A Dissertation

entitled

An Examination of Sensorimotor and Mechanical Factors Contributing to Posttraumatic Ankle Instability

by

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Context: Posttraumatic ankle instability (PAI) is likely a multifactorial condition that results from mechanical and sensorimotor insufficiencies. Recent research has focused on identifying specific factors that make the greatest contribution to the development of PAI, thereby helping elucidate the underlying causes of PAI. However, a limited understanding of this complex pathology still exists because of conflicting results. Using more homogenous cohorts of participants with PAI could help facilitate the identification of and treatment for specific sources of self-reported disability, perceived instability, and recurrent ankle sprains in patients with PAI. Objective: The primary aim for the current study was to determine whether sensorimotor and mechanical variables differ among homogenous groups of participants with PAI established based on the presence of self-reported instability, repeated episodes of “giving-way,” and recurrent ankle sprains. The secondary aim was to identify specific mechanical and sensorimotor factors that would most strongly associate with the major clinical symptoms. Design: A single-blinded, case control. Setting: Research laboratory. Patients or Other Participants: A total 87 participants volunteered for this current study and were
allocated to the five participant groups (recurrent ankle sprains with perceive instability [RAS-PI], recurrent ankle sprainers [RAS], functional ankle instability [FAI], ankle sprain copers, and healthy controls). Twenty-four participants with RAS-PI (14M, 10F; 22.54+4.05yrs; 171.56+8.83cm; 76.38+15.06kg), 11 participants with RAS (5M, 6F; 22.27+4.98yrs; 169.68+9.62cm; 74.35+22.55kg), 12 participants with FAI (4M, 8F; 20.83+1.59yrs; 165.76+6.54cm; 65.67+11.77kg), and 16 ankle sprain copers (6M, 10F; 21.06+3.45yrs; 167.76+11.57cm; 73.00+17.92kg) were compared to 24 healthy control participants (9M, 15F; 21.54+3.30yrs; 166.82 +7.82cm; 67.28+13.49kg). **Methods:** Measures of sensorimotor and mechanical outcomes were conducted. **Main Outcomes:** Sensorimotor outcome measures included 1) spinal reflex excitability assessed with the $H_{\text{max}}: M_{\text{max}}$ ratio calculated from the maximal Hoffman (H)-reflex and muscle-response, 2) the amount of efferent nerve impulses traveling in the alpha motoneuron assessed with the V-wave and maximal muscle –response ($V: M_{\text{max}}$ ratio), 3) corticospinal excitability assessed using the transcranial magnetic stimulation for active motor threshold (AMT) and cortical silent period (CSP), 4) static postural control assessed with center of pressure velocity (COPV) and time-to-boundary (TTB) measures, 5) dynamic postural control assessed with the star excursion balance test in the anterior reach direction (SEBT-A), and movement variability during gait assessed with approximate entropy (ApEn). Mechanical outcome measures included 1) ankle joint laxity measured as displacements in the anterior-posterior directions (mm) and rotation in the eversion-inversion directions (degrees) using ankle arthrometer, 2) weight bearing ankle dorsiflexion range of motion (DF-ROM) using the weight bearing lunge test (WBLT) (cm), and 3) non-weight bearing DF-ROM using a bubble inclinometer (degrees). **Statistical Analyses:** Aim 1: A separate
independent samples Kruskal-Wallis test was used to examine the difference for each outcome variable that was not normally distributed. For sensorimotor outcome variables that were found to be normally distributed, one-way ANOVAs were performed to examine differences between groups. For each mechanical outcome variable, a separate ANCOVA was used to examine difference between groups (covariate=sex). Fisher’s LSD post-hoc or a Mann-Whitney U test was used in the event of statistical significance. Cohen’s d effect sizes with associated 95% confidence intervals (CI) were calculated using the pooled standard deviations. 

Aim 2: The discriminant functional analysis (DFA) was used to investigate the contribution of each significant factor on the determination of group membership. An A priori alpha level was set at $P < 0.05$ using SPSS 21.0 (SPSS, Inc. Chicago, IL.) for Windows for all statistical tests. 

**Results:** 

Aim 1: Spinal reflex excitability ($H_{max}$: $M_{max}$ ratio) was diminished in participants with RAS-PI and FAI compared to those with RAS, ankle sprain copers and healthy controls participants ($F_4, 86=2.643$, $P =0.039$). The $V$: $M_{max}$ ratio did not differ among the groups ($H_4 = 9.069$, $P = 0.059$). However, moderate effect sizes were found for $V$: $M_{max}$ ratio between the RAS-PI and ankle sprain coper groups ($d=-0.79$). For static postural control, the RAS-PI group demonstrated higher COPV in the anteroposterior (AP) ($H_4 = 14.574$, $P = 0.006$) and in the mediolateral (ML) ($H_4 = 10.542$, $P = 0.032$) directions compared to the control and coper groups. For the TTB measures of static postural control, no differences were observed among the groups ($p > 0.05$). However, effect size analysis revealed that the RAS-PI group had lower mean TTB-ML ($d = -0.77$) and SD of TTB-ML ($d = -0.82$) compared to the control group. No significant results were observed for other sensorimotor and mechanical outcome measures ($P > 0.05$). 

Aim 2: Neural excitability
and static postural control measures correctly classified 45.83% of participants with RAS-PI (Wilk’s $\lambda = 0.578$, $\chi^2_{24} = 44.194$, $P = 0.007$). **Conclusion:** Decreased spinal reflex excitability of the soleus and impaired static postural control were observed in participants with PAI. Neural excitability and static postural control measures were shown to be the most influential factors of the selected outcome measures in this study to classify group memberships. The results may lead to therapeutic interventions that target decreased spinal reflex excitability and static postural control to improve clinical outcomes for PAI.
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<tr>
<td>ACL</td>
<td>Anterior Cruciate Ligament</td>
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<tr>
<td>ADL</td>
<td>Activities of Daily Living</td>
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<tr>
<td>AII</td>
<td>Ankle Instability Instrument</td>
</tr>
<tr>
<td>AMT</td>
<td>Active Motor Threshold</td>
</tr>
<tr>
<td>AP</td>
<td>Anteroposterior</td>
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<tr>
<td>ApEn</td>
<td>Approximate Entropy</td>
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<td>ATSF</td>
<td>Anterior Tibial Shear Force</td>
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<tr>
<td>CAI</td>
<td>Chronic Ankle Instability</td>
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<tr>
<td>CNS</td>
<td>Central Nervous System</td>
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<tr>
<td>COP</td>
<td>Center of Pressure</td>
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<tr>
<td>COPV</td>
<td>Center of Pressure Velocity</td>
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<tr>
<td>CV</td>
<td>Coefficient of Variation</td>
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<tr>
<td>DFA</td>
<td>Discriminant Functional Analysis</td>
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<tr>
<td>DF-ROM</td>
<td>Dorsiflexion Range of Motion</td>
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<tr>
<td>FAAM</td>
<td>Foot and Ankle Ability Measure</td>
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<tr>
<td>FAI</td>
<td>Functional Ankle Instability</td>
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<tr>
<td>EMG</td>
<td>Electromyography</td>
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<tr>
<td>GRF</td>
<td>Ground Reaction Force</td>
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<tr>
<td>H-reflex</td>
<td>Hoffman Reflex</td>
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<tr>
<td>IC</td>
<td>Initial Foot Contact with Ground</td>
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<tr>
<td>I-E</td>
<td>Inversion-Eversion</td>
</tr>
<tr>
<td>IdFAI</td>
<td>Identification of Functional Ankle Instability</td>
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<tr>
<td>MAI</td>
<td>Mechanical Ankle Instability</td>
</tr>
<tr>
<td>MAI</td>
<td>Motor Evoke Potential</td>
</tr>
<tr>
<td>ML</td>
<td>Mediolateral</td>
</tr>
<tr>
<td>NWB</td>
<td>Non-Weight Bearing</td>
</tr>
<tr>
<td>NWB-DF</td>
<td>Non-Weight Bearing Dorsiflexion</td>
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</tbody>
</table>
OA..........................Osteoarthritis
OKC-DF.....................open kinetic chain dorsiflexion

PAI..........................Posttraumatic Ankle Instability
PCA..........................Principal Component Scores
PRSII.........................Psychological Response to Sport Injury Inventory

RAS..........................Recurrent Ankle Sprains
RAS-PI.........................Recurrent Ankle Sprains with Perceived Instability

SD .........................Standard Deviation
SEBT-A.........................Star Excursion Balance Test in the Anterior Reach Direction
SF-36..........................Short Form-36

TMS .........................Transcranial Magnetic Stimulation
TTB .........................Time-to-Boundary
TTS .........................Time-to Stabilization

WB ..........................Weight Bearing
WB-DF........................Weight Bearing Dorsiflexion
WBLT .........................Weight Bearing Lunge Test
Chapter 1

Introduction

Participation in sports has an important role in a healthy lifestyle. However, it is associated with an inherent risk of injury. An ankle sprain represents one of the most common injuries in sports and everyday life,\(^1\)-\(^3\) resulting in an annual health care cost approximating $3.8 billion\(^4\) and many long-term complications.\(^5\)-\(^8\) Despite the attention and focus ankle sprains receive, it has been reported that up to 74% of individuals who experience an ankle sprain suffer from some type of residual symptoms, perceived instability (repeated episodes of “giving-way”), recurrent ankle sprains, and/or self-assessed disability,\(^5\),\(^6\),\(^8\) which may be termed as chronic ankle instability (CAI). However, the term of CAI is not necessary to indicate ankle instability following traumatic ankle sprains. Individuals with general joint laxity at the ankle could suffer chronic ankle instability. Posttraumatic ankle instability (PAI) may be better suited than CAI for referring to this ankle pathology.

The presence of PAI decreases activity levels,\(^6\),\(^7\) limits occupational involvements,\(^7\),\(^8\) and adversely impacts quality of life,\(^5\),\(^9\) as well as develops an early onset of degenerative pathology in the ankle,\(^10\),\(^11\) requiring costly medical diagnostic techniques and extensive treatments. Therefore, PAI is a significant public health concern.
in the physically active population and an economic burden of the global health care systems. With increasing government and societal emphasis on physical activity, the incidence of PAI would remain constant or increase as more individuals participate in physical activities. Researchers and clinicians must work together to minimize complications of PAI to maximize the potential health benefits of a physically active lifestyle.

