 to 1.991) and kurtosis (-4.893 to 2.907) were acceptable to apply parametric tests.[261-263] However, based on our visual analysis of the data, non-parametric analyses were also completed and reported.

From the lab portion of our pilot study, preferred gait speed did not correlate with COP change between baseline and posttest ($p>0.05$) therefore, we did not control for gait speed in our analyses. Based on current statistical recommendations[264] and previous gait retraining literature,[17,91,96] we did not correct for multiple comparisons. We used separate two-way analyses of covariance (ANCOVA) to compare between conditions for each subphase of gait. Our independent variables were time (pre, post) and sensor location (lateral heel, 5th MH) and our dependent variable was medial-lateral COP location. The average medial-lateral COP location at baseline was used as a covariate as there were no statistically significant differences in medial-lateral COP location between baseline conditions. The addition of the covariate adjusted for any baseline non-statistically significant differences between conditions.[265] Tukey's Least Significant Difference pairwise tests were used for *post hoc* analyses in the event of significant omnibus tests. For all tests (primary and exploratory analyses), alpha was set *a priori* at = 0.05. Hedge's g effect sizes and 95% confidence intervals were calculated. Effect sizes were interpreted as trivial ($g<|0.2|$), small ($g=|0.2–0.49|$), moderate ($g=|0.50–0.79|$), and large ($g=|\geq0.80|$).[259] The complementary non-parametric analysis for each subphase of gait included Wilcoxon Signed Rank tests 1) between baseline ML-COP and posttest ML-COP location and 2) between the change scores (posttest-baseline) while walking with the FSR in each location.

Separate two-way (FSR location x Time) repeated measures analysis of covariances (rmANCOVAs) were completed to compare ML-COP distance at baseline and while walking between FSR locations for each subphase of gait. The average baseline ML-COP location between conditions was included as a covariate to adjust for any baseline differences between conditions.[265]

Exploratory Analyses

During data collection, gait deviations were noted which suggested that at least 4/10 participants visibly altered their biomechanics at initial contact from a heel strike to a midfoot or forefoot strike while training with the FSR at the heel location. This impacted our primary analysis as those participants utilized unanticipated biomechanical strategies to offload the FSR and avoid feedback stimuli. This prompted additional exploratory analyses of our participant's data to quantify the strategy used. While only 4/10 participants demonstrated biomechanical deviations which were observable, we chose to include the entire cohort to capture more subtle strategy changes. First, we assessed changes in the anterior-posterior COP (AP-COP). Theoretically, a mid or forefoot would cause the person to land with a more plantarflexed ankle and therefore a more anterior COP location at initial contact. The anterior-posterior COP (AP-COP) at initial contact was calculated as the distance along the midline of the foot using the raw resultant COP position, the perpendicular distance between the ML-COP and the midline of the foot, and the Pythagorean theorem. AP-COP was normalized to the length of the truncated foot which was defined as the distance between the calcaneal marker and the midpoint of the 1st and 5th metatarsal markers and expressed as percent foot length (%FL). A two-way (FSR x Time) rmANCOVA was completed between AP-COP at initial contact under each FSR location between baseline and early accommodation timepoints with average baseline AP-COP as a covariate.

Next, we completed a follow up analysis with sagittal plane ankle position as an additional covariate. A mid or forefoot initial contact could be attained by plantarflexing the ankle and could impact the AP-COP results. Then, we completed an analysis which controlled for foot length and is important to normalize the data for between-subjects comparisons. Given that the COP location is derived within a foot projected on the ground[266], a more plantarflexed foot could make a shorter foot length. A one-way rmANCOVA was conducted with average baseline AP-COP and average sagittal ankle position at initial contact as covariates within the heel condition.

Next, we completed an analysis to determine if participants altered their foot position at initial contact by manipulating step length. A shorter step length may allow for a more foot flat initial contact which could limit loading on the FSR under the heel without having to significantly change the ankle position. Step length was calculated as the distance between the heel markers at initial contact for both the involved and uninvolved limb and then divided by height in meters to normalize the data. Wilcoxon Signed Rank tests were completed to assess step length between baseline and early accommodation phases for both the involved and uninvolved limb under the heel condition.

Finally, a visual inspection of the data was completed to assess for any other underlying trends which could shed light on our nonsignificant primary analysis results. AP-COP data at initial contact were plotted for each participant between baseline and early accommodation. Both the magnitude and direction of change between the two time points were assessed.

Aim 2:

Understand how the COP location during gait changes after RW-VF training in those with CAI and how such changes compare to the COP location of healthy controls.

Rationale

Comparing within CAI changes before and after a single and multiple RW-VF training allowed for a greater understanding of how vibration feedback impacted the COP location within this pathology. Looking at within CAI COP retention after 1 week gave us initial information about the latency and amount of motor learning after a short, two-week training period. Given that the goal of this intervention was to alter the gait biomechanics of people with CAI so that they more closely mimic the gait biomechanics of a healthy population including a comparison with a healthy cohort allowed us to objectively determine if the intervention could do that.

Experimental Procedures

In this cohort study a group of CAI participants completed six RW-VF sessions in two weeks with four assessment points (Figure 7). CAI participants enrolled and completed an initial baseline session (B1) to collect gait biomechanics as described above. Twenty-four to 48 hours

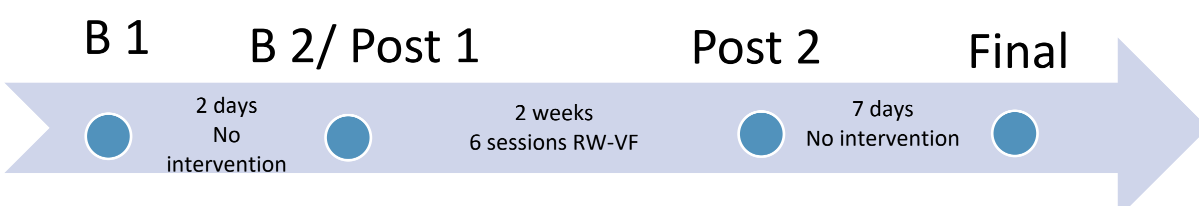


Figure 7: Study design (Aim 2)

later, participants returned for a second baseline (B2) session and the first training session. The B1 and B2 sessions were used to calculate the minimal detectable change (MDC) of COP location changes. Prior to the baseline for B2, the feedback tool was donned with the sensor placed under the 5th MH and calibrated using the methods described above. Baseline data were collected during minute 1-2 of walking with no feedback. Next, the feedback was turned on and participants completed the first of six RW training sessions followed by an immediate posttest (Post 1). During each training session, participants walked a supervised 1-mile loop on campus, in the real world, while receiving feedback. Participants walked all six predetermined 1-mile routes (Appendix B) during the training protocol in a randomized order which was generated using a random number generator. The time to complete the training path, including any adverse events which impacted progress (i.e.: red lights, waiting at cross walks) were recorded for each training session. At Post 1, the feedback tool remained in place but was powered down to minimize the time latency between conclusion of the training and data collection. We believe that leaving the tool in place for B2 and Post 1 did not impact our results as it's been established that people with CAI accommodate to a 0.45 kg mass within 1 minute.[90] As our feedback tool weighs 56.67 grams, and our baseline data collection of the session occurred after participants had been walking for 1 minute, there should have been no impact related to the presence of the tool at these two timepoints.

Over the course of two weeks, participants returned for an additional five supervised training sessions on separate days. A single feedback tool was used for all training sessions for a single participant. Only one participant switched feedback tools during their training due to electronics issues. Using a single tool minimized the need to recalibrate the feedback tool. Twenty-four to 72 hours after the last training session, participants returned to the lab for a posttest assessment (Post 2) during which gait biomechanics were collected. An identical biomechanics lab session was completed 1-week later to assess retention (Final). At Post 2 and Final timepoints, participants completed the same patient reported outcome measures (the IdFAI, the FAAM-ADL, and the FAAM-S) as during their screening.

A secondary analysis was completed on a healthy control database to compare the COP location in people with and without CAI. Biomechanical data for the healthy control cohort were previously collected in a single session using the same methods as above to determine the treadmill speed. A similar marker set up was used with the control participants, however, the foot segment only had three markers: the 1st MH, 5th MH and posterior calcaneus. As these are the same markers which define our rigid foot segment in those with CAI, this did not impact the between group (CAI vs Control) comparisons. During the session, participants walked on the treadmill for 5 minutes. Data were captured during the last 90 seconds, however for our analysis, we isolated the last 60 seconds to match the protocol completed by the CAI group. Data were not available during the first 3:30 of the session.

Data Reduction

Biomechanical data for both the CAI group and the control group were reduced as above.

Sample Size Analysis

Research Question 1: Does the COP location in those with CAI change following a single session of RW-VF training?

Research Hypothesis 1: A single session of RW-VF training will cause a medial shift in the COP in people with CAI and this change will exceed the calculated MDC.

Sample Size Calculation: Effect sizes from previous lab based studies[95,96] and our lab based pilot testing range from 0.1 to 3.04 in both pre-to-post (pilot) and intervention-to-control[95,96] single session analyses. From our single session RW data, effect sizes ranged from 0.1 to 1.01 across the 10 subphases of gait. Therefore, we estimated a conservative effect size of 0.3 following a single session. To determine statistical significance for the within factor analyses (CAI changes over a single session), a sample size of 17 was required with an effect size of 0.3, an alpha level = 0.05 and 80% power (G*Power v. 3.1.9.4).

Research Hypothesis 2: The COP location after a single session of RW-VF will be similar to the COP location of healthy controls while walking.

Sample Size Calculation: The current literature about the COP location in people with CAI compared to controls suggests that effect sizes range from 0.9 to 1.9 across the 10 subphases of gait.[17] Therefore, to determine sample size to address this hypothesis we estimated a conservative effect size of 1.0. When coupled with an alpha ≤ 0.05 and 80% power, our analysis indicated a total of 14 subjects per group were required to detect statistical differences (G*Power v. 3.1.9.4).

Research Question 2: Does the COP location in those with CAI, change following two weeks of RW-VF training?

Research Hypothesis 3: Two weeks of RW-VF training will cause a medial shift in the COP in people with CAI and this change will exceed the calculated MDC.

Sample Size Calculation: Currently, there is no literature comparing multiday treatment sessions on COP behavior. However, we anticipated that effect sizes following multiple trainings would be larger than that of a single session due to a cumulative training effect. Therefore, we conservatively powered the multiday training analyses with an effect size of 0.33. As all within factor comparisons before and after two-weeks of training were completed with a single repeated measures analysis (pre, post, retention) 17 participants were required to determine statistical differences with an effect size 0.33, alpha = 0.05, 80% power, and 3 repeated measures (G*Power v. 3.1.9.4).

Research Hypotheses 4: The COP location after two-weeks of RW-VF will be similar to the COP location of healthy controls while walking.

Sample Size Calculation: Like the sample size calculation for research hypothesis 3, we used the effect sizes from a single training session to calculate the sample size for research hypothesis 4. Therefore, with an estimated effect size of 1.0, alpha = 0.05, and 80% power, 14 participants per group were required to determine statistical differences. (G*Power v. 3.1.9.4).

Research Question 3: Is the COP location retained after 1 week with no intervention?

Research Hypothesis 5: The COP location will be retained for at least 40% of the significant phases identified in RQ 2/ hypothesis 3 following a 1-week retention.

Sample Size Calculation: Currently, our pilot project is the only study to include retention data following sensory feedback for gait retraining. In the real world, we reported fewer significant phases than immediately following training with effect sizes ranging from 0.02 to 1.15. Considering effect sizes from a single session and our pilot data, we estimate a conservative effect size of 0.33. Therefore 20 participants were required to determine statistical differences with an effect size 0.3, alpha = 0.05, 80% power, and 3 repeated measures (G*Power v. 3.1.9.4).

Sample Size Summary

To adequately power this group of Research Questions, we based our enrollment for Aim 2 on 20 participants, which was the largest number of participants indicated of all the sample size calculations. We enrolled a total of 20 CAI participants who all completed the entire training program. The healthy control cohort totaled at 24 participants. We used data from all healthy control participants as a normative reference group.

Statistical Analysis

Prior to statistical analyses, the data were assessed for normality and inspected for outliers, which was defined as any value greater or less than the product of 1.5 times the interquartile range. From the RW portion of our pilot study, preferred gait speed only correlated with COP change between baseline and posttest for a single subphase in gait (phase 9, $r= -0.472$, $p=0.048$). All other correlations were not significant ($p>0.05$), therefore, we did not control for gait speed in our analyses. Additionally, based on current statistical recommendations[264] and previous gait retraining literature,[17,91,96] we did not correct for multiple comparisons in our analyses.

Our independent variable for all analyses was time and our dependent variable was COP location within in the foot. We calculated the MDC (B1 to B2) of the COP location for each stance subphase of the CAI group as:

$$MDC = SEM \times 1.96 \times \sqrt{2}$$

Where 1.96 was the z score associated with a 95% confidence interval and the square root of two accounts for the potential error in each group.[267] The Standard Error of the Mean (SEM) was calculated as:

$$SEM = SD_d/\sqrt{2}$$

Where SD_d is the standard deviation of the difference between B1 and B2.[267]

To determine if the COP location changed in those with CAI following a single session of RW-VF (RQ 1), we used separate Wilcoxon Sign Rank Tests to compare COP data between B2 and Post 1 of the CAI group for each subphase of stance as the data were not normally distributed. COP change scores were calculated (COP Change = Post 1 – B2) and compared to the MDC to confirm our results. Any change score greater than the MDC was considered a result of the intervention and normal variability or error.[267]

To determine how the COP location in those with CAI changed following two weeks of RW-VF training (RQ 2) and if those changes were retained (RQ 3), we used separate Friedman's ANOVAs to compare data from B2, Post 2, and Final for each subphase of gait. COP change scores were compared to the MDC as above. For all tests, alpha was set *a priori* at = 0.05. Wilcoxon Signed Rank Tests were completed as post hoc tests between each time point as the data were not normally distributed. Hedge's g effect sizes and 95% CI were calculated. Effect sizes were interpreted as trivial ($g<|0.2|$), small ($g=|0.2–0.49|$), moderate ($g=|0.50–0.79|$), and large ($g=|\geq 0.80|$).[259] Per current literature[96,111,113] and statistical recommendations[264] we did not control for multiple comparisons.

For our secondary analysis we compared COP baseline, post training (both after a single and multiple sessions) and retention data from the CAI group to the COP of pre-collected control data. First, we compared baseline CAI data to control data using separate Mann-Whitney U tests for each phase of stance as the data were not normally distributed. This allowed us to assess how similar, or dissimilar the two groups were and shed light on the capacity of the CAI participants to change. Next, we compared COP single session posttest data from the CAI group to COP control data using Mann-Whitney U tests for each phase determine how the COP in people with CAI after a single training session relates to the COP of controls (RQ 1). We then compared COP multisession posttest data from CAI to control to assess the impact of cumulative training sessions (RQ 2) using Mann-Whitney U tests. Finally, we repeated the Mann-Whitney U tests using retention COP data from the CAI group and COP data from control to determine how changes were retained following a moderate period of no intervention (RQ 3). For all tests, alpha was set *a priori* at ≤ 0.05. Hedge's g effect sizes and 95% CIs were calculated. Effect sizes were interpreted as trivial ($g=<|0.2|$), small ($g=|0.2–0.49|$), moderate ($g=|0.50–0.79|$), and large ($g=|\geq 0.80|$).[259]

For our tertiary analysis, we compared the baseline COP data to control data to determine if there were any differences between those with CAI and controls before our intervention using Mann-Whitney U tests. Alpha was set *a priori* at ≤ 0.05. Hedge's g effect sizes and 95% CIs were calculated. Effect sizes were interpreted as trivial (g=<|0.2|), small (g=|0.2–0.49|), moderate (g=|0.50–0.79|), and large (g=|≥0.80|).[259]

Aim 3:

Determine the relationship between non-modifiable structural factors of the lower leg/ foot, clinical outcomes, and COP location change during RW-VF training.

Rationale

Structural alignment of the lower leg and foot could alter the relationship between the foot and the ground. For example, excessive tibial varus or a pes planus foot puts the ankle in a pronated position while a pes cavus foot, limited dorsiflexion range of motion, and limited calcaneal eversion maintains the ankle in a supinated position during stance. These structural adaptations may hinder dynamic movement of the foot and therefore may limit the ability to respond to feedback stimuli appropriately. This aim will helped begin to explore how structural alignment may impact the capacity to change the COP during walking.

Experimental Procedure

Tibial varum, FPI, passive rearfoot calcaneal range of motion, WBLT, and SLS with eyes open and closed were collected during one of the two baseline assessments in Aim 1. To measure tibial varum, first the distance from the medial malleolus to the medial tibial plateau was measured in centimeters and one third of the distance was calculated. Next, a mark was be placed on the participant using washable ink at the bisection of the most proximal point of the one third distance and at the bisection of the distance between the malleoli. The marks were connected to create a bisection line of the distal lower leg. Tibial varum was measured with a goniometer as the angle between the plane of the floor and the bisection line of the posterior distal lower leg[114] with the participant in a single limb stance position as this position mimics rearfoot movement during midstance.[257] Participants were asked to move from double to single leg stance multiple times to ensure that they were achieving a lateral weight shift at the pelvis prior to the obtaining the measurement.[257] Participants placed their hands on their hips and were allowed to lightly touch down with the toes of the contralateral limb to maintain balance during the measurement. Degrees of tibial varum were treated as a continuous variable.

The FPI is a reliable[268] and valid[269] clinical method to classify foot type. The outcome of the tool is a composite score derived from six items measured in standing and categorizes the foot as either pes planus, neutral, or pes cavus. Relationships between the FPI and kinetics[270] as well as the FPI and kinematics[270] of the foot during walking have been established. A recent systematic review indicated that evidence relating foot posture to walking was of poor quality but noted that the studies which included higher methodological rigor used standardized measures to classify foot type.[271] For our purposes, foot structure could greatly impact an individual's ability to manipulate foot positions required to successfully respond to the feedback provided in this study. Therefore, the FPI was included as a standardized clinical measure to help understand the variance in COP changes seen with this intervention. The FPI score was treated as a continuous variable.[272]

Passive calcaneal eversion ROM (degrees) was measured with a goniometer with the participant in prone. The participant was instructed to flex and abduct the contralateral limb which vertically aligned the posterior axis of the involved limb. The midpoint between the malleoli on the posterior aspect of the ankle was the landmark for the axis of the goniometer, the stable arm aligned with the midline of the posterior lower leg and the moveable arm was aligned with the midline of the calcaneous.[273] Passive calcaneal eversion was be treated as a continuous variable.

The WBLT is a reliable[274] and valid[274] clinical outcome to measure functional dorsiflexion range of motion at the ankle. This test was be completed as previously described in the literature.[23,55,115,156] Participants stood facing the wall with their involved foot parallel with a tape measurer secured to the floor and the great toe touching the wall. They were asked to lunge forward and touch their anterior knee to the wall while keeping the heel on the ground. If participants were successfully able to complete the task, the foot was be moved backwards along the tape measurer at 1 cm intervals until they were no longer successful at touching the knee to the wall. Using smaller increments, the maximal distance for a successful completion, measured as the distance between the great toe and the wall to the nearest 0.1 centimeter, was determined. Maximal distance in centimeters was treated as a continuous variable.

SLS was collected on a portable force plate with a 1cm x 1 cm grid on top. Participants completed three trials of 10 seconds each with eyes open and eyes closed. The trial was repeated if the foot moved from the static position on the force plate. The COPv in the anterior-posterior and medial-lateral directions were calculated as the total excursion divided by the length of the trial.[186]

Sample Size Analysis

Tibial varum and calcaneal eversion have been included as variables in previous multivariate models to determine the relationship between lower leg structure and plantar pressure.[272,275,276] These models support weak but significant associations (R^2: 0.044 – 0.273) between structure and plantar pressure measures during gait.[272,275,276] The Foot Posture Index score (FPI) has been used as a single independent variable to examine the relationship between structure and peak plantar pressures during walking with R^2=0.067.[272] Therefore, using an estimated R^2= 0.10, our calculated sample size for separate univariate linear regressions with an alpha level set at 0.05 and 80% power is 614 (G*Power v. 3.1.9.4). However, as this aim was exploratory in nature, we enrolled 20 participants. This analysis was completed using the same study as that used for Aim 1. A sample size of twenty participants was selected as the target because it was a feasible number which was close to the initial analysis point for Aim 1. Even though Aim 1 was concluded early, we continued to enroll participants for the single arm of the study which addressed this current Aim.

Statistical Analysis

To determine the relationship between structural adaptations, clinical outcomes, and COP change during training, univariate linear regression analyses were completed with each structural adaptation and clinical outcome as separate independent variables and COP change scores between baseline and the early adaptation phase (minute 1-2 of training) while walking with the sensor under the 5th MH as the dependent variable. The data were not normally distributed, and we removed one participant from this data set because their data qualifies as an extreme outlier (at least 3x the interquartile range) for 50% of stance. Separate spearman's correlations were completed between each structural or clinical measure and the COP change for each subphase of stance. Bootstrap, bias corrected 95% confidence intervals were calculated for each correlation coefficient with 1000 samples. Alpha was set at ≤ 0.05 *a priori* for all analyses and the strength of the correlation was interpreted as 0.01-0.19 negligible, 0.2-0.29 weak, 0.30-0.39 moderate 0.4-0.69 strong, ≥ 0.7 very strong.[277]

CHAPTER 4: MANUSCRIPT 1

The Impact of Feedback Tool Sensor Location on Center of Pressure in People with Chronic Ankle Instability

1. Introduction

Lateral ankle sprains are one of the most common athletic injuries.[278] Approximately 40% of people who sustain a lateral ankle sprain will develop chronic ankle instability (CAI)[3], which is characterized by a history of at least 1 ankle sprain, recurrent episodes of the ankle giving way, persistent pain, and lifelong physical activity limitations.[8] Individuals with CAI demonstrate sensorimotor impairments[8] causing increased ankle inversion, increased plantar pressure under the lateral foot,[157] and a lateral shift in the center of pressure (COP) location during gait.[8] These altered gait biomechanics are thought to contribute to increased risk of future ankle sprains and to post traumatic osteoarthritis (PTOA) development.[154]

Gait retraining interventions using various sensory feedback modalities reduce excessive inversion,[27,113] decrease lateral plantar pressure[95,96] and medially shift the center of pressure (COP) location[96,111] during walking in people with CAI. In-shoe force sensing resistors (FSRs) have been integrated into auditory and haptic feedback tools to control the feedback stimuli during walking[95,111,113], ensuring that the feedback is not constant. Briefly, an individual resistance threshold is set for each participant and the stimulus is delivered while the plantar pressure exceeds the threshold. Within the portable biofeedback gait retraining literature, two locations have been utilized to detect pressure. In people with CAI, three studies[95,111,113] placed the FSR under the 5th metatarsal head (5MH) while in a group of people with knee osteoarthritis

(OA), the FSR was placed under the lateral heel.[110] The location of the FSR dictates when feedback could be delivered during the stance phase of walking. A heel location could deliver feedback during loading response, whereas a 5MH location may not provide feedback until midstance. Both locations have evidence indicating that the COP medially shifts for at least the first half of stance during walking in their respective groups[110,111]. However, given that people with CAI and people with knee OA demonstrate different gait deviations, it is unknown people with how people with CAI will respond to feedback with a heel location and whether it is more effective than a 5MH location. Therefore, the purpose of this investigation is to describe the impact of sensor location on the COP location during walking in people with CAI. Our hypothesis was that the sensor under 5MH would generate either more phases with significant medial COP shifts or larger effect sizes within the significant phases compared to training with the heel location.

2. Methods

This crossover study was approved by the university's Institutional Review Board. Ten participants with unilateral CAI were enrolled from a university setting based on criteria established by the International Ankle Consortium.[4] Participants were between the ages of 18-35 years, had at least one significant ankle sprain more than 1 year prior to enrollment, repeated episodes of giving way of the involved ankle, and self-reported functional limitations as indicated by a score of ≥11 on the Identification of Functional Ankle Instability (IdFAI) questionnaire and ≤ 90% of the Foot and Ankle Ability Measure (FAAM) activities of daily living subscale and ≤ 80% on the FAAM sport subscale. Participants were excluded if they had 1) a history of previous lower extremity surgery or fracture requiring realignment, 2) acute injuries within the past 3 months, 3) a disorder known to impact gait (i.e.: neurological and neurodegenerative disease, diabetes, or peripheral neuropathy) 4) were currently pregnant, or 5) had bilateral CAI.

Following completion of written informed consent, participant's height, mass, and self-selected walking speed were collected. Self-selected walking speed was obtained by taking the average speed during 5 over ground walking trials measured between two timing gates (Dashr 2.0, Dashr Motion Performance Systems, Lincoln, NE). Next, participants donned a custom feedback tool. A full description of the feedback tool has been previously published.[111] Briefly the tool consists of a small force FSR secured to the insole of the shoe, electronics and battery housed in a container on the shoelaces, and a vibration motor to provide the feedback secured to the lateral malleolus with an elastic strap. The presence or absence of feedback during the entire trial was controlled by turning the tool on or off. Under the 5MH condition, the FSR was secured to the shoe insole under the 5MH and for the heel condition, the FSR was secured to the insole under the lateral boarder of the heel cup. All participants completed the study using both FSR locations. The order of condition was randomized for each participant using a random number generator prior to enrollment.

After donning the feedback tool, a custom threshold was set for each participant such that standing in double limb support did not trigger the feedback but standing in single limb support did.[111] Each participant tested the calibration by walking on level ground first with the instruction to "walk normally" or with no changes to their biomechanics to ensure that the participant experienced a stimulus at each step. This was the first indicator that the threshold was correct. Second, participants were given the instruction to "walk so you do not get the vibration."

Additional external feedback cues were provided as needed for each participant. Often, the cue "think about where the sensor is and how to offload it" was given with success. Phrases which gave specific changes such as "roll your foot in" or "shift your weight" were not used to avoid influencing a participant's chosen strategy.[111] With the FSR under the heel, participants often needed additional cues such as "walk as normally as possible" to facilitate a heel strike pattern. The second indicator that the tool was successfully calibrated was when participants were able to walk with minimal feedback stimuli and a heel strike pattern overground. If the tool did not meet this indicator after additional cuing, the threshold was reset. No participant required more than 3 threshold attempts. Thresholds were reset at the beginning of each session as the threshold with the sensor at one location did not suffice for the opposite location. Anecdotally, the 5MH location required a higher threshold than the heel location and participants reported that it was easier to adapt their gait during the 5MH location.

Following calibration, retroreflective markers were placed on the first and fifth metatarsal heads as well as the calcaneus, medial and lateral malleoli, anterior tibia, and medial and lateral epicondyles of the femur. Participants walked on a split-belt treadmill with two 1.75 x 0.5 m force plates embedded under the belt (Bertec, Columbus, OH) at their calculated self-selected speed for two minutes without feedback to collect baseline kinematics and kinetics. Data were recorded during the second minute to allow participants to accommodate to the treadmill and any perceived weight from the tool[90,111,113], which weighed 56.7 g (2 oz). Next, the feedback was turned on and participants walked for a 10-minute training period at their self-selected speed with the instruction to "walk so you do not get the vibration." Data were collected during training for the early (minute 1-2) and late (minute 9-10) accommodation phases. Subsequently, the feedback was turned off and an immediate posttest assessment was completed in which participants walked for 2 minutes without feedback and data were collected during the second minute. Kinetic data were collected at a sampling rate of 2000 Hz and filtered with a 4^{th} order lowpass Butterworth filter with a cut off frequency of 10 Hz. Synchronized marker trajectories were captured at 200 Hz using an 8-camera motion capture system (QTM, Qualysis, Gotebörg, Sweden) and filtered using a 4^{th} order lowpass Butterworth filter with a cut off frequency of 10Hz.

During the heel location sessions, 4/10 participants required additional cues such as "touch your heel down first" in addition to resetting the threshold to attain a heel strike pattern. After cues and resetting the threshold, these participants were able to walk with a visually sufficient heel strike overground but were unable to maintain a heel strike when they walked at their measured self-selected speed on the treadmill. The mid and forefoot strike patterns caused other kinematic changes to be visually identified. Because of these changes, we decided to stop enrollment in this project early as there was enough anecdotal evidence that the 5MH location was a superior option in this group of participants.

2.1 Data Reduction

Data were reduced by isolating all complete steps (i.e.: initial contact followed by toe off) of the involved limb within the 60 second collection period. Initial contact was defined as the moment the vertical ground reaction force ascended past 20 N and toe off was defined as the moment the vertical ground reaction force descended past 20 N. The medial-lateral COP (ML-COP) location relative to the lab was derived in Visual 3D v 7 (C-Motion, Germantown, MD). ML-COP data were then bounded to the foot using a custom MATLAB script (Mathworks, Inc. version 2022b) and expressed as the perpendicular distance, in millimeters, from the midline of the foot. The midline of the foot for each frame was determined by creating a line between the ankle joint center (half the distance between the medial and lateral malleolus) and the midpoint between the 1st and 5th metatarsal head. This technique removes the impact of foot progression angle from the COP location. Positive distances indicate that the COP is lateral to the midline and negative distances indicate the COP is medial to the midline of the foot. The COP data were then normalized to maximal medial-lateral foot width which was calculated as the distance between the 1st and 5th metatarsal head markers during the static trial and expressed as the percent foot width (%FW). For each complete step in the trial, the normalized data were divided into 10 subphases and data within each subphase were averaged to obtain a single point which represents 1/10th of stance.[96,111] Finally the 10 data points for each step were averaged across all steps in the trial.

2.2 Statistical Analysis

All tests were completed in SPSS v27 (IBM Corp, Armonk, NY) with alpha ≤ 0.05 *a priori*. The data were assessed for normality and were found to be overall not normally distributed based on visual inspection of histograms and Kolmogorov-Smirnov tests for Normality (Table 2). Measures of skew and kurtosis ranged from -1.515 to 1.991 and -4.893 to 2.907 respectively (Table 2). Given that data may be considered approximately normal with skew values ranging from -2 to +2[261-263] and kurtosis values range from -7 to +7[262,263], parametric analyses were completed. However, based on our visual analysis of the data, non-parametric analyses were also completed and reported. Finally, based on current statistical recommendations[264] and previous gait retraining literature[17,91,96] we did not correct for multiple comparisons.

The statistical plan for the primary analysis was determined *a priori* and included separate two-way (FSR location x Time) repeated measures analysis of covariances (rmANCOVAs) to compare ML-COP distance at baseline and while walking between FSR locations for each subphase of gait. The average baseline ML-COP location between conditions was included as a covariate as the data were not statistically different for any phase of gait between conditions (W = -0.357 to 1.478, p>0.05). This strategy was used to adjust for any baseline differences between conditions.[265] Non-parametric Wilcoxon Signed Rank tests were completed between baseline ML-COP and posttest ML-COP location and between the change scores (posttest-baseline) while walking with the FSR in each location were for each subphase of gait.

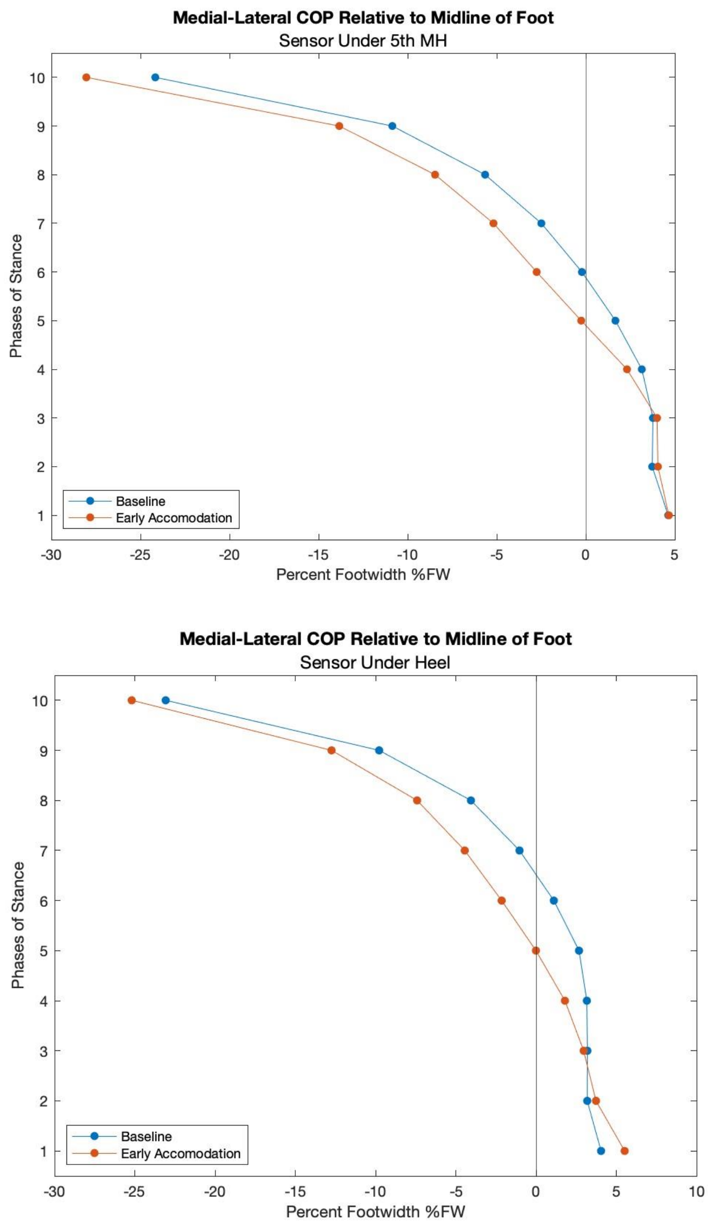


Figure 8: Medial-lateral center of pressure from baseline to early accommodation (Aim 1)

3. Results

3.1 Primary Analysis

There were no significant interactions between time and condition when controlling for baseline ML-COP location for any phase of stance ($p>0.05$, Table 3). Additionally, there were no significant main effects of time or condition when controlling for baseline ML-COP location for any phase of stance ($p>0.05$, Table 3). Non-parametric analyses revealed that there were no significant differences between baseline and posttest ML-COP location ($p>0.05$) or between change in ML-COP location between FSR locations ($p>0.05$, Table 4) for any phase of stance. Hedges g effect sizes were small to trivial ($g=<0.00$ to 0.24, Table 4) for ML-COP location during all phases between baseline and posttest for each FSR location and were also small to trivial ($g=<0.00$ to 0.31, Table 4) for the between conditions change score analysis. Figure 8 illustrates the average ML-COP trace from baseline to posttest for each FSR location.