Posttraumatic ankle instability is likely a multifactorial condition that results from mechanical and sensorimotor insufficiencies.\textsuperscript{12-15} Recent research has focused on identifying specific factors that make the greatest contribution to the development of PAI, thereby helping elucidate the underlying causes of PAI. However, a limited understanding of this complex pathology still exists because of conflicting results\textsuperscript{13,16-33} with similar outcome measures. Most of the investigation in this area has ignored that PAI is a heterogeneous ankle pathology that consists of several homogenous subgroups.\textsuperscript{32,34} Some of the current inconsistencies in sensorimotor and mechanical outcomes between participants with and without PAI may be explained by the lack of utilization of more homogenous subgroups of this complex pathology.\textsuperscript{32,35}

Posttraumatic ankle instability has classically been categorized by two subgroups based on the presence of mechanical (MAI) and functional (FAI) ankle instability.\textsuperscript{15} Recent investigations have considered differences in movement patterns during functional tasks between participants with MAI and FAI.\textsuperscript{36-40} However, the inclusion criteria of participants with MAI did not truly represent a homogenous group of PAI in these studies. Participants with MAI were required to report repeated episodes of “giving-way” and complaints of ankle instability secondary to the initial sprain, suggesting that
MAI is likely associated with deficits in patient perception-oriented measures. Our preliminary data and previously published data investing similar outcome measures of ankle laxity indicate that mechanical ankle laxity is likely present in individuals who have a previous history of ankle sprain but have returned to high-level physical activities without any major clinical symptoms. Furthermore, the relation between mechanical ankle laxity and the levels of self-reported disability has been explored, suggesting that mechanical ankle laxity should be considered as a potential factor contributing to the major clinical symptoms of PAI, instead of a criterion for differentiation between subcategories of PAI. Participants typically have been included in PAI study groups if they report all major clinical symptoms of PAI, including self-reported disability, perception of instability, and recurrent ankle sprains. However, all cases of PAI do not arise from the same condition. Specifically, some patients with PAI may suffer recurrent sprains but have neither perception of instability nor self-reported impairments.

Separating this ankle pathology into subgroups based on the number of ankle sprains, repeated episodes of "giving-way," and the presence of perceived instability may create more homogenous cohorts of participants with PAI. Using more homogenous cohorts of participants with PAI could help facilitate the identification of and treatment for specific sources of self-reported disability, perceived instability, and recurrent ankle sprains in patients with PAI. Therefore, we propose four subgroups of PAI: 1) patients with recurrent ankle sprains with perceived ankle instability that suffer all major clinical symptoms (RAS-PI); 2) patients with FAI that have perceived instability and self-reported impairments but do not suffer recurrent ankle sprains; 3) patients with recurrent ankle sprains that suffer recurrent ankle sprains but have neither repeated episodes of
“giving-way” nor self-reported impairments (RAS); and 4) ankle sprain copers that have a history of a lateral ankle sprain and return to high-level activities without any major clinical symptoms of PAI.

Our long-term goal is to reduce the occurrence and disability associated with PAI. An important step towards this long-term goal is to understand mechanisms that may cause self-reported impairments, recurrent ankle sprains, and perceived instability in patients with PAI, thereby providing valuable information to identify specific targets on which clinicians could focus for interventions of PAI. The overall objective of this study was to identify specific sensorimotor and mechanical factors that would characterize homogenous groups of participants with PAI established based on the presence of self-reported impairment, perception of instability, and/or recurrent ankle sprains. Our central hypothesis was that sensorimotor variables would represent the strongest factors that associate with PAI, and mechanical variables would not provide strong distinction between PAI and healthy participants. The rationale for this project was that: (1) using a heterogeneous population with PAI limits our understanding of what constitutes the development of PAI (AIM 1); and (2) the causes of self-reported impairments and recurrent ankle sprains associated with PAI are multifactorial (AIM 2).

1.1 Specific Aims and Hypotheses

To test the central hypothesis, the following specific aims were addressed:

**AIM 1:** Determine whether sensorimotor and mechanical variables differ among homogenous subgroups of participants with PAI, established by the presence of self-
reported instability, recurrent ankle sprains, and/or repeated episodes of “giving-way” compared to those without PAI.

**Hypothesis 1:** Participants with PAI, who suffer all of the identified characteristics (repeated episodes of “giving-way,” self-reported instability, and recurrent ankle sprains) would exhibit differences in sensorimotor variables compared to other subgroups of PAI and those without PAI. Mechanical outcome measures would be not significantly different between subgroups of PAI and the control group.

Sensorimotor variables included spinal and corticospinal excitability of the soleus muscle, the level of descending efferent motoneuron output to the soleus during maximal muscle contraction, static balance with eyes-closed, dynamic balance assessed by the star excursion balance test (SEBT), and lower extremity joint variability during walking. Mechanical variables included ankle-subtalar-joint laxity and ankle dorsiflexion range of motion (DF-ROM) in both weight-bearing (WB) and non-weight-bearing (NWB) positions.

**AIM 2:** Determine the combination of sensorimotor and mechanical variables that would most strongly link to the major clinical symptoms (self-reported impairments, repeated episodes of “giving-way,” and recurrent ankle sprains) in patients with PAI.

**Hypothesis 2:** Sensorimotor-based outcome measures would have the greatest contribution to PAI, as well as discriminate best between participants with and without PAI.

### 1.2 Significance
Patient-oriented outcome measures have been emphasized in health care.\(^{44}\) Specific to the ankle, patient-oriented measures provide valuable information on how the patient experiences disability due to PAI. Despite the determination of effectiveness of treatment, and the shifting of rehabilitation interventions from clinical and laboratory-oriented outcome measures to more patient-centered ones, it is crucially important to determine what the origins of patient-reported impairments due to PAI are, and how altered sensorimotor and mechanical functions contribute to these impairments that are present following ankle injury.

Various mechanical and sensorimotor measures have been used to distinguish between participants with and without PAI, suggesting the causal mechanism of PAI is multifactorial.\(^{12-14}\) Clinical interventions to address impairments and disability associated with PAI cannot be adequately prescribed without understanding how these factors contribute to the development of PAI. Currently, it remains unknown which mechanical and sensorimotor factors are most strongly associated with the major clinical symptoms in patients with PAI, including self-reported instability, repeated episodes of “giving-way,” and recurrent ankle sprains,\(^ {35}\) and how the deficits interact with each other. Identifying specific factors that make the greatest contribution to PAI clearly helps clinicians determine what factor(s) need addressing to produce the best treatment outcome for patients with PAI. This research was significant because it would: (1) provide important direction toward elucidating the underlying mechanisms of PAI; (2) provide a foundation for continued work to develop the most effective intervention program for PAI; and (3) help to focus future research on variables known to best influence the occurrence of recurrent ankle sprains and self-reported status of patients.
with PAI. This study was a critical step towards our overall goal of preventing disability, improving general health-related quality of life, and increasing activity levels in the physically active population that has suffered an ankle sprain.

1.3 Anticipated Outcomes

**Aim 1:** we expected that PAI participants who suffer all of the identified major clinical symptoms (episodes of “giving-way, self-reported instability, and recurrent ankle sprains) would demonstrate significantly: 1) diminished static and dynamic postural control; 2) diminished efferent neural drive from spinal alpha motoneuron and supraspinal pathways in the soleus muscle (smaller ratio of maximum V-wave to maximum Muscle response compared to the copers subgroups of PAI and healthy controls); 3) less corticospinal excitability (larger active motor threshold and longer cortical silent period compared to the copers subgroups of PAI and healthy controls); and 4) decreased gait variability (less approximate entropy values) compared to the copers subgroups of PAI and healthy controls, indicating deficits in sensorimotor functions.

Secondarily in this aim, we hypothesized that mechanical outcome measures would not be significantly different between subgroups of PAI and the control group. It has been shown previously, that mechanical ankle laxity and ankle hypomobility could coexist following a lateral ankle sprain. Additionally, it has been reported that both mechanical ankle laxity and restricted ankle DF-ROM in the ankle is strongly associated with the perception of instability and functional impairments. We anticipated no differences in measurements of ankle laxity and DF-ROM among subgroups of participants with PAI and those without PAI.
**Aim 2**: Our preliminary study performed discriminant function analysis using dynamic postural control measured by the SEBT, ankle sagittal-plane torque production measures, and ankle laxity measures. Our preliminary data showed measures of dynamic postural control could classify participants with PAI across a wide range of disability, supporting our hypothesis for this aim. Measures of dynamic postural control using the SEBT provided a clinical assessment of sensorimotor deficits that may be present in patients with PAI, and we believed that altered sensorimotor function likely leads to the clinical impairments that patients with PAI have. Therefore, we expected the presence of PAI would have the strongest association with sensorimotor dysfunction.

**Implications of Data to the Future**: This study would serve as proof of concept for identifying specific contributing factors to the major clinical symptoms and impairments of PAI. We anticipated that establishing specific sensorimotor and mechanical contributions to self-reported impairments, perceived instability and recurrent ankle sprain associated with PAI would direct clinicians and future studies at how best to treat PAI, leading to an increase in quality of life and activity level as well as a possible reduction in the incidence of posttraumatic ankle osteoarthritis (OA). Additionally, we expected this information to be the next logical and critical step in prospectively examining the specific contributing factors to explore the time course of the development of PAI. Lastly, we anticipated that our findings would lead to the improvement of prevention strategies for PAI following an initial ankle sprain by developing more effective treatments and rehabilitation that target these specific factors contributing to the major clinical symptoms and impairments associated with PAI.
Chapter 2

Literature Review

The ankle is the most common injury site, with accounting for 11.85% of all self-reported musculoskeletal injuries. Ankle sprain is the most common ankle injury in youth and young adults participating in physical activity. More than 600,000 patients with ankle ligamentous sprains are treated in emergency departments annually in the U.S. Nearly half (53.5%) of all ankle sprains occurred in young populations between the ages of 10 and 24 years, and 49.3% of these sprains occurred during athletic activities. Although the incidence of ankle sprains presenting in hospital emergency department was only between 2.06 and 7.00 per 1000 person/year, the reported emergency department rate for all sports related ankle sprains was only 0.02 per 1000 person/year. These epidemiological reports for an ankle sprain do not include individuals who present in other ambulatory and acute management settings, and it is possible that the incidence rate of ankle sprains would increase with recording data from all health care settings.

Participation in sports has an important role in a healthy lifestyle. However, it is associated with an inherent risk of injury. An ankle sprain was the major specific musculoskeletal injury documented in 33 of 44 sports and accounts for 15% to 44% of all injuries in physically active populations, with 42% to 70% of physical active...
individuals having a history of at least one ankle sprain. In the high school setting, the ankle is the most common location of these lower extremity injuries, with most ankle injuries diagnosed as ligament sprains. Additionally, the ankle is the most common site of recurrent injury in high school athletes. In collegiate athletes, ankle ligamentous sprains accounted for 15% of all injuries in the 15 sports over a 16 year period. With increasing government and society emphasis on physical activity, the number of ankle sprains will remain constant or increase as more individuals participate in physical activities.

An ankle sprain can require costly medical diagnostic techniques and extensive treatments resulting in time loss from sports participation and many long-term complications. It has been reported that 32% to 74% of individuals with a previous history of ankle sprain suffered from some type of residual and chronic symptoms, recurrent ankle sprains, and/or perceived instability, which is often referred to as chronic ankle instability (CAI). However, the term of CAI is not necessary to indicate ankle instability following traumatic ankle sprains. Individuals with general joint laxity at the ankle could suffer chronic ankle instability. Posttraumatic ankle instability (PAI) may be better suited than CAI for referring this ankle pathology. Previous evidence illustrates that the presence of PAI leads to a decrease in activity levels and is a leading cause of posttraumatic osteoarthritis in the ankle. Fifteen to 64% of those with a history of an ankle sprain did not fully recover their function from the initial ankle sprain within three years, and 17.5% of those had residual symptoms persisting for more than 10 years after the injury. Furthermore, individuals that suffered from residual symptoms and perceived ankle instability following an acute ankle sprain reported lower general health quality of
life and more functional limitations compared to those with upper extremity joint injuries\textsuperscript{5} or without PAI.\textsuperscript{9} Therefore, an ankle sprain is a significant public health concern in the physically active population.