3.2 Exploratory Analyses

During data collection, gait deviations were noted which suggested that at least 4/10 participants visibly altered their biomechanics at initial contact from a heel strike to a midfoot or forefoot strike while training with the FSR at the heel location. This impacted our primary analysis as those participants utilized unanticipated biomechanical strategies to offload the FSR and avoid feedback stimuli. This prompted additional exploratory analyses of our participant's data to quantify the strategy used. While only 4/10 participants demonstrated biomechanical deviations which were observable, we chose to include the entire cohort to capture more subtle strategy changes. First, we assessed changes in the anterior-posterior COP (AP-COP). Theoretically, a mid or forefoot would cause the person to land with a more plantarflexed ankle and therefore a more anterior COP location at initial contact. Next, we completed a follow up analysis with sagittal plane ankle position as an additional covariate. A mid or forefoot initial contact could be attained by plantarflexing the ankle and could impact the AP-COP results. Then, we completed an analysis which controlled for foot length and is important to normalize the data for between-subjects comparisons. Given that the COP location is derived within a foot projected on the ground[266], a more plantarflexed foot could make a shorter foot length. Next, we completed an analysis to determine if participants altered their foot position at initial contact by manipulating step length. A shorter step length may allow for a more foot flat initial contact which could limit loading on the FSR under the heel without having to significantly change the ankle position. Finally, a visual inspection of the data was completed to assess for any other underlying trends which could shed light on our nonsignificant primary analysis results.

3.2a Anterior-Posterior COP

The anterior-posterior COP (AP-COP) at initial contact was calculated as the distance along the midline of the foot using the raw resultant COP position, the perpendicular distance between the ML-COP and the midline of the foot, and the Pythagorean theorem. AP-COP was normalized to the length of the truncated foot which was defined as the distance between the calcaneal marker and the midpoint of the 1st and 5th metatarsal markers and expressed as percent foot length (%FL).

The AP-COP data were checked for normality using the Kolmogorov- Smirnov test for Normality and were grossly not normal (Baseline 5th: $D_{1,10} = 0.166$ $p = 0.200$, Posttest 5th: $D_{1,10} = 0.268$ $p=0.040$, Baseline Heel: $D_{1,10} = 0.161$ $p=0.200$, Posttest Heel: $D_{1,10} = 0.210$ $p = 0.200$) however demonstrated acceptable levels of skew and kurtosis[261-263] (Baseline 5th: skew = 0.102, kurtosis = -1.692, Early 5th: skew = 0.512, kurtosis = 0.126, Baseline Heel: skew = 0.569, kurtosis = -1.006, Early Heel: skew = 1.663, kurtosis = 3.976). Therefore, a two-way (FSR x Time) rmANCOVA was completed between AP-COP at initial contact under each FSR location between baseline and early accommodation timepoints. As in our primary analysis, the difference between baseline biomechanics between FSR locations at initial contact was assessed using a Wilcoxon Signed Rank and were not significantly different (W= 37.00, p=0.333) and therefore the average baseline AP-COP was used as a covariate. There were no significant interactions ($F_{1,8}$=4.283 p=0.072) or main effects of FSR condition ($F_{1,8}$=1.392 p=0.272) or time ($F_{1,8}$=0.135 p=0.723) when controlling for average baseline AP-COP at initial contact.

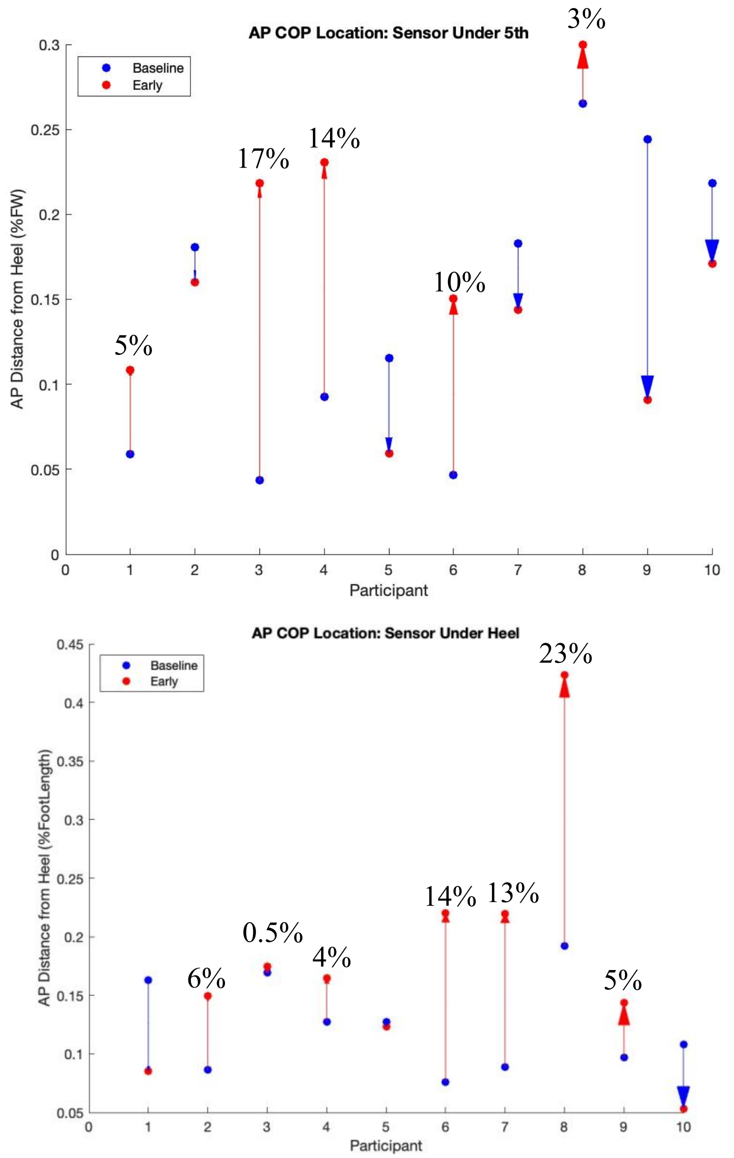


Figure 9: Visual data analysis: Anterior-posterior center of pressure from baseline to early accommodation by participant. (Aim 1)

Red arrows indicate anterior shift, blue arrows indicate posterior shift. % = magnitude of change in %foot length

3.2b Sagittal Plane Ankle Position

Sagittal plane foot position was used as a covariate to further investigate our observations during data collection with the sensor under the heel. First, the difference in sagittal plane ankle position between the baseline and early timepoint was assessed as previously completed to determine whether data from both timepoints were needed as covariates. No significant differences were found between the two timepoints (W=0.663, p=0.508), therefore the average of both timepoints was used as a single covariate of sagittal plane position. A one-way rmANCOVA was conducted with average baseline AP-COP and average sagittal ankle position at initial contact as covariates within the heel condition. The results while controlling for baseline AP-COP and ankle position were not significant ($F_{1,7}$=1.565 p=0.251).

3.2c Step Length

Finally, step length was calculated as the distance between the heel markers at initial contact for both the involved and uninvolved limb and then divided by height in meters to normalize the data. Wilcoxon Signed Rank tests were completed to assess step length between baseline and early accommodation phases for both the involved and uninvolved limb under the heel condition. Results indicate that during the early accommodation phase participants took a shorter step with their involved limb than at baseline (Early Step Length = 0.343 ± 0.023 m, Baseline = 0.357 ± 0.172 m, p=0.005) while the step length for their uninvolved limb remained constant (Early = 0.359 ± 0.015 m, Baseline = 0.356 ± 0.017 m, p = 0.285).

3.2c Visual Inspection & Analysis

Despite no statistical differences in the AP-COP location, a visual analysis of the data did show differences in AP COP location at initial contact between the conditions. While walking with the sensor at the 5MH, 50% (5/10) of the participants experienced an anterior shift in the COP compared to baseline. Similarly, while walking with the sensor under the heel, 70% (7/10) demonstrated an anterior shift in the COP (Figure 9). The range of anterior shift was 3-17 %FL during the 5MH condition and 0.5-23 %FL during the heel condition. Four participants demonstrated an anterior shift under both training conditions, however not always in the same direction. Of the four participants, one decreased the magnitude of the anterior shift from 17 %FL under the 5^{MH} condition to 0.5 %FL under the heel condition, one decreased the magnitude of the anterior shift from 14 to 0.5 %FL, one increased the magnitude of the anterior shift from 10 to 14 %FL, and the final participant increased the anterior shift from 3 %FL under the 5MH condition to 23 %FL under the heel condition. Last, the two participants who increased the anterior-posterior COP magnitude during the heel condition also displayed an increased plantarflexed ankle position at initial contact during early accommodation (mean difference = 6.13°).

4. Discussion

Our purpose was to determine how sensor location impacted ML-COP following a short training in people with CAI. While our lack of significant results is contrary to our hypotheses, visual inspection of the data at the participant level demonstrates that not all people with CAI respond to vibration feedback with the same biomechanical changes regardless of where the sensor is located. Therefore, is important to consider a full kinematic and kinetic analysis of the lower extremities while implementing gait retraining interventions to assess the intervention for both intended and unintended impacts.

4.1 Primary Analysis: ML-COP Between Sensor Locations

Our primary results suggested that there were no differences between sensor locations, however, exploration of the data suggest that this cohort may have included a high proportion of non-responders which could be driving our non-significant results. The methods in the 5MH arm of this study were identical to our previous work[111,113], yet the results were contradictory. In this study, no significant results were noted between baseline and posttest measures while walking within the 5MH condition. However, in a previous cohort of 16 people with CAI, these same methods medially shifted the COP for phases 1-9 following training.[111] This cohort had 7/10 people classified as non-responders, whereas in the previous cohort 2/16 non-responders were identified. For our purposes, a non-responder was defined as a lateral rather than medial COP shift after training in at least 50% of stance phases.

Given that confirmation of CAI for participants in both studies was based on criteria established by the International Ankle Consortium,[4] similar demographic and functional limitation variables were available for both groups. In a tertiary analysis, we compared height, mass, number of ankle sprains, and functional limitations as reported on the IdFAI and FAAM. Additionally, center of pressure velocity during a single limb stance with eyes open and eyes closed were collected for both groups for a different analysis. The tertiary analysis revealed that this cohort had better (i.e.: slower) center of pressure velocity (current cohort: 4.80 cm/s, previous cohort: 5.66 cm/s, p=0.047) in the anterior-posterior direction with eyes closed. This suggests that there could be aspects of neuromuscular control which may be different between cohorts and could have contributed to the different responses to feedback between the groups. Cumulatively, the results of these studies emphasize the need to determine a profile of people with CAI who may be most likely to benefit from gait retraining interventions to improve the application of feedback modalities.

Finally, it is worth noting that participants were given the cue to “walk normally” during their posttest session with no feedback. This could have been detrimental to our posttest results as participants could have interpreted that as to walk without any deviations and to ignore the training they had just completed. However, these identical instructions have been used previously with statistically significant medial shift in the COP at posttest.[111] Therefore, the impact of the verbal instructions remain unclear.

4.2 Exploratory Sensor Location Analysis

Our exploratory analyses attempted to quantify observations of aberrant gait biomechanics observed during training. While we had no statistically significant kinetic or kinematic differences which could confirm the observed changes in foot strike pattern, we were able determine that overall, participants employed shorter step lengths to avoid a heel strike position while walking with feedback. Further visual analysis of the data revealed that more participants did in fact experience an anterior COP shift under the heel condition compared to the 5MH condition while walking with feedback, however, only those with large magnitude shifts also increased their plantarflexion angle at initial contact. These observations provide further evidence that people with CAI may not utilize the same strategy to respond to feedback. We know that CAI occurs from a complex interaction between pathomechanical, motor-behavioral, and sensory-perceptual impairments, however, not every individual presents with the same myriad of impairments[120]. Combinations of different impairments could lead to different constraints at the ankle necessitating different movement strategies within groups of individuals with CAI.

Attempts to tease out different movement strategies in people with CAI is currently in its infancy and only a single study has attempted to identify patterns to date. Hopkins et al[279] assessed a group of 200 individuals with CAI and 100 healthy controls and measured lower extremity biomechanics and ground reaction forces while participants completed a vertical jump landing with immediate side cut task. Researchers identified that participants with CAI could be clustered into six categories based on stereotypical deviations from healthy movement strategies demonstrated during ground contact time.[279] Clusters were derived using a combination of kinetics and kinematics in both the frontal and sagittal plane for all three joints in the lower extremity. The clustering technique and the results from our analyses highlight important factors which should be considered when designing studies and analyzing movement in individuals with CAI. First, the entire limb should be included in the analysis. This could allow identification of mechanistic altered movement strategies or additional clusters of movement across tasks. It is possible that different clusters may respond to feedback differently and could be considered responders or non-responders. This information would improve the implementation of feedback. Second, while we primarily focus on frontal plane movement due to its relationship with the mechanism of injury, a dual-planar analysis, or triplanar analysis may be more important. When categorizing movement strategies, all categories had different combinations of frontal and sagittal plane biomechanics.[279] Similarly, we saw differences in both ML- and AP-COP after training. Multiplanar analysis allows for a more comprehensive understanding of both positive and negative aspects of movement. Last, a control group should be included as often as possible.

Hopkins et al[279] were able to definitively identify variations from healthy participants, however, it is still unknown how healthy participants respond to vibration feedback with the sensor in any location. Future research should aim to quantify clusters of departures from typical movement during walking throughout the global lower extremity in response to feedback.

5. Conclusion

Based on the current data, neither FSR location is better at generated a medial COP shift while walking in people with CAI. Individual variations within these data support the need for comprehensive lower extremity assessments, cluster analyses, and developing non-responder profiles while developing and employing new intervention strategies for people with CAI.

Table 2: Skew & kurtosis values by stance phase (Aim 1)

		5TH			HEEL		
		K-S Test	Skew	Kurtosis	K-S Test	Skew	Kurtosis
Phase 1	Baseline	$D_{(10)}$=0.132 p=0.200	0.294	0.378	$D_{(10)}$=0.26 p=0.042	1.312	2.155
	Posttest	$D_{(10)}$=0.154 p=0.200	0.049	-1.689	$D_{(10)}$=0.17 p=0.200	0.814	-0.205
Phase 2	Baseline	$D_{(10)}$=0.191 p=0.200	0.86	-0.08	$D_{(10)}$=0.264 p=0.047	0.673	-0.982
	Posttest	$D_{(10)}$=0.227 p=0.153	0.85	0.081	$D_{(10)}$=0.72 p=0.200	0.392	-1.161
Phase 3	Baseline	$D_{(10)}$=0.189 p= 0.200	0.735	-0.445	$D_{(10)}$=0.305 p=0.009	0.712	-0.663
	Posttest	$D_{(10)}$=0.167 p=0.200	0.816	0.293	$D_{(10)}$=0.152 p=0.200	0.158	-1.508
Phase 4	Baseline	$D_{(10)}$=0.214 p=0.200	0.488	-0.957	$D_{(10)}$= 0.144 p=0.155	0.367	0.049
	Posttest	$D_{(10)}$=0.227 p=0.155	-0.106	-1.209	$D_{(10)}$=0.119 p=0.200	-0.165	-1.005
Phase 5	Baseline	$D_{(10)}$=0.172 p=0.200	0.184	-1.417	$D_{(10)}$=0.160 p=0.200	-0.341	-0.465
	Posttest	$D_{(10)}$=0.208 p=0.200	-0.005	-2.007	$D_{(10)}$=0.166 p=0.200	0.435	1.194
Phase 6	Baseline	$D_{(10)}$=0.238 p=0.113	0.835	-0.712	$D_{(10)}$=0.223 p=0.172	-0.303	0.206
	Posttest	$D_{(10)}$=0.202 p=0.200	0.917	1.153	$D_{(10)}$=0.170 p=0.200	-0.803	0.572
Phase 7	Baseline	$D_{(10)}$=0.266 p=0.043	1.347	0.674	$D_{(10)}$=0.175 p=0.200	-0.062	0.41
	Posttest	$D_{(10)}$=0.226 p=0.158	1.991	4.893	$D_{(10)}$=0.187 p=0.200	-1.515	2.907
Phase 8	Baseline	$D_{(10)}$=0.177 p=0.200	1.123	0.808	$D_{(10)}$=0.186 p=0.200	-0.736	-0.144
	Posttest	$D_{(10)}$=0.208 p=0.200	0.919	2.293	$D_{(10)}$=0.239 p=0.239	-0.764	-0.034
Phase 9	Baseline	$D_{(10)}$=0.149 p=0.200	-0.076	-0.927	$D_{(10)}$=0.215 p=0.200	1.208	2.097
	Posttest	$D_{(10)}$=0.144 p=0.200	-0.745	-0.043	$D_{(10)}$=0.187 p=0.200	0.602	-0.377