As participation in high school and collegiate sports continues to grow with proportional increases in recurrent ankle injury, there is an increased need to develop more effective intervention programs and preventive measures for reducing the occurrence and recurrence of ankle injury. Important steps toward these goals are to (1) understand the injury mechanism of an acute ankle sprain, (2) identify the risk factors of an ankle sprain, (3) understand the sensorimotor consequence of PAI, and (4) identify the origin of impairments associated with PAI. Therefore, this review examines the causes of ankle sprains and the resultant sensorimotor consequence of PAI.

2.1 Causes of Ankle Sprains

2.1.1 Injury Mechanisms

Establishing the injury mechanisms of ankle sprains is a critical step in the sequence of clinical research. The mechanism of a lateral ankle sprain is traditionally described as excessive plantarflexion, inversion, and internal rotation of the rearfoot, coupled with external rotation of the lower leg.\textsuperscript{15} Biomechanical studies support that increased plantarflexion coupled with inversion and internal rotation of the ankle at initial foot contact (IC) increases the likelihood of suffering a lateral ankle sprain and increases the mechanical strain of the anterior talofibular ligament.\textsuperscript{62} However, these findings were based on a computer simulation model and do not necessarily indicate injury mechanism of an actual ankle sprain incidence case.
While the clinical qualitative injury mechanism of an ankle sprain has been reported as plantar flexion at the talocrural joint with adduction and inversion at the subtalar joint, recent case reports using 3-dimensional (3D) biomechanical data of actual ankle sprain incidences during several functional tasks suggest that the possible injury mechanism to cause an ankle sprain may not be only plantar flexion but also a sudden increase in lateral excursion of COP, ankle inversion, and ankle internal rotation.

Table 2.1 shows a summary of the case reports, and Table 2.2 provides 3D biomechanical data of the actual ankle sprain incidences. However, there are little investigations that prospectively have examined 3D biomechanics during functional tasks, which may be the most predictive of ankle sprain risk. Therefore, it is still unknown whether excessive inversion and internal rotation of the ankle are the causes or the consequences of an ankle sprain mechanism. Future study should consider this information on injury mechanism and prospectively examine 3-D human movement patterns during functional tasks to identify intrinsic risk factors for ankle sprains that may be modifiable.

**Table 2.1 Biomechanical data of each ankle sprain case**

<table>
<thead>
<tr>
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<tbody>
<tr>
<td></td>
<td>Case 1</td>
<td>Case 2</td>
<td>Case 1</td>
<td>Case2</td>
</tr>
<tr>
<td>Peak</td>
<td>142</td>
<td>78</td>
<td>48</td>
<td>23*</td>
</tr>
<tr>
<td>Time to peak</td>
<td>80</td>
<td>80</td>
<td>200</td>
<td>138 (Joint moment)</td>
</tr>
<tr>
<td>Kinetics</td>
<td>-</td>
<td>-</td>
<td>79</td>
<td>-</td>
</tr>
<tr>
<td>Dorsiflexion*</td>
<td>7</td>
<td>13</td>
<td>18</td>
<td>22*</td>
</tr>
<tr>
<td>Internal rotation^</td>
<td>Kinematics</td>
<td>37</td>
<td>27</td>
<td>10</td>
</tr>
</tbody>
</table>

Time to peak values are expressed in msec. Joint moment values are expressed in Nm. * Kinematic values are reported at the time point of peak ankle inversion. ^ Kinematic values are reported at the time point of peak ankle inversion moment. Negative values indicate plantarflexion.
Another critical step in the sequence of establishing the causes of ankle sprains is to obtain information on why a particular individual may be at risk for ankle sprains in a given situation. Determining the primary intrinsic risk factors for lateral ankle sprains may assist clinicians and researchers to develop more effective prevention programs, which in turn may decrease the occurrence and recurrence of an ankle injury.

Previous prospective studies\textsuperscript{71-87} have identified multiple potential risk factors that would make an individual more likely to sprain their ankle or suffer from repeated ankle sprains. While the results of these studies seem divergent and inconclusive (Table 2.3), a
previous history of an ankle sprain is consistently reported as the largest contributing factors that will place individuals at a greater risk for future ankle sprains.\textsuperscript{76-79,83,86-88} 

More specifically, it is documented that individuals with a history of an ankle sprain were two to five times more likely to sustain subsequent ankle sprains.\textsuperscript{76-78,83} 

Currently, it is unclear why individuals with a previous history of ankle sprains may go on to suffer subsequent injury. Furthermore, post-traumatic ankle instability receives abundant attention and focus in clinical practice and research; however, it persists as the most common recurrent injury in the physically active population.\textsuperscript{5,58} The re-injury and secondary or chronic injury following an initial acute injury can be preventable by developing effective intervention strategies for the acute first-time injury. Therefore, it is important for future prospective studies to provide an explanation for the higher injury rate associated with a history of an ankle sprain. 

Lastly, the assessments of static and dynamic postural control have been used in an attempt to predict ankle sprain risk\textsuperscript{84,89} and to identify sensorimotor deficits following ankle sprains\textsuperscript{33,90-94} that may place individuals at a greater risk for PAI. Static postural control is clearly impaired following lateral ankle sprains,\textsuperscript{32,33,90-94} and poor static postural control is likely associated with an increased risk of sustaining ankle sprains.\textsuperscript{52,57} However, some predictive findings were inconsistent with the measures of static postural control during a single-limb stance using center of pressure (COP).\textsuperscript{71,72,87} The task of static single-limb stance may not be challenging enough to elucidate differences in postural control between individuals who did or did not suffer an ankle sprain. The star excursion balance test (SEBT) has been developed as a simple and inexpensive injury screening tool to predict the risk of ankle injury in athletic population by assessing global
dynamic postural control. The poor SEBT performance was strongly predictive of an ankle sprain. However, there is little evidence that provides specific information about what factor(s) influence the SEBT performance and why poor SEBT performance increase a risk for ankle sprains. Therefore, further prospective investigation is needed to establish which modifiable factors that make the greatest contribution to the SEBT performance in individuals with a history of an ankle sprain can predict ankle sprains.

2.2 Sensorimotor Consequence of PAI

2.2.1 Principals Sensorimotor Control

Before discussing the sensorimotor consequence of PAI, it is important for the beginning of this section to understand principals of sensorimotor control. In general, optimal motor performance is achieved through two classes of control in the sensorimotor system: (1) predictive or feed-forward control and (2) reactive or feedback control. Feed-forward control refers to planning actions that occur prior to the event and modify the action of the control systems before the actions take place through predicting the sensory consequence, and anticipating environmental variables with previous experiences and combing inputs from multiple sensory sources together. In contrast feedback control involves the use of sensory inputs from somatosensory, visual, and vestibular systems to update ongoing motor commands.

The sensorimotor system sets up feedback controllers that convert sensory information into motor commands. However, the feedback system cannot be used to
Table 2.3 Summary of studies that investigated risk factors for an ankle sprain.

<table>
<thead>
<tr>
<th>Study</th>
<th>Study design</th>
<th>Participants</th>
<th>Outcomes measured</th>
<th>Main risk factors identified</th>
<th>Follow-ups/duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hiller et al.</td>
<td>Prospective</td>
<td>115 adolescent dancers (94 girls/21 boys, 12-16 y old.)</td>
<td>Ankle sprain, y dancing, hick dancing, flexibility, balance, external hip rotation, foot and 1st metatarsal phalanges ROM, ankle instability, age, inversion recovery</td>
<td>Previous sprain of contralateral ankle (hazard ratio = 3.90, CI 1.49-10.22).</td>
<td>13 months (98.9% follow-up rate)</td>
</tr>
</tbody>
</table>
| McHugh et al.  | Prospective  | 189 high school athletes (68 girls/101 boys, 14-18 y old); football, basketball, soccer, or gymnastics | Previous ankle injury, hip strength, balance ability, brace/tape, no support, sex, BMI | (1) Previous hx of ankle sprain  
(2) Combination of a male being overweight with a hx of previous sprain makes them 9.6 times more likely to experience a sprain than athletes with no previous ankle sprain and of normal weight. | 24 months (100% follow-up rate for 1st year and 52% for 2nd year) |
| Kofotolis et al. | Descriptive   | 336 male amateur soccer athletes (20-29 y old). | Previous ankle injury, Contact/noncontact, Game/practice, time of sport season, time during competition, player position, age, BMI, height | (1) Previous hx of ankle sprain (odds ratio = 1.83, CI 1.46-2.29).  
(2) Contact-noncontact  
(Neither age, body mass, nor height was a risk factor) | 24 months (92.9% follow-up rate) |
| Baumbauer et al. | Prospective  | 145 college athletes (72 female/73 male. 18-23 y old); lacrosse, soccer, or field hockey | Ankle sprain, generalized joint laxity, anatomical foot and ankle alignment, ankle ligament stability, and isokinetic strength | (1) Greater eversion-to-inversion strength ratio,  
(2) Greater PF strength  
(3) Smaller DF-to PF ratio.  
(Previous hx was not a risk factor) | One season |
| Beynon et al.  | Prospective  | 901 high school college athletes (293 male/382 female); soccer, basketball, lacrosse, field hockey | Sex, level of competition, and sport | Sex and sports (women's basketball: relative risk=4.11) | 5 years |
| Fousekis et al. | Prospective  | 100 professional soccer players (23.6±4.2 y old) | Ankle joint asymmetries in isokinetic muscle strength, flexibility, proprioception, stability; BMI, BFMI, somatometric asymmetries, previous injuries, lateral dominance traits | (1) Eccentric isokinetic ankle sagittal plane strength asymmetries (odds ratio = 8.88)  
(2) Increased body mass index (OR = 8.16)  
(3) Increased body weight (OR = 5.72) | 10 months |
Table 2. 3 Cont’d

<table>
<thead>
<tr>
<th>Study</th>
<th>Study design</th>
<th>Participants</th>
<th>Outcomes measured</th>
<th>Main risk factors identified</th>
<th>Follow-ups/duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>de Noronha et al. 2012</td>
<td>Prospective</td>
<td>121 college students (64 females/57 males, 20.9 ± 2.7 y old)</td>
<td>CAIT, the foot lift test, DF-ROM, SEBT, the side recognition task, BMI, hx of previous sprain</td>
<td>(1) hx of previous sprain (hazard ratio = 2.21) (2) The SEBT in the anterolateral direction (hazard ratio = 0.96, 95% CI 0.92–0.99).</td>
<td>12 months (96.8% follow-up rate)</td>
</tr>
<tr>
<td>Tyler et al. 2006</td>
<td>Prospective</td>
<td>152 high school football players</td>
<td>BMI, BM, height, previous hx of ankle sprain, using ankle brace or tape</td>
<td>(1) Previous hx of ankle sprain (2) Higher BMI</td>
<td>1 or 3 seasons</td>
</tr>
<tr>
<td>Willems et al. 2005</td>
<td>Prospective</td>
<td>241 male PE college students (17-28 y old)</td>
<td>Anthropometric characteristics, functional motor performance, ankle joint position sense, isokinetic ankle muscle strength, lower leg alignment characteristics, postural control, and muscle reaction time during a sudden inversion perturbation</td>
<td>(1) Slower running speed (2) Less cardiorespiratory endurance (3) Less balance (4) Decreased DF muscle strength and ROM (5) Less coordination (6) Faster reaction of the tibialis anterior and gastrocnemius muscles</td>
<td>12-36 months</td>
</tr>
<tr>
<td>Willems et al. 2005</td>
<td>Prospective</td>
<td>159 female PE college students (17-26 y old)</td>
<td>Anthropometric characteristics, functional motor performance, ankle joint position sense, isokinetic ankle muscle strength, lower leg alignment characteristics, postural control, and muscle reaction time during a sudden inversion perturbation</td>
<td>(1) Less accurate passive joint inversion position sense (hazard ratio = 1.08) (2) A higher extension ROM at the 1st MTPJ (hazard ratio = 1.03) (3) Less coordination of postural control (hazard ratio = 0.94-0.96)</td>
<td>12-36 months</td>
</tr>
<tr>
<td>Willems et al. 2005</td>
<td>Prospective</td>
<td>223 PE college students</td>
<td>3D gait kinematics, Plantar pressure variables</td>
<td>(1) a longer total foot contact time, (2) a higher loading underneath the medial and less loading underneath the lateral border of the foot, (3) a medially directed pressure distribution at 1st metatarsal contact, forefoot flat and heel off and less pressure displacements in the intervening phases, (4) a delayed knee flexion, (5) a more laterally directed pressure displacement in the forefoot push-off phase and a laterally deviated COP at last foot contact, and finally (6) a greater extension at the 1st MTPJ.</td>
<td>12-24 months</td>
</tr>
</tbody>
</table>
Table 2.3 Cont'd

<table>
<thead>
<tr>
<th>Study</th>
<th>Study design</th>
<th>Participants</th>
<th>Outcomes measured</th>
<th>Main risk factors identified</th>
<th>Follow-ups/duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whichall et al.</td>
<td>Systematic review/meta-analysis</td>
<td>13 published studies</td>
<td>strength, postural control, proprioception, muscle reaction time in response to perturbation, ROM, laxity</td>
<td>(1) Higher postural sway, (2) Lower postural stability (relative risk = 2.06), (3) Lower inversion proprioception, (4) Higher concentric PF strength at faster speeds (4) Lower eccentric eversion strength at slower speeds.</td>
<td>-</td>
</tr>
<tr>
<td>McGinley et al.</td>
<td>Randomized controlled clinical trial</td>
<td>763 high school soccer and basketball players (523 girls/242 boys)</td>
<td>-</td>
<td>(1) Athletes with a hx of an ankle sprain (risk ratio = 2.14) (2) Reduction in ankle sprain rate by 38%</td>
<td>-</td>
</tr>
<tr>
<td>Trojan and McKee</td>
<td>Prospective cohort study</td>
<td>230 high school football, soccer, and volleyball players (80 girls/150 boys)</td>
<td>Positive single leg balance test</td>
<td>(1) Positive single leg balance test (risk ratio = 2.54) (2) Positive single leg balance test without ankle taping (risk ratio = 8.82) (3) A hx of an ankle sprain is not risk factor</td>
<td>-</td>
</tr>
<tr>
<td>McGinley et al.</td>
<td>Prospective cohort study</td>
<td>210 (high school basketball players) (91 girls/119 boys with no hx of ankle and knee injury and who did not did not use prophylactic ankle taping or bracing during the season)</td>
<td>Postural sway (the average degrees of sway per second score (eyes-closed and-opened conditions), gender, leg dominance, BMI, and ankle sprain injury</td>
<td>Higher postural sway scores corresponded to increased ankle sprain injury rates</td>
<td>-</td>
</tr>
</tbody>
</table>

CAIT: Cumberland ankle instability tool, the foot lift test, DF: dorsiflexion, PF: Planter flexion, ROM: range of motion, SEBT: Star Excursion Balance Test, BMI (body mass index), hx: history, PE: Physical education, COP: Center of pressure, MTPJ: metatarsophalangeal joint
initiate the movement because the CNS receives the sensory information regarding the
movement after the completion of the movement.\textsuperscript{100,101} The conduction delays of the
monosyaptic stretch reflex pathway are on the order of 10-40ms, depending on the length
and type of nerve fiber, and this delay may increase by 20-30ms for the cortical
component of the long-latency stretch reflex response.\textsuperscript{102} The electromechanical delay for
the rise in the force generation within a muscle can take another 25 -72ms.\textsuperscript{103,104} Konradsen et al.\textsuperscript{104} reported that a dynamic protective reaction about the ankle from the
fibularis muscles would take at least 126ms to happen after inversion perturbation,
including 54ms for the reaction time of the initial EMG activity and 72ms of the
electromechanically delay needed to generate muscular force.

As a result of delayed or altered feedback responses, the sensorimotor system may
rely more on feed-forward control.\textsuperscript{98} The feed-forward control system can help the
sensorimotor system to take into account the motor commands to interpret sensory
responses.\textsuperscript{97} The feed-forward control system predicts the sensory consequence with
previous experiences and/or information from multiple sensory modalities (e.g., vision)
to estimate the outcome of an action optimally.\textsuperscript{97,99} A main role of the feed-forward
control is to counteract the effects of delays and noise in processing of afferent feedback
that cannot provide motor commands fast enough to correct responses following events.\textsuperscript{97}
Differences between expected and actual outcomes of motor action can be used in order
to modify future motor commands to correct errors as a motor learning process.\textsuperscript{99} The
sensorimotor system is capable of learning to produce optimal motor outputs under
various environments and circumstances.\textsuperscript{105,106}
Central commands for feedback and feed-forward adjustments originate at supraspinal levels.\textsuperscript{107} Information from afferent sources is integrated into the CNS via the dorsal lateral tracts or the spinocerebellar tract.\textsuperscript{96,108} While the dorsal lateral tracts transmit signals from sensory information to the somatosensory cortex in the cerebrum, the spinocerebellar tract terminates in the cerebellum where most nonconscious proprioceptive signals are processed and integrated.\textsuperscript{108} The cerebellum is an important region of the CNS for motor control, learning, and postural control, as it is responsible for the precise coordination of motor control, especially using nonconscious sources (proprioceptive, vestibular, visual, and auditory input).\textsuperscript{108} The cerebellum has been suggested as a regulatory system that modifies motor acts initiated by other regions of the CNS.\textsuperscript{109} While visual, vestibular, and sensorimotor information is integrated in the brainstem in addition to the cerebellum, the control of complex and voluntary movements lies primarily in the cerebral cortex.\textsuperscript{108} The spinocerebellar tract acts as a feedback control system through applying the corrections to integrating motor centers in the brainstem by using both ongoing and static proprioceptive information and taking information from ongoing motor commands.\textsuperscript{108} The cerebrocerebellar tract, which lies between the sensorimotor-motor cortex and the primary motor cortex, is arranged to act as a feed-forward control system through applying the corrections to the red nuclei and the primary motor cortex where the motor command can be influenced before execution of the command.\textsuperscript{108} All of these different areas are efficiently organized into a coordinated motor control system.\textsuperscript{108} Once sensory information has traveled up the ascending pathways to higher CNS levels and is processed, the responding motor commands are sent along the descending pathways to the motor neurons, where they are transmitted to
skeletal muscle fibers via alpha motor neurons or to muscle spindles via gamma motor neurons.  

Dynamic contributions to functional joint stability arise from feedback and feed-forward sensorimotor control over the skeletal muscles crossing joints. Therefore, proper functioning of the feed-forward and feedback sensorimotor control systems during functional tasks is a crucial factor for the maintenance of dynamic joint stability. An initial ankle injury results in immediate changes in the sensorimotor system, affecting the supraspinal temporal and spatial organization of dynamic contributions to dynamic joint stability. Understanding the sensorimotor alterations associated with PAI may provide an insight to as how the presence of PAI influences movement and muscle activation patterns during functional tasks and why individuals with PAI exhibit repeated episodes of “giving way” and recurrent ankle sprains.

2.2.2 Altered Sensorimotor Control Associated with PAI

The ability to detect motion in the lower extremity and to respond by adjusting postural control has been believed to play a crucial role in the prevention of ankle injury. It has been long thought that damage to the lateral ligamentous complex in the ankle disrupts the somatosensory component of the sensorimotor system through “articular deafferentation” that results from altered functions of mechanoreceptors, proprioceptors, and joint receptors, which can influence feedback control mechanism. Suppressed joint mechanoreceptor activation and deafferentation alter gamma motoneuron activity and muscle spindle sensitivity, influencing dynamic restraint activations. Altered feedback sensorimotor control in individuals with PAI has
been demonstrated by quantifying muscular strength, joint position sense, force sense, and static postural control measures. Recent literature has indicated that altered afferent inputs from the peripheral joint receptors in the ankle following an ankle sprain influence biomechanics and magnitude/timing of muscle activation during functional tasks, including: (1) an increased ankle inversion, decreased foot-floor clearance, laterally deviated COP, late tibialis anterior muscular activation, and a greater loading on the lateral forefoot during gait; (2) diminished and delayed fibularis longus activation after inversion perturbation during walking; and (3) deficits in dynamic stability during a single leg jump-landing tasks.

Hertel pointed out that theory of “articular deafferentation” assumes a feedback model of articular proprioception and sensorimotor control. The feedback model only explains that efferent motor control deficits following an ankle sprain arise only after the damaged afferents fail to detect that the ankle is in or moving toward a potentially injurious position. When the afferent input from the somatosensory system is altered following an ankle injury, the CNS adapts by relying on other sources of afferent information, such as vision and vestibular system, previous experience with tasks, as well as learned responses. However, this re-organization of the CNS with altered feedback responses following an ankle sprain may globally influence movement and muscle activation patterns during functional activities. Central and global changes in sensorimotor control have been associated with PAI as a consequence of damage to the ankle joint. It has been shown that alterations in peripheral receptors in the lateral ankle complex due to existing PAI altered conscious perception of joint and functional joint stability, creating a centrally mediated feed-forward compensatory
mechanism affecting spatiotemporal movement and muscle activation patterns in the entire lower extremity joint during various dynamic tasks in PAI patients.\textsuperscript{29,30,37,118,135-140}

Furthermore, previous research has demonstrated bilateral alterations in postural control,\textsuperscript{141} knee kinematics,\textsuperscript{30} gait termination,\textsuperscript{121} and hip muscle activation patterns\textsuperscript{142} in participants with unilateral PAI. The altered alpha motoneuron pool\textsuperscript{123,143-145} and cortical excitability\textsuperscript{146,147} of the lower extremity muscles in individuals with PAI also have been documented in previous investigations, suggesting that central changes in both spinal-and supraspinal-level sensorimotor control mechanisms are likely present in PAI patients. However, links between feedback (local) and feed-forward (global) alterations in sensorimotor control remain unknown, and this link should be investigated in future studies.