Phase 10	Baseline	$D_{(10)}$=0.141 p=0.200	0.181	-1.461	$D_{(10)}$=0.158 p=0.200	-0.627	1.153
	Posttest	$D_{(10)}$=0.167 p=0.200	0.038	-0.407	$D_{(10)}$=0.230 p=0.142	-0.882	0.552

K-S test = Kolmogorov-Smirnov Test for Normality, 5TH = sensor under 5th metatarsal head HEEL = sensor under lateral heel

Table 3: Repeated measures ANCOVA results (Aim 1)

	Repeated Measures ANCOVA					
	Interaction $F_{(1,8)}$	p value	Condition $F_{(1,8)}$	p value	Time $F_{(1,8)}$	p value
Phase 1	2.719	0.134	5.093	0.054	4.103	0.077
Phase 2	0.277	0.613	0.697	0.428	0.008	0.931
Phase 3	0.042	0.843	0.004	0.952	0.496	0.501
Phase 4	0.021	0.888	0.009	0.927	0.377	0.377
Phase 5	0.003	0.961	0.162	0.698	0.039	0.849
Phase 6	0.015	0.906	0.018	0.897	0.009	0.927
Phase 7	0.078	0.787	0.052	0.825	1.008	0.345
Phase 8	1.091	0.327	0.214	0.656	4.117	0.075
Phase 9	1.36	0.277	0.732	0.417	1.676	0.232
Phase 10	0.001	0.973	0.247	0.633	0.011	0.917

ANCOVA = analysis of covariance

Table 4: Wilcoxon Sign Rank results with Hedges g effect sizes (Aim 1)

	Within Subjects						Between Subjects		
	Wilcoxon Sign Rank				Hedges g		Wilcoxon Sign Rank		Hedges g
	5th W	p value	Heel W	p value	5th	Heel	W	p value	
Phase 1	0.357	0.721	0.968	0.333	0.07	0.00	0.764	0.445	0.03
Phase 2	0.764	0.445	1.172	0.241	0.15	0.24	0.357	0.721	0.01
Phase 3	0.357	0.721	0.764	0.445	0.11	0.24	0.051	0.959	0.01
Phase 4	0.663	0.508	0.866	0.386	0.02	0.19	-0.051	0.959	0.10
Phase 5	-0.051	0.959	0.651	0.575	0.15	0.14	0.357	0.721	0.23
Phase 6	0.663	0.508	0.153	0.878	0.07	0.01	-0.255	0.799	0.04
Phase 7	0.561	0.575	0.051	0.959	0.00	0.10	-0.051	0.959	0.16
Phase 8	0.153	0.878	0.051	0.959	0.01	0.06	0.255	0.799	0.07
Phase 9	-0.153	0.878	0.459	0.646	0.12	0.14	1.172	0.241	0.31
Phase 10	-0.153	0.878	0.663	0.508	0.16	0.10	0.153	0.878	0.00

W = Wilcoxon sign rank test statistic

CHAPTER 5: MANUSCRIPT 2
Feasibility of two-weeks of real-world gait retraining on the center of pressure in people with chronic ankle instability

1. Introduction

Chronic ankle instability (CAI) develops in approximately 40% of individuals after an initial lateral ankle sprain.[1] Long-term deficits in people with CAI are due to complex interactions between sensory-perceptual, pathomechanical, and motor behavioral impariments[120] which can lead to limited range of motion, strength, balance, proprioception, and altered movement patterns.[8] In regards to walking gait, people with CAI have demonstrated increased inversion[157] and a lateral center of pressure (COP) throughout stance of up to 7.5 mm compared to controls.[17] These altered biomechanics are thought to increase recurrent ankle sprain risk[154] and ankle joint contact forces during walking.[219] Both may contribute to early onset joint degeneration and post traumatic osteoarthritis development long term.

Sensory-based gait retraining is a new intervention strategy for people with CAI which employs the use of visual,[27,96] vibrational,[111,113] or auditory[95] stimuli to provide feedback to the user regarding their foot position during stance. Specifically, a single session of visual and vibrational feedback decreases excessive inversion[113] and medially shifts the COP[96,111] during and after gait retraining. Additionally, a single session of vibration feedback reduces mechanical joint loading while training.[112] These preliminary, single session studies suggest that these interventions may be promising rehabilitation strategies to restore gait biomechanics and potentially slow the progression of PTOA in people with CAI. However, single session interventions do little to guide clinical practice.

Gait retraining using visual feedback about foot inversion position at initial contact is the only sensory-based feedback technique which has been integrated into a multiday intervention to mimic a clinical model of treatment for people with CAI. Koldenhoven et al[27] compared an impairment-based rehabilitation program with and without the inclusion of visual feedback gait retraining. Results indicated that the group who received visual gait retraining in addition to an impairment-based rehabilitation program demonstrated a less inverted foot position at initial contact and greater improvements in self-reported function following training. While this study took an important step towards clinical integration by modeling clinical rehabilitation in research, we continue to lack information about the long-term retention effects of gait retraining for people with CAI. To maximize long term learning or retention, researchers suggest incorporating variability into training.[111] Training in a real-world environment rather than a controlled laboratory or clinical environment introduces variability due the inconsistencies in surface orientation and material, height, etc. To date, vibration feedback is the only sensory-based intervention which has been investigated using real-world training, and demonstrated retention of the medially shifted COP.[111] However, only a single training session was conducted and the retention period was only 5 minutes.[111] Exploring longer retention intervals following cumulative training sessions will provide additional insights into protocol development which can eventually be integrated into clinical practice. Therefore, our purpose was to investigate the immediate and short term (1-week) retention effects of two-weeks of real-world vibration feedback gait retraining. We hypothesized that the two-week training protocol would cause a medial shift in the COP after both a single session and two-weeks of training which would exceed the minimal detectable change (MDC). Additionally, we hypothesized that the COP location after a single and multiple training sessions in people with CAI would have shifted medially to resemble the COP location of controls more closely.

2. Methods

2.1 Participants: CAI

Table 5: Participant Demographics (Aim 2)

	CAI		Control	
	Mean	SD	Mean	SD
Age (yrs.)	24.80	5.59	21.83	3.78
Height (cm)	174.76	9.85	171.94	8.00
Mass (kg)	86.21	14.91	69.7	13.59

a) demographic variables shared between groups, SD = standard deviation CAI = chronic ankle instability, yrs. = years, cm = centimeters, kg = kilograms

	Involved		Uninvolved	
	Mean	SD	Mean	SD
# of Sprains	4.05	2.78	1.35	0.93
IdFAI	20.25	4.52	9.25	6.38
FAAM-ADL (%)	85.90	5.10	97.20	3.03
FAAM-S (%)	71.50	7.30	92.40	8.55

b) CAI specific outcome measures for involved limb and uninvolved limb

This study was approved by the Institutional Review Board at the University of North Carolina at Chapel Hill prior to initiation and was registered a-priori with www.clinicaltrials.gov (NCT05327244). Twenty participants (Table 5) with CAI volunteered. Participants completed a screening survey prior to enrollment to determine if they had CAI per the selection criteria recommendations published by the International Ankle Consortium.[4] Participants were between the ages of 18 – 35 years and had a history of at least 1 significant lateral ankle sprain which occurred at least 12 months prior to enrollment. A significant lateral ankle sprain was defined as a sprain which caused at least 1 day of interrupted physical activity. Participants also had a history of recurrent sprains and/or episodes of "giving way". Participants also had a sense of ankle instability measured by a score of ≥ 11 on the Identification of Functional Ankle Instability outcome (IdFAI), and had self-reported functional limitations measured by a score of < 90% of the Foot and Ankle Ability Measure (FAAM)-Activities of Daily Living (ADL) subscale and < 80% on the FAAM-Sport (S) subscale.[4] Participants were excluded if they had evidence of bilateral CAI using the criteria above, had a history of previous surgery in either lower extremity, had a history of a fracture requiring realignment in either lower extremity, had an acute (< 12 weeks from enrollment) injury to either lower extremity, had any condition known to affect gait such as peripheral neuropathy, diabetes, neurological disorders, or neurodegenerative diseases, or were knowingly pregnant.[4] All participants provided written informed consent prior to enrollment.

2.2 Participants: Control

Data from 24 healthy controls (Table 5) was collected as part of an unrelated project and acted as a reference group for the COP location in uninjured walking. Inclusion criteria for healthy control participants were as follows: 1) between the ages of 18-35 years, 2) no previous history of lower extremity surgery, 3) no lower extremity injury history in the past 6 months, 4) no history of neurological disorders (i.e.: stroke, cerebral palsy, multiple sclerosis, etc.), and 5) not knowingly pregnant. Patient reported outcomes were not collected in the original investigation and are therefore not available for comparison.

2.3 Study Procedures: CAI

After enrollment, self-selected walking speed was measured for each participant as the average of walking 5 trials between two timing gates (Dashr 2.0, Dashr Systems, Lincoln, NE, USA) placed 1 meter apart. Average self-selected walking speed was used for each treadmill assessment throughout the study. The participant then completed the first baseline session to capture gait biomechanics. Retroreflective markers were placed on the following landmarks of each participant: bilateral ASIS, a sacral cluster containing bilateral PSIS and a sacral marker, between L4 and L5 spinous process, bilateral greater trochanters, bilateral anterior mid-thigh, medial and lateral medial epicondyles, bilateral tibial tuberosities, bilateral medial and lateral malleoli, bilateral posterior calcanei, bilateral 1st, and 5th metatarsal heads. Participants then walked on a split-belt instrumented treadmill with two embedded 1.75 x 0.5 m force plates (Bertec, Columbus, OH, USA) sampled at 1200 Hz. Marker trajectories were captured using an 8-camera motion capture system (Qualysis Tracking Manager, Qualysis, Göteborg, Sweden) sampled at 120 Hz. Participants walked for two minutes at their average self-selected speed and data were collected during the second minute.

At least 24-72 hours later, participants returned for a second baseline using the same data collection procedures and self-selected speed. However, prior to walking on the treadmill, participants were fitted with a custom made vibration feedback tool.[111-113] The tool consists of a small force sensing resistor (FSR) (Model 402, Interlink Electronics, Inc, Carmarillo, CA) secured to the foot bed of the shoe under the 5th metatarsal head and a small 200 Hz vibration motor placed over the lateral malleolus with a custom elastic strap. The battery and electronics were secured to the shoelaces of the shoe using a custom enclosure. The feedback tool was then calibrated to each participant so that the feedback stimulus occurred when excess pressure was applied to the lateral foot. Calibration procedures have been previously described.[111,113] Briefly, an individualized resistance was set for each participant so that when standing in double limb support there was no feedback but standing in single limb support with contralateral toe touch for balance triggered the stimulus. Participants tested the calibration by walking on level ground with the cue to "walk normally with minimal vibration". If participants were able to successfully manipulate their foot position to decrease the frequency or completely avoid the stimulus, the tool was successfully calibrated. No participant required more than three calibration attempts.

After completing calibration, the feedback tool was turned off and participants walked on the treadmill with the feedback tool in place as previously described for a second baseline testing session. The difference between data from the two baseline sessions were used to calculate the MDC to determine if any observed change was due to true change rather than normal variability or measurement error. It is known that participants with CAI accommodate to a 0.45 kg (1-lb) weighted object on their shoe while walking in less than 1 minute,[90] therefore, the weight of our feedback tool (2 oz) did not impact walking biomechanics during biomechanics collection of the second baseline.

Immediately following the second baseline, participants completed their first of six gait retraining sessions within two-weeks. Training sessions consisted of a 1-mile supervised walk with vibration feedback in the real-world. During training sessions, participants encountered variable surfaces including sidewalks, uneven brick terrain, inclines/ declines, and stairs. Each participant walked the same six routes but the order for each participant was randomized using a random number generator. All walking routes were supervised by the study PI or a trained research assistant for navigation and participant safety. Following the first training session, the feedback tool was turned off and participants completed an identical posttest assessment (P1) on the instrumented treadmill prior to removing the feedback tool. Over the next two weeks, participants completed the five other training routes with a member of the research team. Training sessions were scheduled within a participants' availability, however, a maximum of three training sessions could be completed in a row. The same feedback tool was used for all training sessions completed by a participant. Within 24-72 hours of the last training session, patients returned for a second posttest assessment (Post 2) on the treadmill and one week later for a retention session (Follow Up). Procedures for Post 2 and Follow Up sessions were identical to the first baseline assessment.

2.4 Data Collection Procedures: Controls

Control participants walked on the same instrumented treadmill for 5 minutes with the same marker arrangement. In the original project, data were collected for the last 90 seconds of the 5-minute walking period. We isolated the last 60 seconds of walking data to best match our CAI protocol.

2.5 Data Reduction

Data for the CAI and Control groups were processed in the same manner. The COP location relative to the lab coordinate system and the foot marker trajectories for all complete steps were exported from the data collection systems and filtered at 10 Hz.[111,113] The beginning of a step was defined as the moment the vertical ground reaction force (vGRF) ascended past 20 N and ended when the vGRF descended past 20 N. To determine the location of the COP within the foot, we subtracted the perpendicular distance between the COP location and the midline of the foot (COP – midline) such that positive values indicated the COP was lateral to the midline and negative values indicated that the COP was medial to the midline. The midline of the foot was defined as the line between a point half the distance between the medial and lateral malleoli and a second point half of the distance between the 1st and 5th metatarsal heads during each frame. All COP locations within the foot were normalized to maximum foot width and expressed as a percent of maximal foot width (%FW). The maximal foot width was calculated as the distance in millimeters between the 1st and 5th metatarsal heads which were obtained from the static calibration file. Next, the COP distance for each stance phase was divided into 10 subphases each representing 10% of stance.[17,91,96] Data within each subphase were averaged to obtain a single point representing the average COP distance during that subphase. The 10 discrete points were then averaged across each step obtained during the collection period.

2.6 Statistical Analysis: COP changes within CAI

First, data were assessed for outliers. While outliers were present, no single participant demonstrated outliers in more than three consecutive subphases of gait, therefore, all data were retained for this analysis to minimize data loss. Data were assessed for normality and were found to be not normally distributed based on the Kolmogorov-Smirnov Test for Normality and visual inspection of histograms. To compare the COP location before and after a single session of real-world vibration feedback, separate Wilcoxon Signed Rank tests were completed for each subphase of gait. Next, to compare the change in COP over time among the second baseline, Post 2, and Follow Up, separate Friedman's tests were completed for each subphase of gait. Post hoc analyses were completed using separate Wilcoxon Signed Rank tests. Hedges g effect sizes and

95% CI of the effect size were calculated for each result and were interpreted as trivial (g<0.02), small (g=0.2-0.4), moderate (g=0.5-0.7), and large (g>0.8). Per current literature[96,111,113] and statistical recommendations[264] we did not control for multiple comparisons.

Significant results were compared against the MDC calculated between the two baseline sessions for each subphase of gait. The MDC was calculated as:

$$MDC = SEM \times 1.96 \times \sqrt{2}$$

Where 1.96 is the z score associated with a 95% confidence interval and the square root of two accounts for the potential error in each measurement,[267] The Standard Error of the Mean (SEM) was calculated as:

$$SEM = SD_d/\sqrt{2}$$

Where SD_d is the standard deviation of the difference between the baseline sessions.[267]

2.7 Statistical Analysis: CAI vs. Control

To compare the COP location from people with CAI after a single and multiple training sessions and the COP location of controls while walking, separate Mann-Whitney U tests were completed between the posttest after a single session (Post 1) and control data as well as the posttest after multiple training sessions (Post 2) and control data. Alpha was set at 0.05 *a* priori and hedges g effect sizes and 95% CI of the effects were calculated.