\textbf{2.2.2.1 Specific Alterations in Sensorimotor Control}

Chronic ankle instability, while often used as a homogenous description, is a heterogeneous pathology\textsuperscript{15,34} and has commonly been separated into mechanical and functional insufficiencies.\textsuperscript{15} However, the development of PAI is multifactorial in nature. Hubbard et al.\textsuperscript{14} examined various mechanical and functional variables to identify which factors make the greatest contribution to PAI. In their study, a discriminant analysis revealed that specific sets of mechanical (joint laxity) and functional (strength and postural control) variables explained approximately 46\% of the total variance between PAI and healthy participants and correctly predicted group membership for 87\% of PAI and healthy participants. However, these findings indicate that approximately 54\% of the variance observed in the PAI group membership remains unexplained. Sefton et al.\textsuperscript{13}
performed a multivariate approach to determine contributing sensorimotor factors that possibly distinguish between PAI and healthy participants. These findings of the diversity of mechanical, functional, and sensorimotor factors that discriminated between copers (who have a history of an ankle sprain but return to high level of physical activity without any residual symptoms) and individuals with PAI indicated that the causal mechanism of PAI appears to be multifactorial. Their work revealed that the measures of static balance and motoneuron pool excitability can correctly categorize over 86% of PAI participants. These investigations utilizing the multivariable approach are important as they provide the direction toward identifying specific contributing factors that may be most associated with PAI. Identifying specific factors that make the greatest contribution to PAI may help clinician to find what factor(s) need addressing to produce the best treatment outcome for patients with PAI. However, it remain unknown whether these factors can predict the development of PAI after an initial lateral ankle sprain as well as how these mechanical, functional, and sensorimotor contributing factors to PAI influence biomechanical and neuromuscular joint control during dynamic tasks.

Understanding the differences in biomechanical and sensorimotor characteristics during functional tasks between individuals with and without PAI will help elucidate the underlying consequence of PAI. Mounting retrospective investigations\textsuperscript{29-31,37-40,113,117-121,123-132,135-140,148-163} have examined biomechanical and sensorimotor characteristics of participants with PAI during functional tasks to identify kinematic, kinetic, and electromyographic (EMG) factors that may be associated with PAI. While these investigations\textsuperscript{72,79-81,83,84,86-97,100-108,119-136} have demonstrated that the presence of PAI locally and globally alters the coordinative ability of the sensorimotor control system...
during functional tasks, there are conflicting results regarding differences in kinematic, kinetic, and EMG variables during functional tasks between PAI and healthy participants. Most previous ankle instability research has combined individuals with mechanical and functional subgroups; however, it is more likely that PAI is a result of the combination of multiple factors representative of PAI subgroups. Several retrospective studies have established that participants with functional instability used different movement patterns to complete various functional tasks compared to those with mechanical instability, suggesting that using more homogenous groups of participants with PAI may demonstrate alterations or deficits in movement patterns more clearly. Therefore, inconsistent findings in literature when comparing kinematic, kinetic, and EMG factors between PAI and healthy participants may be attributable to the lack of differentiation between PAI subgroups. Furthermore, a recent work identified as many as 7 PAI subgroups, and some individuals with PAI may suffer recurrent sprains but have neither mechanical nor functional instability. Therefore, it is important for future investigations to identify specific sensorimotor impairments and alterations contributing to each subgroup of PAI using more homogenous groups of participants with various levels of ankle instability and injury history, as well as establish overlaps, links, or interactions between these subgroups.

While the subgroups of PAI appear to affect sensorimotor control differently, some of the conflicting results may be related to task demand differences that influence dynamic restraint requirements during functional tasks. Caulfield et al. and Delahunt et al. reported that participants with PAI demonstrated a significant decrease in fibularis longus muscle activation prior to IC during a single-leg drop landing task compared to
controls, resulting in more inverted position of the ankle. However, Gutierrez et al.\textsuperscript{137} found that those with PAI demonstrated a significant increase in fibularis longus activation before landing with two legs, but with the testing leg on a supinating platform designed to simulate an inversion ankle sprain mechanism compared to healthy controls. Although these findings conflict, these alterations in preparatory fibularis longus could be explained through a centrally mediated, feed-forward mechanism. In Caulfield et al.\textsuperscript{139} and Delahunt et al.\textsuperscript{29} studies, participants dropped off a 35cm-or 40cm-height-box and simply landed on a force plate only with their testing leg. Gutierrez et al.\textsuperscript{137} theorized that individuals with PAI may not activate fibularis muscles appropriately during situations which they may consider safe. Subsequently, the decreases in the preparatory fibularis longus activation observed in the studies of Caulfield et al.\textsuperscript{139} and Delahunt et al.\textsuperscript{29} may result from centrally mediated alteration in feed-forward control via spinal motor control mechanisms. Therefore, the spinal level alterations in sensorimotor control may represent a more constrained sensorimotor system that is perhaps ineffective at reacting to changes needed for the organization of movement.\textsuperscript{90,166} In Gutierrez et al.\textsuperscript{137} study, participants were aware they were landing on a supinating device that gives perturbation; thus, it is possible that increased fibularis longus before landing in those with PAI results from re-organization of pre-programmed feed-forward mechanisms that employs muscle pre-activation to prepare for up-coming events and promote dynamic restraints as a protective manner to avoid placing their ankle in an injurious position. The suprapsinal adaptations to sensorimotor control may increase the individual to cope with changing task and environmental demands. In contrast, recent gait studies observed the global neuromuscular and biomechanical control were impaired in participants with PAI during
gait initiation\textsuperscript{136} and gait termination,\textsuperscript{121} indicating that the presence of PAI negatively alters supraspinal aspects of sensorimotor control system during gait. Changes in the task demands with the presence of PAI appear to affect CNS as kinematic, kinetic, and muscle activation patterns are mediated via spinal and supraspinal sensorimotor control mechanisms. However, the retrospective design does not permit a causal link to be established between PAI and the identified alterations in the sensorimotor control system; thus, it remains unknown whether altered suprapsinal aspects of sensorimotor control associated with PAI is helpful or harmful. Clearly, long-term mechanical and neurologic consequences of a constrained sensorimotor system after an initial lateral ankle sprain should be a focus of future prospective investigations.

\textbf{2.2.2.2 Altered Dynamic Postural Control}

Evaluations of dynamic postural control have frequently been used to estimate sensorimotor function in individuals with PAI. Dynamic postural control requires the integration of somatosensory, visual, and vestibular afferent inputs and appropriate motor outputs to control muscle activity in the trunk and extremities in an effort to maintain balance.\textsuperscript{133}

Variations on Time-to-Stabilization (TTS) have been used to measure dynamic postural control in individuals with and without PAI during a single-leg jump landing task.\textsuperscript{30,31,124-126,128,130-132,156} This jump landing task requires individuals to create a steady base of support as quickly as possible after making contact with ground during a single-legged landing.\textsuperscript{31} Researchers\textsuperscript{30,31,124-126,128,130-132,156} have established that participants with PAI took a longer period of time to dissipate and control the experienced GRFs after
landing compared to controls, indicating that a diminished level of dynamic postural stability was present in those with PAI. While there are consistent results regarding differences in the TTS variables between individuals with and without PAI, the majority of these investigations did not quantify what sensorimotor, mechanical, and functional factors may be associated with the diminished level of dynamic postural control.

Several studies suggested that proximal joint adaptation may play a role in the diminished dynamic stability in PAI participants. Gribble and Robinson found reduced knee flexion angle at the points of initial contact (IC) and 100ms prior to IC in a group of individuals with PAI simultaneously with deficits in dynamic stability. Marshall et al. identified a relation between delayed trunk muscle reflexes and a TTS variable. In addition, Brown et al. assessed electromyography (EMG) of ankle musculature simultaneously with TTS, and identified significantly less activation levels of the soleus muscle after landing in the PAI group compared to healthy control groups. Together, these results suggest that the presence of local and proximal neuromuscular alterations in individuals with PAI may be associated with the reduced level of dynamic stability during jump landing tasks. However, the TTS analysis is a laboratory-based measure and may be not feasible in most clinical settings. Future research is needed to determine the clinical utility of the TTS variables as outcome tools to track progress over time as well as evaluation tools to predict the development of PAI after an initial ankle sprain.

The SEBT has also been used to identify sensorimotor deficits associated with PAI by assessing dynamic postural control. The SEBT requires individuals to maintain stability while simultaneously reaching maximally without compromising the base of
Sensorimotor control during the SEBT is reflected by the distance reached in eight directions, with an increase in reach distance normalized by the leg length reflecting greater sensorimotor control. It has been consistently documented in the literature that patients with PAI had diminished dynamic postural control as measured by shorter reaching distances on the SEBT, particularly in the anterior direction, than did healthy controls. Gribble et al. showed that a reduced anterior reaching distance during the SEBT was associated with decreased knee and hip flexion angles in participants with PAI on the involved side compared to both their uninvolved leg and the matched control participants. In our preliminary study, participants with unilateral PAI exhibited an increased ankle inversion and a decreased knee valgus in the involved limb during the SEBT in the anterior reach direction compared to both their uninvolved limb and the uninjured controls simultaneously with significant decreased reach distance. Together, these findings suggest that a diminished level of dynamic postural control, as measured with the SEBT, may be a consequence of global and local alterations in the sensorimotor control system.

Deficits in SEBT performance may also be the results of local impairments of range of motion (ROM) at the ankle joint. A recent investigation has demonstrated that anterior reach of the SEBT was moderately and positively correlated with the availability of ankle dorsiflexion motion measured by the weight bearing lunge test (WBLT) in participants with PAI. Our preliminary data also found a moderate and positive correlation between the WBLT and anterior reach of the SEBT in participants with PAI, but a weak correlation between open-kinetic-chain measure of dorsiflexion (OKC-DF) and the SEBT performance. These findings suggest that restricted ankle
weight-bearing dorsiflexion (WB-DF) associated with ankle pathology may be responsible for shorter anterior reach distance of the SEBT.\textsuperscript{27,171} Therefore, mechanical constraints limiting movement solutions may also be associated with poor SEBT performance observed in individuals with PAI.

In summary, the SEBT appears to be a useful clinical tool to assess the ability of individuals with PAI to organize various components of sensorimotor functions and ROM to accomplish movement goals. The poor SEBT performance demonstrated by those with PAI may be the result of sensorimotor and/or mechanical constraints that limit movement solution, functional capacity, and joint coordination. However, it is currently unclear how the degree of constraint in the sensorimotor system influences the amount of available movement solutions used during the SEBT to make postural corrections in individuals with PAI. Therefore, future investigations should attempt to determine (1) the effect of PAI on the amount of variability and functional capacity in joint coordination during the SEBT and (2) how these factors influence the SEBT performance and risk for re-injury.

\subsection{Discriminating Individuals with PAI and Copers}

Individuals who have a history of a lateral ankle sprain return to high-level activities without recurrent injury, functional impairments, and/or the development of perceptive instability and repetitive episodes of giving way, referred as copers.\textsuperscript{12} By determining the differences between copers and individuals with PAI, it will help to understand the underlying mechanism of PAI and identify those who are more likely to go on to suffer PAI. Understanding the contributing factors that enable some individuals
with a history of an ankle sprain to return to high-level activities without the development of PAI helps clinicians and researchers to develop more effective interventions targeting those at risk for PAI.

Several authors have identified differences in perceptual, mechanical, functional, and sensorimotor variables between copers and people with PAI. A recent investigation incorporating the diagnostic utility of perceptual, mechanical, and sensorimotor outcome measures and demonstrated that perceptual and sensorimotor outcomes had a greater ability to discriminate between copers and individuals with PAI compared to mechanical outcomes. Croy et al. also suggested that mechanical laxity alone may not characterize the condition of PAI; but rather sensorimotor components may have a greater impact on the condition of PAI. In their study, using diagnostic stress ultrasonography, a similar length change of the anterior tibiofibular ligament during the anterior drawer test and ankle inversion was observed between copers and participants with PAI; but both pathological groups had greater laxity to healthy controls. Furthermore, a recent jump-landing study reported that copers exhibited significant decreases in preparatory and reactive fibularis longus EMG while on a supinating platform designed to simulate an inversion ankle sprain mechanism compared to participants with PAI, indicating that the number of available degree of freedom in the sensorimotor system following ankle injury may be related to the development of PAI. A specific compensatory strategy is apparently necessary for individuals with PAI to protect the ankle during external perturbed landing, but this may not be required in copers. Wikstrom et al. suggested that copers have a greater number of solutions available to compensate successfully for damage to the lateral
ligaments following an initial ankle sprain. However, these retrospective studies cannot fully explain an exact coping mechanism after an initial ankle sprain and do not permit a causal link to be established between the development of PAI and the identified alterations in sensorimotor functions. Long-term prospective investigations are needed to explore the time course of the development of PAI.

While perceptual and sensorimotor outcome measures appear to provide the ability to discriminate between copers and individuals with PAI, it is yet unknown whether these outcome measures can accurately predict the development of PAI and which modifiable factors best lead to improved perceptual and sensorimotor outcomes. It is important for future research to determine if perceptual and sensorimotor outcome measures can be used to predict future injuries following an initial ankle sprain and how these outcomes can be improved.

### 2.2.2.4 Movement Variability Associated with PAI

Movement variability is inherent within all biological systems and essential for the function of the sensorimotor control system under changing conditions. Movement variability has been referred to as the normal variations that occur in motor performance across multiple repetitions of a task. Movement variability has been considered as both detrimental and beneficial to skilled coordinated movement and suggested as a factor contributing to developing and perpetuating injury. Exploring variability provides an insight into movement analysis, not relying on standard means, peak or minimum kinematic or kinetic variables. Optimal state of variability is necessary for movement to be functional and efficient as well as should be included in
intervention strategies if variability is pathological in a particular clinical population.\textsuperscript{181} Normal efficient movements have deterministically chaotic characteristics but not stochastic (random) variations, which can fluctuate within an optimal range.\textsuperscript{177,181} Deterministic chaos is defined as mathematically predictable when the initial conditions are known, but qualitatively appearing random.\textsuperscript{179,181}

According to the generalized motor control theory, variability is identified as error in movement, planning, execution, and the ability to predict proper parameters to achieve the optimal movement pattern and is associated with motor redundancy.\textsuperscript{182,183} It has been suggested that variability could be minimized with practice that allows an individual to identify the proper parameters as well as optimize the accuracy and efficiency of the movement pattern through trial and error.\textsuperscript{183}

In contrast, the dynamical systems theory states that movement variability is a beneficial subconscious compensatory system that self-organizes according to organismic, task, biomechanical, and environmental constraints to find the most stable solution for coping with changes, maintaining stability, and attaining higher levels of skills.\textsuperscript{176,184,185} The sensorimotor system is constantly changing and attributable to the interaction of multiple external and internal stimuli, such as complex systems, constraints, the environmental conditions, degrees of freedom, and the neuromuscular and musculoskeletal systems.\textsuperscript{176,184,185} In order to accomplish a given motor task, the sensorimotor control system has numerous options and pathways within the involved degrees of freedom that can be utilized.\textsuperscript{185,186} In the dynamical systems theory, large amounts of variability of movement indicate loss of stability, while small amounts of variability indicates a highly stable behavior.\textsuperscript{176} The dynamical systems theory suggests
that the sensorimotor system becomes highly unstable and switches to use a new, more stable movement pattern, which implies that lack of movement variability may reduce the flexibility and degrees of freedom into an effective movement solution, thereby limiting the ability to adapt to new situations or changing situations. However, a critical limitation of the dynamical systems theory is that it does not provide an explanation for some biological behaviors that appear to be highly stable but are paradoxically performed in variable ways (high variability).\textsuperscript{179}

In the theoretical model of variability proposed by Stergiou et al.,\textsuperscript{177,179} desired movement variability is nonlinear, and there is an optimal zone of variability that is characterized by deterministically chaotic patterns and associated with high complexity. This complexity is necessary for systems to adapt to changing condition over time and is defined as highly variable fluctuations in physiological processes resembling chaos. The presence of chaotic temporal variations describes that output of a healthy biological system can represent the underlying physiologic capability to make flexible adaptations to everyday stresses placed on the human body.\textsuperscript{187,188} Thus, the chaotic pattern associated with the higher complexity is reflective of a healthy system.\textsuperscript{178} A decrease in this optimal zone is characterized by a periodic structure that is more predictable with less variability and high regularity, more repeatable, and demonstrates less complexity, which ultimately creates a system that is more rigid and less adaptable to different perturbations. In contrast, an increase in the optimal zone is characterized by a random structure with high variability, is less predictable, regular, and complex, which results in a noisy and unstable system.\textsuperscript{177}
There are a number of methods to quantify variability in the moving system. One traditional, commonly used method is the linear analysis technique, such as the standard deviation normalized to the mean of the score distribution and the coefficient of variation in relative terms. Another method is the nonlinear tool, including approximate entropy, sample entropy, correlation dimension, largest Lyapunov exponent, and detrended fluctuation analysis. While the linear analysis technique quantifies the amount or magnitude of movement variability, the nonlinear analysis technique quantifies the structure or organization of movement variability.

Movement variability has been assessed with linear analysis in patients with PAI to find an explanation for recurrent ankle sprains and repeated episodes of instability. Kipp and Palmieri-Smith found that individuals with PAI displayed greater inter-trial variability of ankle kinematics in the sagittal plane before IC and in the frontal plane during the entire single-leg landing task compared to healthy individuals when analyzed with principal component scores (PCA). Brown et al. attempted to determine if differences in movement variability exist at the ankle, knee, hip, and trunk as well as GRF variability in three planes of motion with the coefficient of variation (CV) and average standard deviation (SD) of the ensemble curve between participants with FAI, MAI, and copers during a stop jump task. They found that the FAI group displayed greater ankle frontal-plane kinematic variability during a stop jump compared to the MAI and coper groups, and that the MAI group exhibited greater anterior-posterior GRF variability than the FAI group. As follow up to their previous study, Brown et al. examined movement variability at the ankle, knee, hip, and trunk in 3 planes of motion between participants with FAI, MAI, copers, and controls during a single leg jump.
landing in anterior, lateral, and medial directions. They found that the FAI and coper
group demonstrated greater variability for knee rotation prior to IC than the control
group, and the FAI group showed less variability for knee rotation after IC than the
control groups.\textsuperscript{37} The copers were less variable for knee flexion during the single-leg task
in the anterior direction compared to the controls. The control group exhibited greater
variability for hip flexion during lateral jumps compared to the FAI group as well as for
hip abduction during anterior jumps compared to the FAI and MAI groups. These
investigations of movement variability with linear analysis technique during jump-
landing tasks suggest that individuals with PAI appear to have greater movement
variability at the ankle and less variability at the knee and hip compared to controls,
assuming that increases in the amount of variability in movement during functional tasks
equate with increase in instability. However, linear variability analysis such as the SD,
CV, and PCA, cannot adequately represent the complexity of the system and does not
accurately define constructs importance in movement, such as stability.\textsuperscript{181} Moreover,
linear tools do not provide information regarding what optimal movement variability is.
The implications of increased or decreased variability for risk of recurrent ankle sprain
are still unclear.

Additionally, evaluating the amount of COP oscillation on a force plate with liner
analysis technique has been commonly used to identify postural instability, with more
COP displacement indicating a higher degree of instability.\textsuperscript{189} Recent meta-analysis\textsuperscript{32}
reported that investigations using traditional COP measures identified greater COP
displacement during static balance with an eyes-closed condition in recurrent ankle
sprainers, indicating the presence of greater postural variability and instability. In
contrast, several studies\textsuperscript{90,166,174,190} have used a spatiotemporal COP analysis referred to as time-to-boundary (TTB) to detect postural control deficits during a single-leg stance in individuals with PAI and identify lower TTB value in those with PAI compared to healthy controls. TTB quantify the amount of time to make a postural correction and the magnitude of constraint experienced by the sensorimotor system while maintain balance within a base of support.\textsuperscript{190,191} The lower TTB value indicates postural instability, as individual has less time and fewer movement solutions to make postural corrections and maintain postural stability in a single-limb stance.\textsuperscript{90} Thus, the lower TTB values exhibited by individuals with PAI indicates that the presence of PAI may reduce postural variability and stability, resulting in the inability to respond appropriately to external perturbations in the maintenance of balance.\textsuperscript{90}

Furthermore, using a variety of TTS variables, several researchers have demonstrated that individuals with PAI have a greater dynamic postural variability and a diminished level of dynamic postural stability during a single-legged jump landing task compared to healthy controls. However, evidence shows that body sway during a single stance with large or small variability implies neither a highly stable system nor instability.\textsuperscript{192,193} From nonlinear dynamical perspective, variability and stability represent different properties within the sensorimotor system.\textsuperscript{179} While variability refers to the ability of the sensorimotor control system to reliably perform in a variety of different environmental and task constraints, stability refers to the dynamic ability to control posture against an external perturbation.\textsuperscript{179} More and less constraints do not necessarily mean a decrease in postural stability because an individual might have a highly efficient sensorimotor system or effective motor learning skill within the number of available
degrees of freedom. Therefore, the amount of variability does not equate the degree of postural stability.

Although linear variability analysis is considered most appropriate for quantifying the total variability within a system during dynamic tasks, it provides information only regarding the amount or magnitude of variability and masks the true structure or organization of variability. Linear analysis measures variability (standard deviation) around mean and typically average kinematic, kinetic, and COP data to generate a mean picture of movement patterns. Using linear variability analysis assumes that each cycle of movement is independent of past and future cycles as well as variations between repetitions and cycles of a task are random, which has been shown to be an incorrect interpretation of variability.

Stergiou et al. pointed out that ideal variability and healthy motor control has characteristics of nonlinearity, and nonlinear variability analysis focused on understanding how a movement pattern changes over time. They believe that variability is an emergent property of the self-organizing behavior of the nonlinear dynamical properties within the sensorimotor system, and nonlinear variability analysis determines whether a chaotic structure and complexity are present in movement by quantifying the structure or organization of the variations present in a time series such as changes observed in gait fluctuations and postural sway oscillations over time. Therefore, using nonlinear analysis for exploring movement variability may provide a better understanding of variability and how it relates to pathology.

The structure of movement variability has been examined with nonlinear analysis on several musculoskeletal conditions such as anterior cruciate ligament (ACL) injury,
cerebral concussion, and knee osteoarthritis. Previous studies of ACL injury reported that individuals with ACL deficiency demonstrated a decrease in the optimal state of movement variability at the knee during walking, which is a more predictable, rigid, and repeatable behavior, while those with ACL-reconstruction exhibited an increase beyond optimal variability at the knee, which is a noisy, irregular, unpredictable behavior. From these findings, Stergiou and Drecker theorized that patients with ACL deficient knee may feel more careful during walking to try to eliminate or minimize any excessive movements, while those with ACL reconstructed knee may feel secure to increase and add extra movement. However, the temporal structure of movement variability at the knee during walking may be not restored to normative levels because of lack of the proper proprioceptive inputs. Interestingly, Yakhdani et al. and Tochigi et al. found a similar structure of movement variability in patients with knee OA to those with ACL deficiency. Therefore, exploration of movement variability with nonlinear dynamics provides an insight into biomechanical and sensorimotor impairments in clinical populations, such as individuals with musculoskeletal pathology.