3. Results

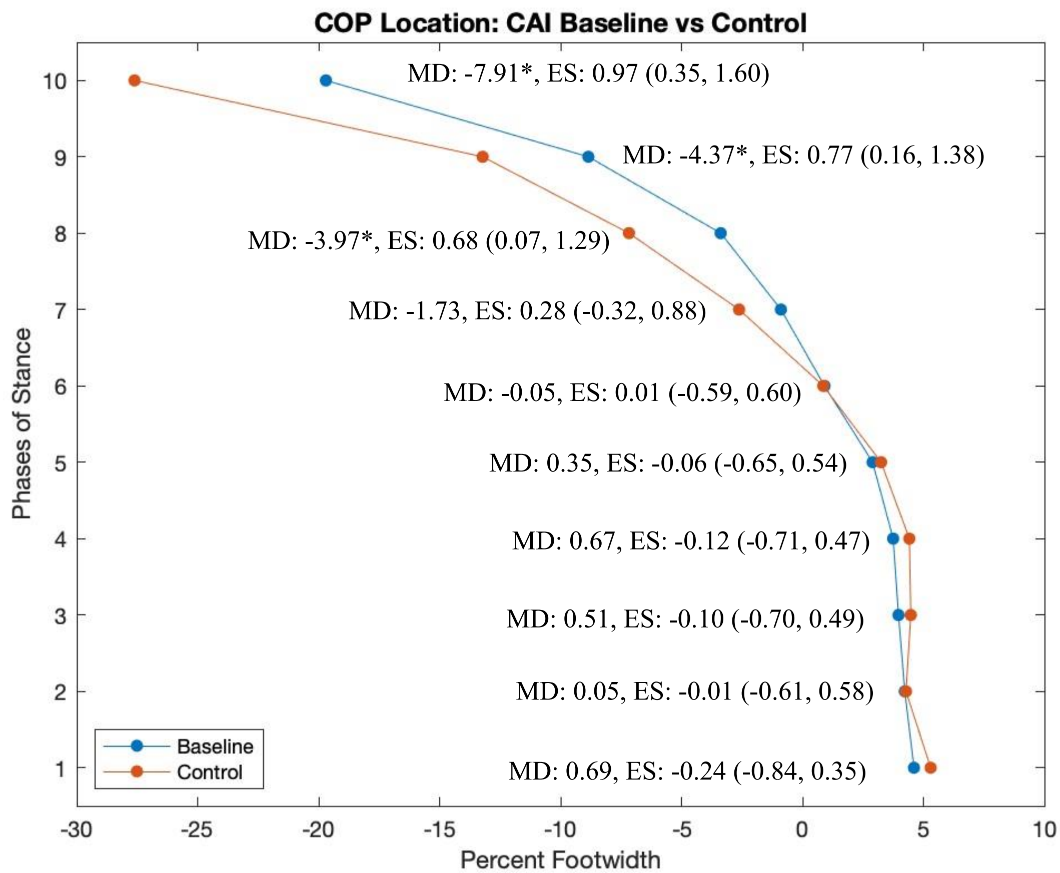


Figure 10: Center of pressure location between CAI at baseline and control (Aim 2)

**=p<0.05*

3.1 CAI vs Control at Baseline

At baseline, CAI participants had a more lateral COP in stance phases 8-10. (Figure 10, Phase 8 CAI = -3.38 ± 1.48 %FW, Control -7.17 ± 2.67 %FW, p=0.003, Phase 9 CAI = -8.85 ± 1.91 %FW, Control = -13.22 ± 7.33 %FW, p=-0.002, Phase 10 CAI = -19.70 ± 5.66 %FW, Control = -27.61 ± 9.46 %FW, p=0.002). Associated Hedge's g effect sizes for phases 8-10 were moderate to large (g=0.68-1.29) with 95% CI that do not cross zero. There were no significant differences between the COP in people with CAI and healthy controls for phases 1-7 (p>0.05).

All means, standard deviations, statistical trends, and differences can be seen in Figure 10 and Table 7.

3.2 Change in COP After Single RW-VF Training Session

There were significant differences in the COP location of CAI participants between baseline and posttest after a single session for stance phases 7-10. The COP was more lateral at Post 1 compared to baseline for phases 7-10 (Mean Difference (MD) Phase 7 = 0.97 %FW, Phase 8 = 1.88 %FW, Phase 9 = 3.39 %FW, Phase 10 = 3.32 %FW, $p<0.04$), however, only phases 7-9 exceeded the MDC. Effect sizes for phases 7-9 were small to moderate (g=0.32-0.67) with CIs that did not cross zero for phases 8 and 9. Compared to controls, the COP in people with CAI was more medial in phase 1 (MD: 2.41 %FW, $p=0.001$, g=0.70) and more lateral after training in phases 8-10 (MD Phase 1 Phase 8 = -3.79 %FW, Phase 9 = -4.37 %FW, Phase 10 = -7.91 %FW, $p<0.004$) but was not statistically different for phases 2-7 ($p>0.05$). Control to Post 1

Table 6: Center of pressure locations: baseline to 1-session posttest (Aim 2)

Phase	Baseline Mean ± SD	Posttest Mean ± SD	p value	Hedges g	Effect Size 95% CI	MDC
1†	4.61±2.43	2.99±1.11	0.06	-0.50	(-1.02, 0.03)	0.80
2	4.23±2.66	3.32±1.50	0.09	-0.46	(-0.99, 0.06)	1.75
3	3.97±2.62	3.49±1.56	0.31	-0.20	(-0.73, 0.32)	2.47
4	3.75±2.51	3.24±2.28	0.25	-0.16	(-0.68, 0.36)	2.15
5	2.9±2.63	2.98±3.66	0.71	0.02	(-0.50, 0.54)	0.82
6†	0.91±2.13	1.55±3.19	0.22	0.20	(-0.32, 0.73)	0.46
7*†	-0.89±2.03	0.08±2.96	0.02	0.32	(-0.21, 0.84)	0.21
8*†	-3.38±1.48	-1.5±3.30	0.004	0.640	(0.11, 1.17)	0.35
9*†	-8.85±1.91	-5.46±6.06	0.01	0.67	(0.14, 1.21)	1.28
10*	-19.7±5.66	-16.38±7.94	0.04	0.53	(0.00, 1.06)	15.27

SD = standard deviation, CI = Confidence Interval, MDC = Minimal Detectible Change
* $p<0.05$, † COP change exceeded the MDC

effect sizes for phases 1 and 8-10 were moderate to large (g = 0.7 – 1.25) with effect sizes that did not cross zero. All means, standard deviations, statistical trends, and differences can be seen in Table 6, Figure 11, and Table 7.

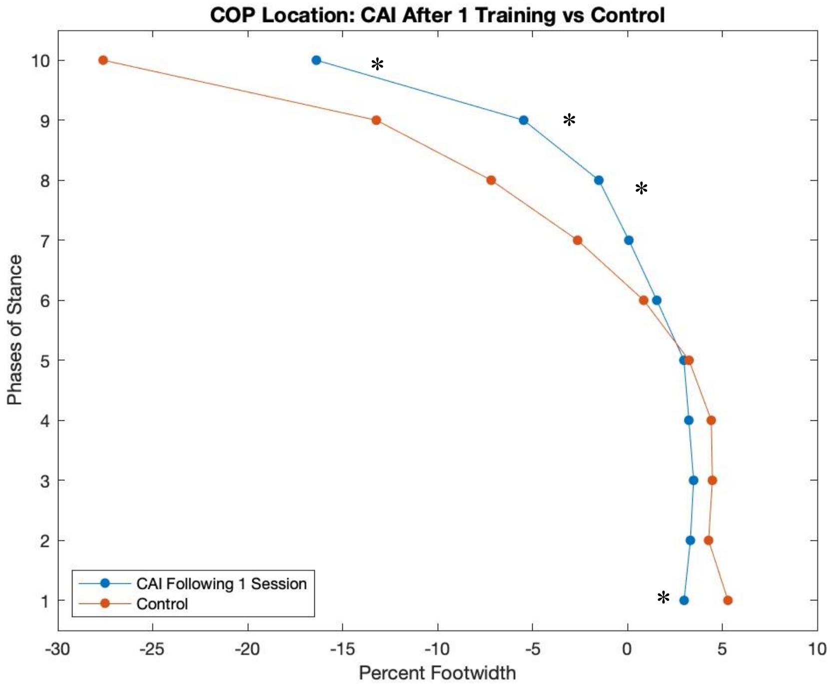


Figure 11: Center of pressure location between 1-session posttest and control

**=p<0.05*

3.3 Change in COP After Two-Weeks of RW-VF

There were statistically significant differences among baseline, Post 2, and Follow Up timepoints for stance phases 1-5 (p=<0.001 – 0.041). Post hoc testing revealed that Post 2 COP locations were more lateral for phases 1-4 (MD Phase 1 = 1.82 %FW p=0.005 g=1.11, Phase 2 = 2.33 %FW p<0.001 g=1.41, Phase 3 = 2.61 %FW p=0.001 g=0.99, Phase 4 = 1.87 p=0.005 g=0.58) compared to baseline, however, only phases 1-3 exceeded the MDC. There were no significant differences between baseline and Post 2 for phases 5-10 (p>0.05, g≤0.45). Post hoc results also revealed that the COP remained more lateral in phases 2-4 at retention compared to

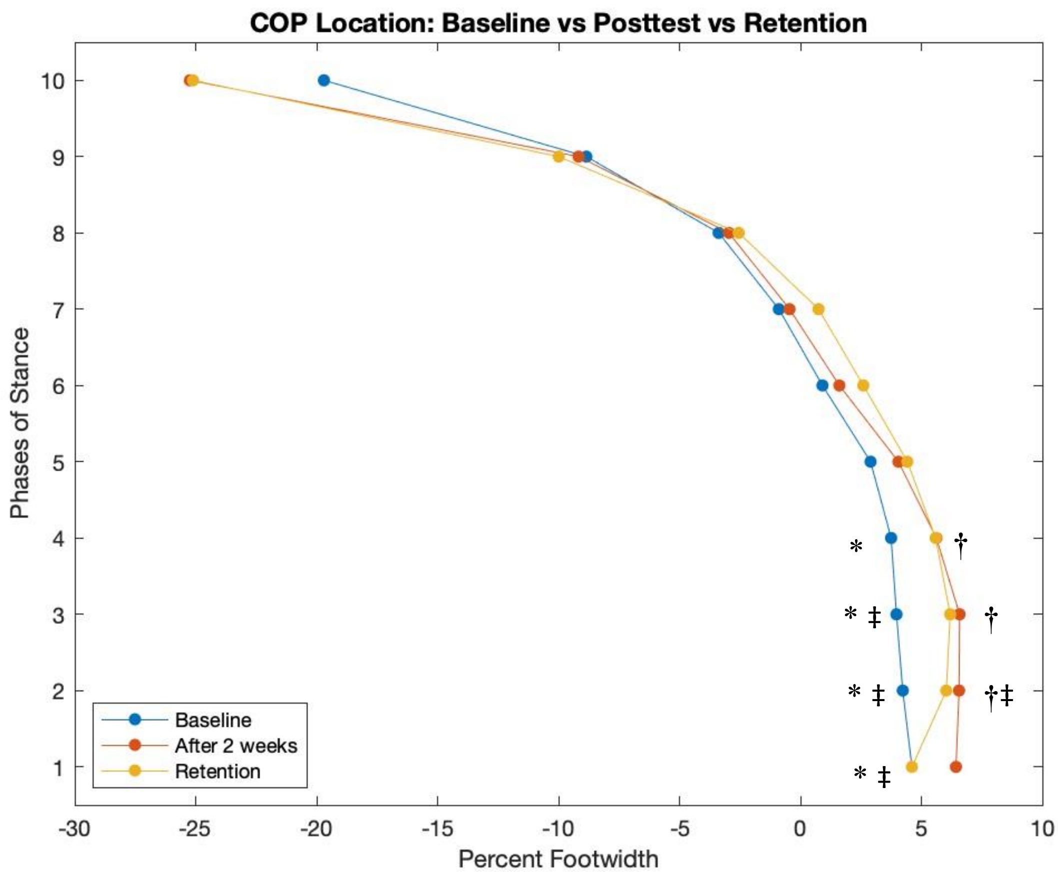


Figure 12: Center of pressure location among baseline, posttest, and retention (Aim 2)

**=p<0.05 for baseline v posttest comparison,†= p<0.05 for baseline v follow up comparison, ‡= COP change that exceeds minimal detectable change*

baseline (Figure 12), and was not statistically different compared to Post 2 in the same phases (MD Baseline vs Follow Up: Phase 2 = 1.80 %FW p=0.028 g=0.57, Phase 3 = 2.22 %FW p<0.001 g=0.64, Phase 4 = 2.15 %FW p=0.002 g=0.47, MD Post 2 vs Follow Up: Phase 2 = -0.53 %FW p>0.05 g=0.17, Phase 3 = -0.39 p>0.05 g=0.12, Phase 4 = -0.03 %FW p>0.05 g=0.01) suggesting that the lateral COP position was retained. When comparing baseline to Follow Up, only the lateral shift in phase 2 exceeded the MDC and no results exceeded the MDC when comparing Post 2 to Follow Up (Figure 12). Furthermore, phases 2-4 at both Post 2 and Follow Up were not statistically different from the COP location of control (p > 0.05) All means, standard deviations, statistical trends and differences can be seen in Figure 12, Table 7, and Table 8.

4. Discussion

The purpose of this study was to determine how cumulative, RW-VF training impacted the COP location in people with CAI. We aimed to not only quantify the COP shift, but to determine if the shifted COP location following training was similar to that of healthy controls. The results of this study suggest that this cohort of people with CAI has COP locations similar to healthy controls for the first 70% of stance at baseline. Further, both a single session and two-weeks of training with RW-VF caused lateral COP shifts across various phases of stance rather than the anticipated medial shift in the COP location. These results partially support our hypotheses because multiple training sessions of variable RW-VF training caused a shift in the COP which was retained after one week of completing the training intervention. However, contrary to our hypotheses the shift experienced by this cohort was lateral rather than a medial shift in the COP location.

4.1 COP in CAI vs Control at Baseline

First, our results are contradictory to previously published results suggesting that the COP location is different in those with CAI and healthy controls. Koldenhoven et al[17] reported that the COP while walking in people with CAI compared to controls ranges from 2.9 mm more lateral in phase 1 to 7.5 mm more lateral at its maximum during midstance/ phase 5.[17] However, in this cohort, the CAI participants had an average COP location which was essentially the same as controls at baseline for the same phases. The participants in this study had COP locations 0.4

mm more medial in phase 1 and 0.12 mm more medial in phase 5. Though not statistically assessed, a comparison of the demographics between this CAI cohort and the published demographics from Koldenhoven et al[17] suggest that these groups were similar. Comparisons were able to be made for age, anthropometrics, functional limitations (IdFAI and FAAM) and number of ankle sprains. Additionally, their healthy control participants had no history of ankle sprains and appeared to be matched based on sex assigned at birth.[17] However, as our control dataset was generated from a separate project, participants were not excluded based on a history of ankle sprain, only a recent injury in the past 6 months. Therefore, it is possible that our control group could have included some individuals with an ankle sprain history from greater than 6 months before data collection.

Our results indicate that not all people with CAI have a lateral COP in phases which contain important gait events such as initial contact and midstance while walking relative to controls. This suggests that there may be a subset of people with CAI who can successfully compensate for their impairments in early and midstance to make their COP location remain within a typical location while walking. At this time, it is unclear if such a compensation results in other downstream biomechanical adaptations and what the consequences of such adaptations could be, if any. The lack of lateral COP shift relative to controls, may also explain why the hypothesized medial shift post training was not observed. Future research is needed but this suggests that gait retraining protocols may need to include a pre-training screening to determine the outcome that should be targeted in the patient's rehabilitation plan. While speculative, some individuals with CAI may benefit from a program that targets reductions in ankle inversion at initial contact or foot contact time as they have been suggested to increase the risk of ankle sprains.[21,171]

4.2 Change in COP After Single Training Session

Though not statistically significant the COP location after a single training session was trending more medial than at baseline for the first 40% of stance. Additionally, in phase 1, the post training COP was more medial than controls with a moderate effect size. This is important as the COP location at initial contact, which is encompassed in phase 1, has been suggested to increase the risk of lateral ankle sprains.[21] This trend could support the existing literature using sensory based gait retraining. Torp et al[96] used a visual crosshair laser during a single session of gait retraining to medially shift the COP for the first 80% of stance while walking with feedback. Similarly, Migel and Wikstrom[111] concluded that a single session of vibration feedback medially shifted the COP in the first 90% of stance when training occurred in a controlled lab setting and the first 70% of stance when training occurred in a real world environment. Previous studies used pre-to-post cohort designs and did not include a control group for baseline comparison. Therefore, we are assuming that they had a lateral COP at baseline and thus a greater capacity for COP change in response to feedback. This study is the first to include a baseline comparison between people with CAI and controls.

It is possible that the differences between the results from this study and previous literature could be due to methodological changes between the studies. For example, this cohort and the cohort from Migel and Wikstrom[111] completed almost identical study procedures except for a small change in the feedback tool calibration technique. In this study, the feedback tool calibration was completed with participants in a single limb stance position with contralateral toe touch for balance rather than a fingertip touch as was completed in the first study. The toe touch procedure, adapted from McPoil & Cornwall,[257] was intended to facilitate a lateral weight shift at the pelvis to make the single limb stance position more similar to that during gait. While there is no way to determine the impact of this methodological change retrospectively, it is possible that this change could have impacted the feedback threshold. A systematically higher or lower threshold would have changed the magnitude of lateral pressure and therefore the COP location required to activate the stimulus while training.