However, it is currently unclear what effects PAI has on the structure or organization of movement variability in a time series, such as changes observed in gait fluctuations and postural sway oscillations over time. It will be important in future investigations, using nonlinear variability analysis, to determine how movement patterns, characteristics, or structure changes over time in individuals with PAI, what the sources of altered variability are, and whether the variation in movement observed in those with PAI increase the risk for recurrent ankle sprains and repeated episode of “giving way.”
2.3 Potential Inter-injury Relationship

Although there is limited information, there is a potential link between a history of ankle sprain and risk of injury at the proximal joints. The presence of PAI alters proximal joint neuromuscular control and biomechanics in the knee, hip, and trunk. It is possible that these proximal joint alterations associated with PAI may increase a risk of future injuries in these proximal joints. Backman reported that there was a trend a higher incidence of patellar tendinopathy in legs with two or more ankle sprains as compared to with those with a history of one or no ankle sprains. Nadler et al. found that athletes with a knee or ankle joint instability were more likely to experience low back pain. Kramer et al. examined a potential relation between ACL injury risk and previous ankle sprain history. Although an ankle sprain history did not primarily predict an ACL injury history, 52% of patients with ACL injury had a previous history of ankle sprain and there were common factors that predicted both the ACL injured and ankle sprained groups. Soderman et al. reported that 60% of patients that suffered an ACL injury had experienced an ankle sprain during the 3 months preceding the study period.

In our previous work, individuals with PAI demonstrated significantly less knee flexion angle at peak anterior tibial shear force (ATSF), a slightly higher peak ATSF, and faster time to peak ATSF compared to the controls; however these differences in peak ATSF and time to peak ATSF were not statistically significant. Although in our study knee flexion angle was significantly and inversely correlated with peak ATSF, posterior GRF was the strongest predictor of peak ATSF in the PAI group, and there was no difference in posterior GRF at peak ATSF between the PAI and control groups. This indicates that a position of greater knee extension with similar posterior GRF may
be not enough to produce a significantly greater amount of peak ATSF in the PAI group compared to the control group. Based on our findings, decreased knee flexion at peak ATSF associated with PAI may indicate that individuals with PAI may exhibit one of the conditions necessary for increasing peak ATSF. Further work in this area is needed to determine if biomechanical and sensorimotor characteristics associated with PAI provides insight regarding future proximal joint injury mechanisms in PAI population. Identifying common contributing factors to PAI and proximal joint injuries will provide a foundation for continued work to develop more effective preventions for lower extremity injuries.

2.4 Considerations for Intervention

Identifying potential points of intervention to improve the sensorimotor function, mechanical degrees of freedom, and kinetic-chain relation that are altered due to the presence of PAI is critical in clinical practice and research. Ankle instability is a multifactorial pathology;\textsuperscript{15,34} thus, it is important for clinicians and researchers to address multifactorial aspects of impairments associated with PAI. A potential relation between mechanical and functional alterations associated with PAI has been suggested.\textsuperscript{27} Hoch et al.\textsuperscript{27} and our laboratory\textsuperscript{171} found a correlation between the WB-DF and SEBT performance in participants with PAI, suggesting that restricted ankle dorsiflexion may also contribute to the functional impairments associated with PAI by reducing sensory inputs to the sensorimotor system. Deficits in postural control may be associated with not only altered feedback and feed-forward controls in the sensorimotor system but also altered arthrokinematic function and mechanical degree of freedom associated with PAI.
Previous investigators\textsuperscript{207,208} utilized joint mobilization techniques to address altered mechanical impairments and excitability of spinal reflex. Hoch et al.\textsuperscript{208} identified significant improvements in WB-DF and the SEBT performance in the anterior, posteromedial, and posterolateral directions following multiple dosages of Maitland Grade III posterior talar glide joint mobilization technique in participants with PAI. Their findings indicate that multiple dosages of joint mobilization may be able of improve the ability to incorporate additional mechanical degrees of freedom into the movement strategies on the SEBT.\textsuperscript{208} Additionally, the investigators\textsuperscript{208} speculated that the improvements in the SEBT performance in the posteromedial and posterolateral reach directions following the joint mobilization interventions may be attributable to an increase in knee and/or hip flexion based on joint coupling between WB-DF and knee and hip sagittal-plane motion.

Previous researchers\textsuperscript{209} determined that knee and hip flexion ROM significantly affect performance on the posteromedial and posterolateral reach distance. Furthermore, less knee and hip flexion during the SEBT was observed in PAI population.\textsuperscript{18,167} These findings imply that the joint mobilization may be able to increase knee and/or hip sagittal-plane kinematics during the SEBT through improving WB-DF availability, possibility resulting in SEBT performance improvements in anterior, posteromedial, and posterolateral reach directions. However, Hoch et al.\textsuperscript{208} did not quantify kinematics in the lower extremity during the SEBT. While Green et al.\textsuperscript{210} reported that posterior talar glide joint mobilizations improved gait parameters in patients with an acute lateral ankle sprain, there is little evidence that has examined movement patterns during the SEBT, gait, and jump-landings following joint mobilization interventions in patients with PAI.
Therefore, exploring how improvements in mechanical impairments associated with PAI following a joint mobilization are incorporated into movement strategies during functional tasks (e.g., quantifying pre-and post-intervention lower extremity kinematics during the SEBT) should be investigated in future studies.

As altered sensorimotor control system at both spinal-and supraspinal- levels are associated with the presence of PAI,\textsuperscript{123,136,145,147} it is important to explore how rehabilitation protocols influence sensorimotor system function. The sensorimotor control system integrates information from multiple modalities.\textsuperscript{97} While reactive feedback control rapidly drives motor responses but cannot be easily modified, supraspinal pathways of the sensorimotor control mechanism can be modified and tuned through experience and learning.\textsuperscript{97} Therefore, addressing impaired movement abilities and learning various movement patterns may allow the sensorimotor control system to correctly tune the downstream neuromuscular control to temporal organization and feedback delays, potentially providing the beneficial results for improving movement patterns and sensorimotor function during functional tasks.

Signals that drive motor learning can arise in different sources, such as through vision or proprioception.\textsuperscript{97,99} Both proprioceptive and visual feedback systems affect the learning response; however, these sensory modalities have differential importance in driving motor learning.\textsuperscript{99} Proprioceptive feedback predominately drives generalization of dynamics, while visual feedback may be responsible for learning the direction of planning and movement, which likely influences re-mapping of path planning.\textsuperscript{211-213} Wei et al.\textsuperscript{214} suggested that feedback should be designed such that it indicates to the sensorimotor control system that both visual and proprioceptive cues are relevant for
movement production instead of being artificially manipulated. Rozzi et al.\textsuperscript{215} reported that participants with PAI demonstrated significant improvements in sensorimotor functions following balance training with visual feedback. Visual feedback during functional tasks impacts higher brain center. Previous literature reported that the posterior parietal cortex in being involved in the sensorimotor integration of optic flow perception and its impact on movement patterns.\textsuperscript{216} The manipulation of visual inputs during locomotion has been shown to impact kinematic and kinetic gait parameter as well as the amount and temporal organization of the gait variability.\textsuperscript{217-220} However, the effects of manipulation of visual inputs during functional tasks on movement and muscle activation patterns in individuals with PAI are unclear. Future investigation of the effects of manipulations of visual inputs on sensorimotor functions in PAI population could be beneficial in the rehabilitation for individuals with PAI.

Although spinal reflexes cannot be easily modified, interestingly, reflex conditioning protocols have been recently developed to reeducate the regenerated lower motor neurons and synapses that are needed to restore motor function and improve locomotion in patients with partial spinal cord injuries and other chronic neuromuscular pathologies.\textsuperscript{221-223} It was proposed that H-reflex operant conditioning protocol with visual feedback of how well the He-reflex is controlled promotes increased effort and awareness of the patient to actively control spinal reflexive excitability, resulting in improvement in motor function.\textsuperscript{223} Thompson et al.\textsuperscript{223} demonstrated that H-reflex operant conditioning protocols with visual feedback correctly modulated the soleus H-reflex in healthy individuals during standing and waking and induced plasticity in the spinal cord, which leads to improvements in motor function.
Previous literature has reported altered spinal reflexive excitability in the soleus and fibularis muscles following ankle sprains. Delayed onsets of muscle activation in the fibularis muscles have been previously shown among PAI populations. Furthermore, Sefton et al. found that motoneuron pool excitability were a sensorimotor factor strongly contributing to PAI. However, the effect of H-reflex operant conditioning protocols with visual feedback on spinal reflexive excitability of the soleus and fibularis in patients with PAI is unknown. In order to potentially target the neural mechanisms, it may be beneficial for future research to determine if H-reflex operant conditioning protocols have an effect on the spinal reflex pathways that are influential to motor function following ankle sprains.

Evidence has shown that the presence of PAI may affect movement variability and coordination. Therefore, exploring intervention strategies which optimize movement variability and manipulate constraints may provide significant insight into rehabilitation practice and research in human movement as well as provide the best results for improving efficacy of movement patterns, functional capacity, and movement solution variability.

From a movement variability perspective, clinician may not set the goal of intervention as achieving an ideal movement pattern or strategy that is common to all patients because each individual has a slightly different set of conditions to a motor problem, and the optimal solution to that problem may be unique to that individual. Some patients with PAI may have laxity, impaired arthokinematics or degenerative changes, while others may have insufficiencies in proprioception, neuromuscular control, postural control or strength. Ankle instability may be associated with various factors that
need to be addressed on an individual basis. The findings from our preliminary data\textsuperscript{225} and a recent systematic review\textsuperscript{226} have suggested that clinicians need to consider what may be the contributing factors to mechanical and functional impairments associated with PAI in order to select the most appropriate treatments and interventions. Therefore, individualized treatments and interventions may be more important when treating a patient than using the “cookie-cutter method” to treat all individuals with PAI.

\subsection*{2.5 Considerations for Future Work}

Recurrent ankle sprains and residual symptoms after an initial ankle sprain, which include repeated episodes of “giving way,” pain, and decreased functions, have been most commonly termed PAI.\textsuperscript{15,35} However, it is not well understood what actually constitutes PAI. Delahunt et al.\textsuperscript{35} reported that there are inconsistencies in definition, inclusion criteria, and exclusion criteria for PAI reported across previous studies, leading to heterogeneous population and making it difficult to compare results across studies. It has been also reported that mechanical and functional components of PAI exhibited different sensorimotor functions during dynamic tasks.\textsuperscript{36-40} Furthermore, a recent systematic review\textsuperscript{32} based on homogenous cohort of participants found that recurrent ankle sprainers exhibit radiographic changes in the talus, decreased concentric invertor strength, increased postural sway during a single-leg balance with the eyes-closed, altered foot positioning during gait, and a diminished dynamic stability during a jump-landing task, compared with healthy controls. The findings of this review indicate that examining more homogenous components of participants with PAI may clarify what alterations or impairments are most associated with each component of PAI. However, overlap or links
among subgroups of PAI have not been established yet. Therefore, more comprehensive research is needed examining numerous variables in individuals with a history of ankle sprain to (1) establish overlap or links among subgroups of PAI, (2) identify exact contributing mechanism to PAI, (3) establish the standard definition and more uniform inclusion and exclusion criteria for each subgroups of PAI, and (4) determine characteristics of each subgroup of PAI.