The data between this study and Migel and Wikstrom[111] also had a change in COP processing techniques. Migel and Wikstrom[111], calculated the COP as the frontal plane distance between the medial-lateral COP coordinate in the laboratory space and a line created by connecting the 5th metatarsal head marker and the posterior calcaneal marker for each frame which represented the lateral foot. The Migel & Wikstrom[111] technique expressed the COP in the laboratory coordinate space, or the global coordinate space. In the current study, the COP was expressed relative to the midline of the foot, which defines the COP within the long axis of the foot, called the foot progression angle coordinate system. Research has shown that expressing the COP in the global coordinate system will change the medial-lateral COP position during static single leg stance as you change the foot progression angle within the global coordinate space.[280] However, expressing the COP within the foot progression angle coordinate system does not create significant differences in the COP location as the foot progression angle changes.[280] Therefore, it is possible that the individuals in the current study manipulated the foot progression angle to offload the FSR but because the data were expressed within the foot progression angle coordinate system, this could have masked COP location changes.

Currently, there is little understanding of how the foot progression angle is impacted by CAI. To our knowledge, there is only a single study[176] which reports an increase in foot progression angle in those with CAI who were undergoing surgical intervention because of failed conservative treatments. Mechanical instability was confirmed intraoperatively in this group.[176] Given that not all individuals with CAI have mechanical instability,[120] it remains unknown how foot progression angle presents or changes within the larger CAI population. In the event that foot progression angle is different between people with CAI and healthy controls, there is evidence that using vibration or haptic feedback can change foot progression angle[281,282] and step width[281] after a single session of retraining in healthy participants while walking using an ankle bracelet with vibration motors or an in-shoe vibration system. Additionally, a six-week gait retraining program using in-shoe haptic feedback in people with medial knee osteoarthritis immediately decreased the knee adduction moment, changed foot progression angle, decreased pain, and improved self-reported function. These changes were also retained for one month.[283] Perhaps most importantly, preliminary data using vibration or haptic feedback outside the lab has been shown to decrease foot progression angle and knee adduction moment in healthy participants[284] providing initial proof of concept for real-world interventions targeting foot progression angle. Future research is needed to fully explore foot progression angle and other 3-dimensional biomechanical changes following RW-VF to better understand how those with CAI change their gross biomechanical movement patterns and if other targeted biomechanics can be modified using RW-VF gait retraining.

4.3 Change in COP After Two-Weeks of RW-VF

Given that our CAI cohort was not different from controls at baseline, it is challenging to draw conclusions about the impact of cumulative training on medially shifting the COP location, however, we can glean insights into vibration training utility. The significant changes and large effect sizes in early stance phases after training suggest that, while the COP changed in the opposite direction for this cohort, RW-VF gait retraining is a feasible and effective intervention to modify gait biomechanics during key stance phases in people with CAI. In the current study, we also noted that the COP changes were retained, however, only a single phase exceeded the MDC. This suggests that the current study parameters (e.g., duration, volume, etc.) of variable, real-world training as the sole intervention starts to change COP but is not enough to make lasting biomechanical changes. Future research should work to assess retention following longer and/or higher volume gait retraining programs in people with CAI or RW-VF integrated into more comprehensive rehabilitation protocols.

5. Conclusion: The Future of RW-VF

Our research confirms that a single session of RW-VF leads to a shift in the COP location. Additionally, two-weeks of RW-VF gait retraining causes immediate COP changes with moderate retention but should not be used in isolation as the retention of changes diminishes over time. This study has unique features in that our sample of individuals with CAI walked with a similar COP location to that of healthy controls. This suggests that participants should complete a screening session to determine if the feedback target is present before enrollment in the study. We also employed different processing techniques. Either, or both, of these two factors may have impacted the COP shift in our results. These conclusions provide justification for longer and/or multimodal intervention strategies for people with CAI as well further exploration of COP processing techniques and the impact of gait retraining interventions on subgroups of people within the broader CAI classification.

Table 7: Center of pressure location between CAI and controls (Aim 2)

Center of Pressure Locations (%FW) Between CAI and Control Participants					
Phase	Baseline Mean ± SD	After Single Session Mean ± SD	After Two-Weeks Mean ± SD	1-Week Follow Up Mean ± SD	Control Mean ± SD
1	4.61±2.43	2.98±3.39*	6.43±3.39	4.61±1.87	5.3±3.07
2	4.23±2.66	3.32±2.58	6.56±2.58	6.03±3.07	4.28±4.17
3	3.97±2.62	3.49±2.03	6.58±6.58	6.19±3.60	4.48±6.07
4	3.75±2.51	3.24±2.68	5.62±2.68	5.59±4.33	4.42±7.06
5	2.9±2.63	2.98±3.61	4.05±3.61	4.42±6.00	3.25±7.94
6	0.91±2.13	1.55±4.27	1.61±4.27	2.6±7.37	0.86±8.64
7	-0.89±2.03	0.08±4.23	-0.45±4.23	0.75±7.89*	-2.62±7.96
8	-3.38±2.48*	-1.50±3.91*	-2.96±3.91*	-2.55±6.94*	-7.17±7.26
9	-8.85±1.91*	-5.46±4.09*	-9.17±4.09*	-9.99±7.67	-13.22±7.33
10	-19.7±5.66*	-16.38±13.1*	-25.24±13.1	-25.11±14.84	-27.61±9.46

a) * p<0.05, %FW = percent foot width, SD = Standard deviation

Hedge's g Effect Sizes and 95% CI			
Baseline v Control			
	g	Lower	Upper
Phase 1	-0.24	-0.84	0.35
Phase 2	-0.01	-0.61	0.58
Phase 3	-0.10	-0.70	0.49
Phase 4	-0.12	-0.71	0.47
Phase 5	-0.06	-0.65	0.54
Phase 6	0.01	-0.59	0.60
Phase 7	0.28	-0.32	0.88
Phase 8	0.68	0.07	1.29
Phase 9	0.77	0.16	1.38
Phase 10	0.97	0.35	1.60
Single Session Post Test v Control			
Phase 1	-0.70	-1.32	-0.09
Phase 2	-0.24	-0.84	0.35
Phase 3	-0.21	-0.80	0.39
Phase 4	-0.21	-0.80	0.39
Phase 5	-0.04	-0.64	0.55
Phase 6	0.10	-0.50	0.69

Phase 7	0.41	-0.19	1.00
Phase 8	0.93	0.31	1.56
Phase 9	1.25	0.60	1.90
Phase 10	0.98	0.35	1.61
Two-Week Post Test v Control			
Phase 1	0.34	-0.25	0.94
Phase 2	0.58	-0.03	1.18
Phase 3	0.44	-0.16	1.04
Phase 4	0.21	-0.38	0.81
Phase 5	0.12	-0.47	0.72
Phase 6	0.11	-0.49	0.70
Phase 7	0.33	-0.27	0.92
Phase 8	0.69	0.08	1.30
Phase 9	0.65	0.04	1.26
Phase 10	0.21	-0.39	0.80
1-Week Follow Up v Control			
Phase 1	-0.26	-0.86	0.33
Phase 2	0.42	-0.18	1.02
Phase 3	0.33	-0.27	0.93
Phase 4	0.19	-0.40	0.79
Phase 5	0.16	-0.43	0.76
Phase 6	0.21	-0.38	0.81
Phase 7	0.42	-0.18	1.02
Phase 8	0.64	0.03	1.25
Phase 9	0.42	-0.18	1.02
Phase 10	0.20	-0.39	0.80

b) CI = Confidence Interval

Table 8: Results of omnibus and post hoc analyses (Aim 2)

Phase	Baseline Mean ± SD	After Two-Week Training Mean ± SD	Follow Up Mean ± SD	$X^2(2)$	p value	MDC
1	4.61±2.43	6.43±3.39	4.61±1.87	9.3	0.01	0.8
2	4.23±2.66	6.56±2.58	6.03±3.07	13.9	0.001	1.75
3	3.97±2.62	6.58±2.03	6.19±3.60	17.1	<0.001	2.47
4	3.75±2.51	5.62±2.68	5.59±4.33	13.3	0.001	2.15
5	2.90±2.63	4.05±3.61	4.42±6.00	6.4	0.041	0.82
6	0.91±2.13	1.61±4.27	2.6±7.37	1.9	0.39	0.46
7	-0.89±2.03	-0.45±4.23	0.75±7.89	2.7	2.59	0.21
8	-3.38±1.48	-2.96±3.91	-2.55±6.94	1.2	0.55	0.35
9	-8.85±1.91	-9.17±4.09	-9.99±7.67	0.4	0.82	1.28
10	-19.7±5.66	-25.24±13.10	-25.11±14.84	4.3	0.12	15.27

a) SD = Standard deviation, MDC = minimal detectable change

POST HOC ANALYSES					
Baseline v Posttest					
Phase	W	p value	Absolute COP Change	Hedges g	Effect Size & 95% CI
1	-2.84	0.005	1.82*	1.11	(-0.55, 1.67)
2	-3.73	<0.001	2.33*	1.41	(0.83, 2.00)
3	-3.4	0.001	2.61*	0.99	(0.44, 1.54)
4	-2.8	0.005	1.87	0.58	(0.05, 1.12)
5	-1.94	0.052	1.15*	0.26	(-0.26, 0.79)
6	-1.23	2.18	0.7*	0.17	(-0.35, 0.69)
7	-0.56	0.575	0.44*	0.12	(-0.40, 0.69)
8	-0.747	0.455	0.42*	0.14	(-0.38, 0.64)
9	-0.523	0.601	0.32	-0.11	(-0.64, 0.41)
10	-2.17	0.03	5.54	-0.45	(-0.98, 0.07)
Baseline v Follow Up					
Phase	W	p value	Absolute COP Change	Hedges g	Effect Size & 95% CI
1	-0.11	0.911	0	0	(-0.52, 0.52)
2	-2.2	0.028	1.8*	0.57	(0.04, 1.10)
3	-3.7	<0.001	2.22	0.64	(0.10, 1.17)
4	-3.02	0.002	1.84	0.47	(-0.06, 1.00)

5	-1.38	0.167	1.52*	0.3	(-0.23, 0.82)
6	-1.27	0.204	1.69*	0.28	(-0.24, 0.80)
7	-0.93	3.51	1.64*	0.26	(-0.27, 0.78)
8	-0.41	0.681	0.83*	0.15	(-0.37, 0.67)
9	-1.01	0.313	1.14	-0.18	(-0.71, 0.34)
10	-1.27	0.204	5.41	-0.43	(-0.96, 0.09)
Posttest v Follow Up					
Phase	W	p value	Absolute COP Change	Hedges g	Effect Size & 95% CI
1	-2.28	0.023	1.82*	0.6	(0.07, 1.13)
2	-1.12	2.63	0.53	0.17	(-0.35, 0.69)
3	-1.008	0.313	0.39	0.12	(-0.40, 0.64)
4	-1.12	0.263	0.03	0.01	(-0.51, 0.53)
5	-1.157	0.247	0.37	-0.07	(-0.59, 0.45)
6	-1.31	0.191	0.99*	-0.15	(-0.67, 0.37)
7	-1.46	0.145	1.2*	-0.17	(-0.69, 0.35)
8	-0.6	0.55	0.41*	-0.07	(-0.59, 0.46)
9	-0.523	0.601	0.82	0.12	(-0.40, 0.64)
10	-0.11	0.911	0.13	-0.01	(-0.53, 0.51)

b) post hoc analyses. *=change exceeds MDC

CHAPTER 6: MANUSCRIPT 3

Functional range of motion and postural control associate with center of pressure changes during gait retraining with haptic feedback in people with chronic ankle instability: An exploratory analysis

1. Introduction

Chronic ankle instability (CAI) results from mechanical and functional insufficiencies following a lateral ankle sprain.[120] Persistent impairments include altered movement patterns such as increased inversion and a lateral center of pressure (COP) during gait.[120] Altered gait biomechanics are a known risk factor for subsequent injury[22] and may lead to altered cartilage loading. Given that walking gait is an important activity of daily living, restoring typical gait biomechanics is imperative to potentially slow the negative cascade from lateral ankle sprain to post-traumatic ankle osteoarthritis.

Treatments using sensory biofeedback for gait retraining have emerged for people with CAI in response to persistent alterations in gait biomechanics. Visual,[27,96] and vibration[111,113] biofeedback can successfully mitigate both excessive inversion and medially shift the COP trace. However, effectively using sensory feedback relies on an individual's ability to change their foot position while walking. Structural and/ or functional adaptations may hinder dynamic mobility of the foot/ankle complex and therefore may limit the ability for some people with CAI to respond to feedback stimuli appropriately. For example, excessive tibial varus or a pes planus foot can cause a pronated ankle position and therefore an inability to further pronate in response to feedback stimuli. A pes cavus foot, limited dorsiflexion range of motion, and limited calcaneal eversion could also limit a person's ability to pronate. Additionally, poor neuromuscular control may impede a person's ability to dynamically alter the amount of pronation in response to feedback while walking. Therefore, an individual's structural factors, range of motion restrictions, and/or sensorimotor function could limit their ability to shift their COP trace medially in response to feedback stimuli.

While determining treatment efficacy for new interventions is important, perhaps equally important is providing a framework to identify patients who are most likely to benefit from the intervention[285] with the intent of identifying profiles of responders and non-responders. Therefore, the purpose of this preliminary analysis, is to explore potential relationships between structural factors and clinical measures with changes in the COP location in response to vibration feedback during walking in those with CAI. Our structural factors include tibial varum during single leg stance and the Foot Posture Index score (FPI). Our clinical outcomes include passive calcaneal eversion, dorsiflexion range of motion measured by the weight bearing lunge test (WBLT), and postural control measured by the COP velocity (COPv) during single leg stance. We hypothesized that increased FPI (i.e.: a pronated foot), increased tibial varum, and increased COPv would associate with lesser COP change. We also hypothesized that decreased passive calcaneal eversion and decreased WBLT would associate with lesser COP change.

2. Methods

Twenty participants with unilateral CAI[4] volunteered for the study. After providing written informed consent, anthropometrics (height & mass) and overground self-selected walking speed were measured. Foot posture was categorized as pronated, neutral, or supinated in bilateral standing using the FPI.[269] The FPI quantifies shank, calcaneal, arch, and forefoot positioning in quiet bilateral standing to generate a composite score which categorizes the foot posture. Tibial varum was measured as the angle between horizontal and the bisection of the lower 1/3 of the leg in single limb stance[257] with contralateral toe touch for added stability to improve the measurement accuracy. Passive calcaneal eversion was measured with the participant lying prone and the contralateral leg in flexion, abduction, and external rotation to position the involved limb in the frontal plane.[286] The calcaneus of the involved limb was moved into maximal eversion and measured as the angle between the bisection of the gastroc and the bisection of the calcaneus. Functional dorsiflexion was measured using the WBLT.[287] The participant was positioned facing a wall with the great toe of the involved foot on a tape measurer and the contralateral limb behind in a mini lunge position. Participants were instructed to lunge forward attempting to touch their knee to the wall while keeping their heel in contact with the floor. Three successful trials of the maximal distance between the great toe and the wall were averaged. Static postural control was measured by placing the participant's foot in the center of a force plate equipped with a grid of 1 x 1 cm squares (AMTI Inc, Watertown, MA). The COPv in the anterior-posterior (COPv-AP) and medial-lateral directions (COPv-ML) were captured with the participant standing in single limb stance with their hands on their hips for 3 trials of 10 seconds with both eyes open (EO) and eyes closed (EC). The COPv was then averaged within each direction for visual condition.

After obtaining structural and clinical outcomes, the vibration feedback tool was placed on the dorsum of the participants' shoe with the force sensing resistor under the 5th metatarsal head as previously described.[111] The tool was calibrated to each participant with the lowest resistance such that participants received vibration feedback while in a single leg stance and maximally loading the sensor but not in bilateral stance.[111] Baseline kinetics (2000 Hz) and kinematics (200 Hz) of the lower leg and foot were collected while participants walked on a split belt treadmill (Bertec, Columbus, OH) at their self-selected walking speed for 2 minutes with no feedback. Baseline data were captured during the second minute of walking to allow participants time to accommodate to the feedback tool placement.[90,111,113] Then, the feedback tool was turned on and participants walked for 10 minutes with vibration feedback and instructions to walk as normally as possible with minimal vibration stimuli. Data were collected during the early accommodation phase (minute 1-2) while the participant walked with feedback.

The COP was extracted from two 1.75 x 0.5 m force plates embedded under the treadmill and marker locations of the 5th metatarsal head, 1st metatarsal head, medial and lateral malleoli were exported. All data were filtered with a 4th order Butterworth filter with a cut off frequency of 10 Hz and reduced using a custom MATLAB script (Mathworks Inc., Natick, MA, Version 2022b). The COP location was expressed as the perpendicular distance between the location and the midline of the foot. The midline of the foot which was defined as a line between the center of the fore and rear foot. The forefoot center was located half the distance between the 5th and 1st metatarsal head markers while the rearfoot center was half the distance between the medial and lateral malleolus marker for each frame of data. Data from participants with CAI of their left ankle was reflected so that all positive COP values represent points lateral to the midline and negative COP values represent points medial to the midline. The COP location within the foot was then normalized to the maximal foot width which was defined as the distance between the 5th and 1st metatarsal markers from the static calibration file. Lastly, the COP locations were divided into 10 subphases of stance and averaged within each subphase so one data point represented 10% of stance.[27,96,111] Phase 1 represents initial contact and loading response, phase

5 represents midstance, and phase 10 represents preswing and toe off.[111] See Figure 13 for processing steps.

Statistical Analysis: Our a priori sample size calculations for separate bivariate regressions with an estimated R^2= 0.10, [272,275,276] an alpha level set at 0.05 and 80% power suggested that 614 participants were required to find statistical significance. However, this exploratory analysis was performed with data collected from 20 participants as part of a larger project. To maximize the number of participants in the analysis, we chose to keep data from mild outliers (1.5 x interquartile range) and only removed data from 1 participant which was classified as an extreme outlier (greater than 3 x interquartile range for more than 50% of the subphases of stance). Therefore, our final sample size included 19 participants with CAI. As our data were not normally distributed, separate spearman's correlations were completed for each structural and clinical measure and the COP change for each subphase of stance. Bootstrap, bias corrected 95% confidence intervals were calculated for each correlation coefficient with 1000 samples. Strength of the correlation was interpreted as 0.01-0.19 negligible, 0.2-0.29 weak, 0.30-0.39 moderate 0.4-0.69 strong, ≥ 0.7 very strong.[277]

3. Results

The final data analysis included 19 participants. One participant had data which qualified as outliers for the first five subphases of gait and was therefore removed from the analysis. Demographics can be found in Table 9. The results of the correlations can be found in Table 11.

Table 9: CAI demographics (Aim 3)

a) Demographics

	Mean	SD
Age (yrs.)	23.6	4.71
Height (cm)	170.275	10.10
Mass (kg)	75.43	14.31
Number of Ankle Sprains	5	2.58

SD= Standard Deviation

b) Baseline patient reported outcomes

	Involved Limb		Uninvolved Limb	
	Mean	SD	Mean	SD
IdFAI	21.95	5.87	7.7	5.88
FAAM-ADL	82%	9%	95%	8%
FAAM-S	59%	19%	89%	13%

SD = Standard Deviation, IdFAI - Identification of Foot and Ankle Instability, FAAM = Foot and Ankle Ability Measure, ADL = Activities of Daily Living, S = Sport

There was a moderate negative correlation between the FPI and the COP change (r_s =-0.315) during phase 10 (preswing/ toe off) which was not significant. Passive calcaneal eversion demonstrated moderate positive correlations with COP change in phases 2-4 (loading response/ midstance: phase 2(P2): r_s =0.364, P3: $r_s = 0.378$, P4: $r_s = 0.369$) though none of the correlations reached statistical significance. There were moderate, positive, non-significant correlations between WBLT and the COP change (P2: $r_s = 0.335$, P3: r_s =0.371) during phases 2-3 (loading response/ midstance). Postural control demonstrated moderate to strong negative correlations with the COP change during phase 1 (initial contact/ loading response: COPv- AP-

EO r_s = -0.389, COP-ML-EC r_s = -0.574), phase 6 (terminal stance: COPv-AP-EC r_s =-0.328) phase 7 (terminal stance: COPv-AP-EC r_s =-0.340), and phase 10 (preswing/ toe off: COPv-AP-EO r_s =-0.312). Of the moderate to strong results, only the correlation between COPv-ML-EO during phase 1 and the COP change reached statistical significance (p=0.010). Means and standard deviations for each variable are located in Table 10.

Table 10: Means and standard deviations (Aim 3)

Variable	Mean ± SD
Foot Posture Index	4.80 ± 3.56
Tibial Varum	8.40 ± 3.09˚
Calcaneal Eversion	2.90 ± 2.97˚
AP COPv Eyes Open	2.36 ± 0.78 cm/sec
ML COPv Eyes Open	2.39 ± 0.98 cm/sec
AP COPv Eyes Closed	4.80 ± 1.41 cm/sec
ML COPv Eyes Closed	5.36 ± 1.36 cm/sec
Weight Bearing Lunge Test	7.26 ± 3.48 cm
COP Change: Phase 1	1.96 ± 2.25 %FW
COP Change: Phase 2	1.74 ± 2.05 %FW
COP Change: Phase 3	2.15 ± 2.27 %FW
COP Change: Phase 4	2.24 ± 2.50 %FW
COP Change: Phase 5	2.91 ± 2.80 %FW
COP Change: Phase 6	3.69 ± 3.03 %FW
COP Change: Phase 7	3.88 ± 3.02 %FW
COP Change: Phase 8	3.93 ± 2.98 %FW
COP Change: Phase 9	4.43 ± 3.19 %FW
COP Change: Phase 10	7.43 ± 6.19 %FW

SD = standard deviation, AP = anterior posterior
ML = medial lateral, COP = center of pressure
%FW = percent foot width

4. Discussion

The purpose of this study was to explore relationships between structural and clinical measures and the capacity to change the COP trace in people with CAI while walking with vibration feedback. Our results partially support our hypotheses as participants with a pronated foot on the FPI (i.e.: increased FPI), decreased calcaneal eversion, decreased WBLT, and worse postural control (i.e.: large COPv) have moderate to strong associations with smaller medial shifts of the COP trace meaning less capacity to change. Contrary to our hypotheses, tibial varum measurements did not associate with the COP change. Our results suggest that range of motion and neuromuscular control may influence the ability to utilize biofeedback during walking. This is particularly important as people with CAI have less dorsiflexion during walking,[157] and worse postural control[120] compared to uninjured controls. Appropriate range of motion and neuromuscular control are essential for both typical gait biomechanics and the ability to respond to haptic feedback. Furthermore, structural alignment either did not associate (tibial varum) or only associated during phase 10 in which the participant was not receiving feedback (FPI).

A recent systematic review[131] investigating the alignment of the foot and ankle in people with CAI identified contradictory results as to whether people with CAI had differences in foot morphology compared to healthy controls. Some studies in the review concluded that people with CAI had cavovarus feet and hindfoot varus using 2D image analyses while others reported no differences between the foot morphology of people with and without CAI using clinical tests such as the FPI and arch height index.[131]

While tibial varum is not as thoroughly investigated in this population, a single study showed excessive tibial varum in a non-weight bearing position in people with chronic ankle instability at $16.09 \pm 2.82°$ compared to $15.01 \pm 3.07°$ in healthy controls.[288] Compared to normative values, our participants demonstrated a slightly more pronated foot on the FPI (mean FPI = 4.8 ± 3.56, normative mean value = 4[289]), and limited calcaneal eversion (mean passive calcaneal eversion = $2.9 \pm 2.97°$, normative passive eversion = $10 \pm 4°$[290]), and a greater tibial varum position in weight bearing (mean tibial varum = 8.4 ± 3.08, normative bilateral weight bearing angle = $6 \pm 2°$[290]). Our results support studies which report morphological differences of the foot and hindfoot in people with CAI, but not the lower leg. However, based on our results, we can conclude that even if an individual’s foot does present in a particular posture, non-modifiable factors (i.e.: tibial alignment and foot classification) may not impact the ability of the individual to respond to sensory feedback while walking.

Structural alignment seems to be an independent factor and not related to the COP change; however, our results support the importance of restoring range of motion early. The purpose of our feedback tool is to decrease excessive supination during walking in people with CAI. Users must be able to achieve a certain level of pronation to effectively respond to the feedback. Calcaneal eversion and dorsiflexion are both important components of pronation during gait, and, in fact, our results showed that people with more range of motion generated larger COP shifts. Therefore, increasing calcaneal eversion and dorsiflexion range of motion early in rehabilitation protocols could improve an individual's response to gait biofeedback at more advanced stages of rehabilitation. Interestingly, people with CAI don't always demonstrate limitations in dorsiflexion range of motion when measuring ankle range of motion in isolation.[291] However, the WBLT consistently finds limitations in this population and can be improved with joint mobilizations.[56,62,64] Improving WBLT could increase an individual's ability to utilize gait biofeedback and potentially lead to improved long term outcomes. Similarly, hindfoot varus, or decreased calcaneal eversion is thought to be present in this population.[131] However, it remains unclear as to whether that is a non-modifiable adaptation within CAI. If the adaptation is modifiable, calcaneal eversion mobilizations may be important to include in rehabilitation to improve an individuals' ability to utilize gait biofeedback. Future research should aim to determine the ability to change hindfoot positioning and how that impacts gait biomechanics in people with CAI.

Finally, in this study, people with better frontal and sagittal plane postural control (i.e.: small COPv in the medial-lateral and anterior-posterior directions) had larger COP trace shifts medially during stance. We identified a single statistically significant correlation between the medial-lateral COPv with eyes closed and the COP change during phase 1 of stance. Phase 1 is particularly important for the gait cycle as it encompasses both initial contact and the beginning of loading response which starts the first foot rocker and sets up the biomechanical profile for the remainder of stance. Furthermore, alterations in foot position at initial contact and loading response have been linked to an increased risk of subsequent ankle injuries[171]. Changing the foot position in phase 1 of stance could have significant impacts on subsequent injury rates and long-term joint health. Balance training interventions consisting of a 4-week progressive training program are able to improve COP distributions during static stance in people with CAI so they are more similar to healthy controls.[175] Interestingly, when gait biomechanics were measured after completing the same balance training program, no changes were noted.[43] While a therapeutic goal of rehabilitation should be to improve postural control, our results suggest that a comprehensive rehabilitation program that includes movement retraining, which allows patients to learn how to use their improved postural control system, is needed to improve gait biomechanics.

This study has some limitations which must be mentioned. First, our power analysis indicated that we needed 617 participants to detect an R^2 of 0.1. This suggests that our study could be underpowered and thus we might have failed to find significant correlations. In response to our low participant number, we intentionally chose analytical techniques which supported an exploratory analysis maximizing the potential to find relationships which are easy to interpret clinically. These include, 1) only removing data from a single extreme outlier and leaving data classified as mild outliers in the analysis and 2) using a liberal relationship strength classification scheme. These two strategies maximized our potential to identify moderate to strong relationships that we believe warrant further investigation. Additionally, we chose to complete all non-parametric analyses rather than transforming the data, which is not currently recommended.[264] However, leaving the data in the original form improves clinical interpretation and implementation which is important as this is the first study to assess structural and clinical factors in relation to a gait biofeedback intervention. Last, structural and range of motion measures were obtained barefoot, however, participants walked with their own shoes on the treadmill. An individual's ability to change their COP location in response to feedback could have been impacted by the construction and/or wear patterns of the individual's shoes and thus impacted our results. Future research should aim to increase sample sizes to confirm or refute the initial observations from this study and to better understand the implications of shoe construction and wear on the capacity to change COP location in response to feedback.

5. Conclusion

Our results suggest the ability of an individual with CAI to respond to vibration feedback during walking is related to modifiable factors including range of motion and postural control but not non-modifiable structural factors. Integrating vibration feedback for gait retraining after addressing limited range of motion and poor postural control in CAI patients could improve the utility of haptic feedback during walking gait for people with CAI.

Table 11: Correlations between structural & clinical outcomes, and center of pressure change during walking with vibration feedback (Aim 3)
Spearman's rho with bootstrapped 95% confidence intervals

Phase	1	2	3	4	5	6	7	8	9	10
FPI	0.077 (-0.425, 0.558)	0.074 (-0.479, 0.640)	0.250 (-0.297, 0.692)	0.004 (-0.686, - 0.524)	0.076 (-0.514, 0.551)	0.225 (-0.277, 0.640)	0.189 (-0.364, 0.648)	0.163 (-0.338, 0.609)	0.063 (-0.407, 0.550)	**-0.315** **(-0.746, 0.266)**
Tibial Varum	0.067 (-0.503, 0.606)	0.134 (-0.389, 0.678)	-0.053 (-0.533, 0.461)	-0.089 (-0.608, 0.523)	-0.043 (-0.540, 0.486)	-0.102 (-0.557, 0.387)	-0.128 (-0.646, 0.442)	-0.184 (-0.699, 0.352)	-0.098 (-0.642, 0.461)	-0.057 (-0.513, 0.461)
Calcaneal Eversion	0.100 (-0.429, 0.615)	**0.364** **(-0.156, 0.721)**	**0.378** **(-0.023, 0.187)**	**0.369** **(-0.077, 0.659)**	0.185 (-0.424, 0.664)	0.112 (-0.437, 0.635)	0.098 (-0.525, 0.638)	0.009 (-0.551, 0.479)	-0.157 (-0.664, 0.377)	-0.139 (-0.694, 0.455)
WBLT	-0.149 (-0.588, 0.348)	**0.335** **(-0.130, 0.724)**	**0.371** **(-0.142, 0.720)**	0.265 (-0.361, 0.735)	-0.155 (-0.590, 0.356)	-0.119 (-0.526, 0.229)	-0.211 (-0.635, 0.283)	-0.277 (-0.659, 0.175)	-0.244 (-0.640, 0.237)	-0.022 (-0.532, 0.469)
COPv-AP-EO	**-0.389** **(-0.809, 0.232)**	-0.209 (-0.696, 0.305)	-0.296 (-0.738, 0.226)	0.053 (-0.461, 0.518)	0.018 (-0.465, 0.489)	-0.132 (-0.574, 0.355)	-0.179 (-0.633, 0.364)	-0.240 (-0.692, 0.318)	-0.147 (-0.633, 0.483)	**-0.312** **(-0.726, 0.253)**
COPv-ML-EO	-0.270 (-0.637, 0.194)	-0.139 (-0.659, 0.456)	-0.102 (-0.579, 0.453)	0.207 (-0.370, 0.662)	0.123 (-0.405, 0.571)	0.084 (-0.431, 0.537)	0.081 (-0.466, 0.522)	0.009 (-0.472, 0.468)	0.100 (-0.330, 0.607)	-0.288 (-0.760, 0.330)
COPv-AP-EC	-0.140 (-0.668, 0.466)	0.105 (-0.391, 0.595)	-0.168 (-0.690, 0.374)	-0.125 (-0.668, 0.411)	-0.130 (-0.662, 0.382)	**-0.328** **(-0.749, 0.298)**	**-0.340** **(-0.732, 0.202)**	-0.268 (-0.716, 0.275)	-0.207 (-0.676, 0.396)	-0.042 (-0.536, 0.500)
COPv-ML-EC	**-0.574*** **(-0.813, - 0.033)**	-0.132 (-0.543, 0.345)	-0.063 (-0.560, 0.446)	-0.109 (-0.532, 0.382)	-0.049 (-0.550, 0.477)	-0.182 (-0.708, 0.497)	-0.135 (-0.614, 0.370)	-0.117 (-0.625, 0.330)	-0.032 (-0.531, 0.460)	-0.196 (-0.679, 0.394)

FPI = Foot Posture Index, WBLT = weight bearing lunge test, COPv = center of pressure velocity, AP = anterior-posterior, ML = medial-lateral, EO = eyes open, EC = eyes closed. Bold type indicates a moderate to strong correlation, * indicates p< 0.05

CHAPTER 7: CONCLUSION

The overall goal of this study was to examine the immediate and delayed effects of real-world gait retraining on gait biomechanics in those with CAI. We aimed to optimize feedback by modifying the FSR placement, examine medial-lateral COP outcomes after multiday RW-VF gait retraining and explore relationships between non modifiable structural factors and modifiable clinical outcomes of the leg and COP changes. While accomplishing our goals, we discovered various unanticipated results which add to the understanding of gait biomechanics in people with CAI and factors to consider when designing RW-VF intervention strategies.

First, we determined that the sensor location (i.e.: under the 5th MH v under the heel) modified gait variables outside of the COP. During data collection, we observed that people with CAI walked with a mid to forefoot strike pattern while training with the sensor under the heel. Objectively, we did not see changes to the COP position in either medial-lateral or anterior-posterior direction with the sensor in either position. However, we did identify changes in step length with the heel location generating a shorter step length. This project demonstrates the need to assess a broad range of biomechanical factors when developing a new movement retraining intervention. The purpose of movement retraining is to minimize the long-term impact of aberrant biomechanics. This goal can only be successfully achieved by implementing training strategies that reduce excess or facilitate limited movement without introducing deleterious changes at any segment within the kinetic chain.

Next, we implemented a two-week RW-VF gait retraining program and assessed COP outcomes following a single training, six trainings, and after 1-week with no training. We compared each biomechanics assessment timepoint to a database of healthy control data. Our results indicate that a two-week RW-VF training can modify the COP in people with CAI. However, our sample of CAI participants were not significantly different than controls before the intervention during key points of gait. This could have limited their capacity to respond to the training as expected. Altered movement strategies is a known impairment in people with CAI, however the current model of CAI acknowledges that not all people with CAI will have the same impairments.[120] The results from this study reinforce the importance of patient specific feedback targets and participant level analyses as appropriate.

Finally, we explored relationships between modifiable and non-modifiable factors which could influence the capacity of people with CAI to change the COP in response to gait retraining. Both structural (i.e.: amount of pronation) and clinical outcomes (calcaneal eversion mobility, WBLT, and static postural control) were related to the capacity to change. The results from this analysis provide potential therapeutic targets which can be integrated into a comprehensive treatment to maximize an individual's ability to respond to vibration feedback.

Cumulatively, the results of this project provide new insights and new questions into the application of gait retraining. While our pilot work did not compare the COP at baseline to controls, feedback targeting the COP location was able to shift the COP medially after training, suggesting that people with CAI can recall the correct biomechanics after training. However, the baseline comparison in this project brings up new questions which had not been previously considered. First, there is some evidence that COP processing techniques can impact COP location in static tasks,[280] however, it is unknown if the conclusions stand in dynamic tasks. Therefore, the first step in continuing to understand gait retraining targeting COP location in people with CAI is to determine how our processing techniques may have impacted our results. If the processing technique did not impact our result, it suggests that there is a group of people with CAI who do not have a lateral COP at baseline. Therefore, all participants should complete a screening session as part of feedback studies going forward to ensure that the feedback target is actually different than controls.

In addition to including a screening session, other feedback targets may need to be explored and identified in people with CAI. Previous research has shown positive feedback results targeting inversion and plantar pressure. The data sets in this project have full 3-D biomechanics which have not been fully explored at this time. Other potential targets could be kinematics, especially of the frontal plane ankle, or center of mass deviations, either of which could explain the changes observed in Aim 1 of this project. Ankle kinematics have been successfully changed previously with real time feedback of ankle position at initial contact. It is possible that our feedback technique could have changed inversion based on our pilot work, however, that analysis has yet to be completed.

Foot progression angle also shows promise as a new target based on literature from patients with medial knee osteoarthritis. It is currently unknown if the FPA is different between people with CAI and controls. Therefore, after determining alternate strategies to provide feedback on the COP location (i.e.: assessing processing techniques and positive reinforcement) it is essential to determine if the FPA in people with CAI is different than controls. If so, this could be a new feedback target which could be cued throughout the entire gait cycle, however, it would require further development of the feedback tool. As of right now, we are only able to cue plantar pressure and associated variables, such as the COP location during stance. However, a tool redesign using inertial measurement units would allow for more utility of the tool such as the ability to track 3-D motion during training. Finally, moments may be a better feedback target as moments can be manipulated without restricting specific kinetics or kinematics. Perhaps cueing moments is an effective strategy in those with CAI given the different constraints individuals may experience based on impairments. The first moment target to explore is the eversion moment. Decreasing an eversion moment could lead to a medially shifted COP.

Regardless of feedback targets, it is also crucial to explore the impact of positive reinforcement and negative reinforcement/ punishment feedback strategies. The studies in this project utilized a negative reinforcement strategy to deliver feedback, meaning that the participant received the feedback when they had too much pressure under the lateral foot. Positive reinforcement strategies would deliver the feedback when the participant loaded the medial column on their foot. It is possible that our participants could have demonstrated a lateral shift in the COP because they were looking for the feedback, or the boundary of the acceptable COP path. However, because there was no feedback at the post training timepoints, participants never found that boundary, and thus the COP remained more lateral. Furthermore, our feedback tool provides feedback during the stance phase with the intent to impact the subsequent step. Cueing for FPA could allow feedback to be provided throughout the entire gait cycle. Providing feedback at terminal swing and initial contact at a minimum may be able to influence the same step and improve the utility of our feedback.

Based on the heterogeneous nature of impairments which lead to CAI, long-term, it is important to identify who will respond to what type of feedback. It is possible that there is a target yet to be identified which may be suitable for all people with CAI or it is highly likely that specific groups of people with CAI will respond to different targets because CAI is derived from combinations of pathomechanical, sensorimotor, and perceptual deficits. Based on our results in Aim 3, it appears that people with better functional range of motion into dorsiflexion, better calcaneal mobility, and better balance will respond better to COP location feedback. Based on our unpublished work, people with better inversion proprioception had less inversion after a similar training protocol. However, static foot and lower leg alignment and plantar cutaneous sensation do not impact the ability to use feedback. Cumulatively, people with better outcomes respond better to COP location feedback. More importantly, the outcomes which appear to be important in this profile are all modifiable, which is promising for integrating COP location feedback into comprehensive treatment programs for those who have a lateral COP at baseline. Previous literature suggests that single items related to a sense of instability on commonly used patient reported outcomes in people with CAI may also be worth investigating. This profile of individuals who may be more likely to respond to COP location feedback could be very effective because it addresses as least one component each category of impairment in CAI (Pathomechanical: range of motion limitations, sensory-perceptual: proprioception and possible changes in sense of stability, and moto-behavioral: balance). Including multifactorial predictors in a model of who may best respond is important because gait included both sensory and motor control.

APPENDIX A: FSR DATA SHEET

INTERLINK ELECTRONICS®

Sensor Technologies

FSR 402 Data Sheet

FSR 400 Series Round Force Sensing Resistor

Description

Interlink Electronics FSR™ 400 series is part of the single zone Force Sensing Resistor™ family. Force Sensing Resistors, or FSRs, are robust polymer thick film (PTF) devices that exhibit a decrease in resistance with increase in force applied to the surface of the sensor. This force sensitivity is optimized for use in human touch control of electronic devices such as automotive electronics, medical systems, and in industrial and robotics applications.

The standard 402 sensor is a round sensor 18.28 mm in diameter. Custom sensors can be manufactured in sizes ranging from 5mm to over 600mm. Female connector and short tail versions can also be ordered.

Features and Benefits

- Actuation Force as low as 0.1N and sensitivity range to 10N.
- Easily customizable to a wide range of sizes
- Highly Repeatable Force Reading; As low as 2% of initial reading with repeatable actuation system
- Cost effective
- Ultra thin; 0.45mm
- Robust; up to 10M actuations
- Simple and easy to integrate

Industry Segments

- Game controllers
- Musical instruments
- Medical device controls
- Remote controls
- Navigation Electronics
- Industrial HMI
- Automotive Panels
- Consumer Electronics

Figure 1 - Force Curve

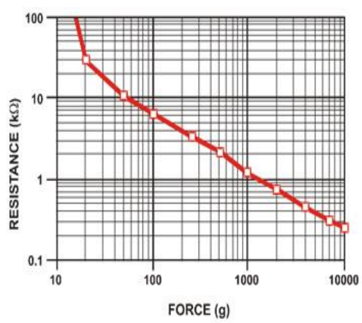
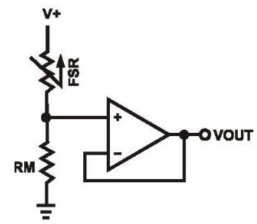


Figure 2 - Schematic



Interlink Electronics - Sensor Technologies

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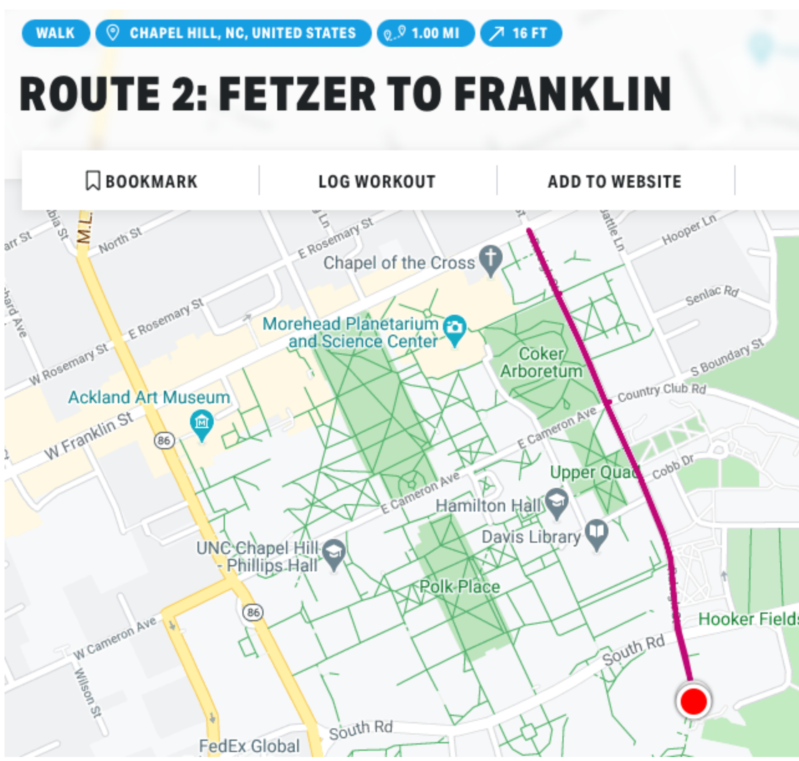
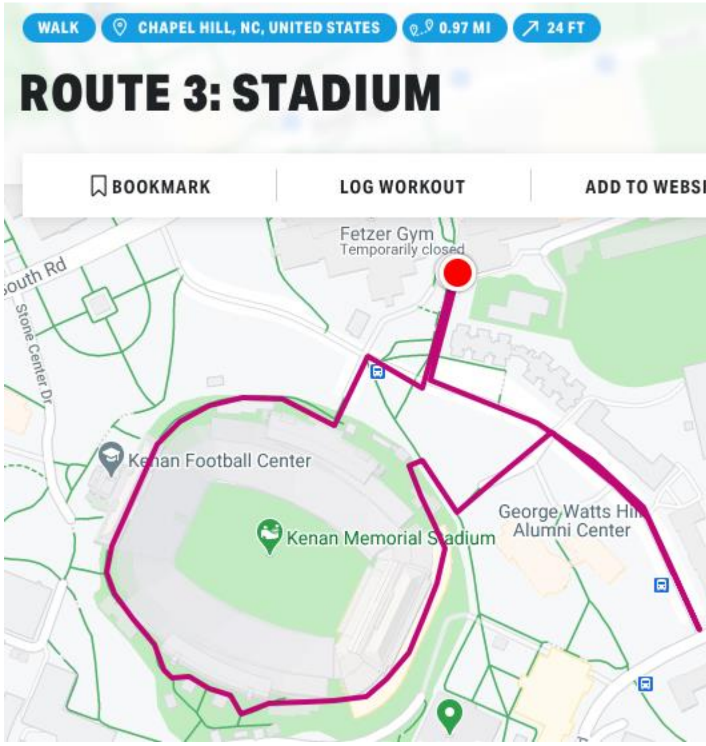
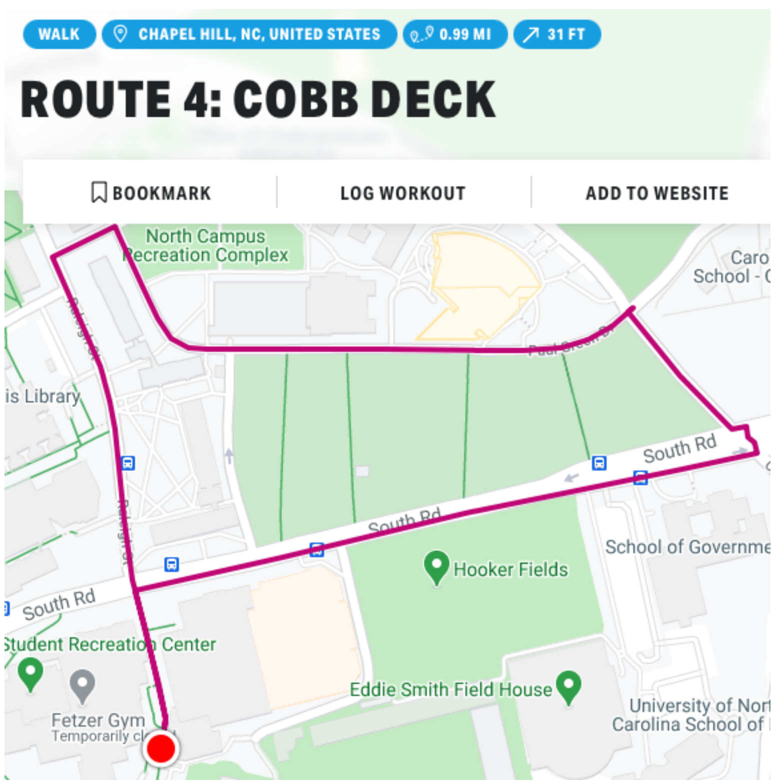
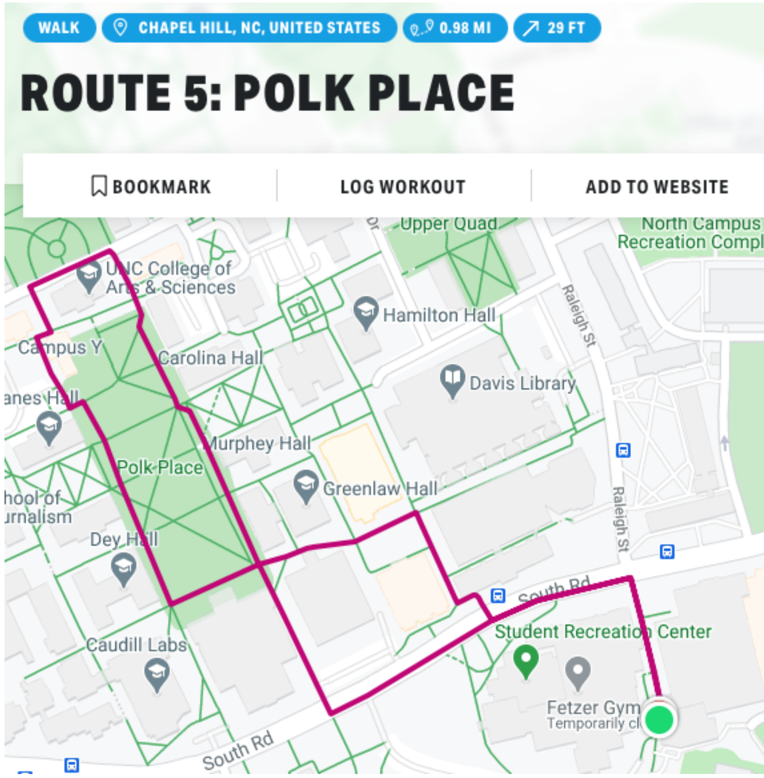
APPENDIX B: TRAINING ROUTES




WALK
CHAPEL HILL, NC, UNITED STATES
0.97 MI
24 FT
ROUTE 3: STADIUM
BOOKMARK
LOG WORKOUT
Fetzer Gym
Temporarily closed
Stone Center Dr
Kenan Football Center
Kenan Memorial Stadium
George Watts Hill
Alumni Center


WALK
CHAPEL HILL, NC, UNITED STATES
0.99 MI
31 FT
ROUTE 4: COBB DECK
BOOKMARK
LOG WORKOUT
ADD TO WEBSITE
North Campus
Recreation Complex
South Rd
South Rd
South Rd
Hooker Fields
School of Governme
Student Recreation Center
Eddie Smith Field House
Fetzer Gym
University of Nort
Carolina School of


WALK
CHAPEL HILL, NC, UNITED STATES
0.98 MI
29 FT
ROUTE 5: POLK PLACE
BOOKMARK
LOG WORKOUT
ADD TO WEBSITE
Upper Quad
North Campus
UNC College of Arts & Sciences
Hamilton Hall
Raleigh St
Campus Y
Carolina Hall
Davis Library
Murphey Hall
Polk Place
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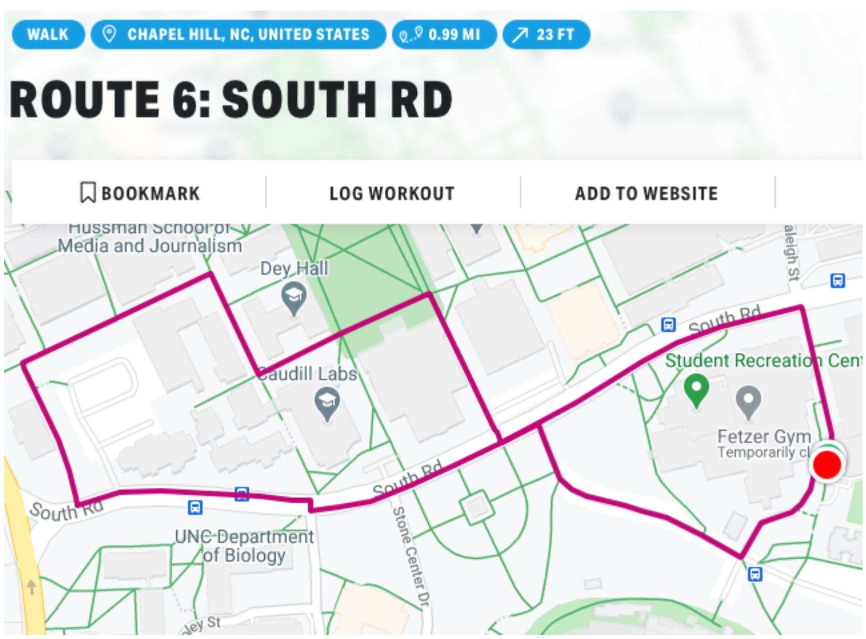
Dey Hall
South Rd
Student Recreation Center
Caudill Labs
Fetzer Gym
South Rd


WALK
CHAPEL HILL, NC, UNITED STATES
0.99 MI
23 FT
ROUTE 6: SOUTH RD
BOOKMARK
LOG WORKOUT
ADD TO WEBSITE
Media and Journalism
Dey Hall
South Rd
Caudill Labs
Fetzer Gym
South Rd
South Rd
UNC Department of Biology
Stone Center Dr

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