Additionally, it is difficult to determine in the findings in the retrospective studies if the sensorimotor and biomechanical characteristic observed during functional tasks in individuals with PAI exacerbate the pathology or are protective to the unstable ankle. Previous literature suggested a history of lateral ankle sprain as a significant risk factor of future lateral ankle sprain.\textsuperscript{88} Therefore, prospective cohort studies that examine sensorimotor function and biomechanics during functional tasks in the lower extremity in individuals with a history of ankle sprain who go on to suffer PAI and/or proximal joint injury may provide additional clinical applications to improve injury prevention protocols.

### 2.6 Conclusion

Although ankle sprains receive abundant attention and focus in clinical practice and research, they persist as the most common injury that leads to recurrent injury in athletic activities. Understanding the cause of recurrent injury is crucial in implementing therapeutic interventions to ankle injury and reducing recurrent injury rate. Although excessive plantar flexion with inversion and external rotation in the ankle has been believed as the mechanism of an ankle sprain, it appears that the ankle sprain injury
mechanism excessive rearfoot inversion and internal rotation coupled with ankle dorsiflexion.

While various studies have shown that there are feed-forward and feedback alterations present in individuals with PAI as manifesting altered movement organization and muscle activation patterns during functional tasks, it is unclear whether these alterations are the result of the injury or initially contributed to it due to the lack of prospective studies. It is possible that compromised feedback responses, which may have been caused by the initial ankle sprain, contribute to the altered feed-forward control.

Ankle instability appears to be linked to multiple aspects of insufficiencies. However, the potential synergistic relation between mechanical and function impairments associated with PAI are unclear. It is important for future investigations to identify the source of alterations associated with PAI, determine exact characteristics of subgroups of PAI, and identify exact factors that cause recurrent and secondary injury for developing more effective intervention and injury prediction model. Interventions that address multifactorial aspects of impairments associated with PAI also are essential for improving both patient-oriented and clinician-oriented functional measures, decreasing disability, and preserving long-term healthy in individuals with PAI.
Chapter 3

Methods

3.1 Research Design

This study used a single-blinded, case-control design to identify specific mechanical and sensorimotor deficits associated with self-reported PAI. The case groups were comprised of participants with self-reported PAI, subdivided into four subgroups: 1) participants that suffer all major clinical symptoms of PAI; 2) participants that have repeated episodes of “giving-way” and perceived instability but not suffer recurrent ankle sprains; 3) participants that suffer recurrent ankle sprains but have neither repeated episode of “giving-way” nor self-reported instability; and 4) ankle sprain copers that have a history of a lateral ankle sprain and return to high-level activities without any major clinical symptoms of PAI. The control groups included healthy participants with no history of lower extremity injuries. Participants were screened by an investigator for inclusion criteria and group allocation. Two investigators with previous experience using the selected outcome measures conducted the assessments. The same investigators conducting the assessments
analyzed all outcome measures. The investigators measuring and analyzing the selected outcome measures were blinded to group membership of the participants using the code being retained by the investigator screening participants until analysis was completed.

### 3.2 Participants

Participants between the ages of 18 and 45 years were recruited from the University community. All participants read and signed an informed consent approved by the University of Toledo Institutional Review Board. All participants had no: 1) diagnosed balance or vestibular disorders; 2) previous history of low back pain in the previous six months; 3) previous history of surgery in the lower extremity; 4) history of seizures; 5) history of a concussion in the past six months; 6) history of neurological injuries or diseases; and 7) previous history of any self-reported musculoskeletal and neurovascular injuries and disorders in the lower extremity other than lateral ankle sprains in the previous two years.

Participants in this study were classified into five groups (four subgroups of self-reported PAI and healthy control) according to the presence of: 1) a previous history of an acute lateral ankle sprain (which caused swelling, pain, and temporary loss of function); 2) repeated episodes of “giving-way” (perceived instability) in the 6 months prior to study enrollment; 3) recurrent ankle sprains; and/or 4) self-reported instability assessed by the Ankle Instability Instrument (AII) and Identification of Functional Ankle Instability (IdFAI) (Table 3.1). The AII (Appendix B) and IdFAI (Appendix C) have been shown as highly reliable and valid self-assessed
questionnaires to diagnose those with PAI. Additionally, participants in the ankle sprain coper group were required to report that they had not modified physical and occupational activity levels due to their ankle injury. No participant with PAI had acutely sprained their ankle in the three months before testing. In the event participants reported a bilateral history of ankle sprains, the limb with the greatest reported functional impairments on the AII and IdFAI was included in the study. A test limb for the control group was randomly selected.

In addition to the AII and IdFAI, participants completed the Foot and Ankle Ability Measure including activities of daily living (FAAM-ADL) and sport sections (FAAM-S) (Appendix D) to examine their self-assessed functional levels of this current study.

Table 3.1 Five Groups and inclusion criteria (IC) for each group

<table>
<thead>
<tr>
<th>Group</th>
<th>IC</th>
<th># of previous ankle sprains</th>
<th>Repeated episodes of “giving-way”</th>
<th>AII&lt;sup&gt;207&lt;/sup&gt;</th>
<th>idFAI&lt;sup&gt;228&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>PAI</td>
<td>RAS-PI</td>
<td>≥ 2</td>
<td>At least two episodes in previous 6 months</td>
<td>≥ 4</td>
<td>≥10</td>
</tr>
<tr>
<td></td>
<td>FAI</td>
<td>1</td>
<td>At least two episodes in previous 6 months</td>
<td>≥ 4</td>
<td>≥10</td>
</tr>
<tr>
<td></td>
<td>RAS</td>
<td>≥ 2</td>
<td>No</td>
<td>&lt; 4</td>
<td>&lt;10</td>
</tr>
<tr>
<td></td>
<td>Coper</td>
<td>1</td>
<td>No</td>
<td>&lt; 4</td>
<td>&lt;10</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>0</td>
<td>No</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

PAI = Posttraumatic ankle instability; RAS-PI = Recurrent ankle sprain with perceived instability; FAI = Functional ankle instability; RAS = Recurrent ankle sprain; AII = Ankle instability instrument; IdFAI = Identification of functional ankle instability

Additional exclusion criteria for the transcranial magnetic stimulation (TMS)
were assessed for all participants. In accordance with the transcranial magnetic stimulation (TMS) safety guidelines outlined by the National Institutes of Neurological Disorders and Stroke, the exclusion criteria for transcranial magnetic stimulation included: 1) having a history of heart disease, stroke, cardiac pacemaker or implanted cardiac defibrillator, epilepsy or seizures, migraines or severe headaches, cancer in brain or leg muscles, diagnosed psychiatric disorder, and intracranial metallic clips; 2) currently pregnant or breastfeeding; 3) currently taking pain relieving medication or neuroinhibiting or stimulating medication; 4) having metal implants anywhere in the head, neck, or shoulders (excluding dental work); 5) having a personal or familial history of seizures or epilepsy; 6) having ocular foreign objects or cochlear implants; 5) having implanted brain stimulators, aneurysm clips, implanted medication pumps, intra-cardiac lines, or cardiac pacemakers; 7) having a history of or is currently abusing illicit drugs or alcohol or is currently withdrawing from any substance; 8) taking any medication that may lower seizure threshold (including, but not limited to, tricyclic antidepressants, neuroleptic agents, Baclofen, and Tramadol); and 9) having a history of serious head injury or increased intracranial pressure. If participants meet the exclusion criteria for corticospinal excitability assessments using TMS were not conducted on them.

Lastly, participants were asked to complete the following questionnaires to better understand their perceptual characteristics, including previous history of the lower extremity injury, levels of physical activity, fear of re-injury, and quality of life. The questionnaires were: 1) a health history questionnaire (Appendix E); 2) the Short-form 36 (Appendix F); 3) Global Physical Activity Questionnaire.
(Appendix G); 4) Tampa Scale of Kinesiophobia\textsuperscript{2,34} (Appendix H); and 5) Psychological Response to Sport Injury Inventory\textsuperscript{2,35} (PRSII) (Appendix I).

3.3 Data Collection and Analysis for Outcome Measures

Data collection took place in two sessions. The following clusters of outcomes were assessed for the involved limb in one of two testing sessions: 1) sensorimotor assessment; and 2) mechanical assessment. The order of the testing sessions was counterbalanced. The session of sensorimotor assessment was divided into two clusters, including: 1) spinal and corticospinal excitability measures; as well as 2) gait analysis and static/dynamic postural control assessment. Excitability measures were conducted first to ensure that movement associated with walking and balance testing did not interfere with results of spinal reflex and corticospinal excitability testing. The order of outcome measures within a cluster was also randomized. All outcome measures were collected in the Musculoskeletal Health and Movement Science research laboratory.

3.3.1 Neural Excitability Measures

3.3.1.1 Spinal Reflex Excitability

Spinal reflex excitability of the soleus muscle was assessed using previously published methods for eliciting Hoffman-reflex (H-reflex) and muscles responses (M-wave).\textsuperscript{2,34,36} The soleus muscle was selected because the soleus muscle is influential in maintaining upright posture and providing ankle stability,\textsuperscript{2,37} and decreased soleus
alpha motoneuron excitability has been demonstrated in patients with ankle injury.\textsuperscript{143,144} Participants were positioned on a dynamometer seat (Biodex System II Pro; Biodex Medical Systems, Shirley, NY) at 90° of hip flexion, knee flexion, and ankle dorsiflexion (Figure 3-1).

![Figure 3-1. Position of a Participant during Neural Excitability Testing](image)

Soleus H-reflex and M-wave were recorded using a biological signal data acquisition system (MP150 MSW; BIOPAC Systems, Santa Barbara, CA). Two 10mm, pre-gelled Ag-AgCl (EL503, BIOPAC Systems, Inc., Goleta, CA) surface electromyography (EMG) electrodes were placed approximately 2 cm apart and parallel to muscle fiber orientation over the midline of the soleus in the distal third of the lower leg.\textsuperscript{238} Surface EMG electrode preparation included shaving, debriding, and cleansing the skin with alcohol. The reference electrode was positioned on the medial malleolus of the non-testing leg. A 2 mm shield disk electrode (EL254S BIOPAC Systems, Inc., Goleta CA, USA) was used to deliver electrical stimuli and positioned over the posterior tibial nerve in the popliteal fossa and secured with hypoallergenic
tape, and a self-adhesive carbon impregnated dispersive pad was positioned over the quadriceps muscles.

Acknowledging BIOPAC software (BIOPAC Version 3.7.3, BIOPAC Systems, Inc., Goleta CA, USA) was used to visualize the EMG signals. Reflex measurements were elicited via a Digitimer DS7AH constant current stimulator with a 200 μs max pulse duration (Digitimer Ltd., Hertfordshire, England), which is a non-invasive device that delivers electrical stimuli transcutaneously through an electrode attached to skin. The raw EMG signal was amplified (gain set at 1000, common mode rejection ratio = 110 dB, input impedance = 1MOhms) and digitally converted at 2000 Hz of the sampling rate. The signal was band-pass filtered from 10 to 500 Hz.

To determine the peak-to-peak maximum H-reflex (H<sub>max</sub>) and M-wave (M<sub>max</sub>) of the soleus, stimulus intensity was gradually increased, with lower intensity stimulus depolarizing Iα afferents resulting in an H-reflex and higher intensity stimuli depolarizing motor axons resulting in an M-wave (Figure 3-2). Stimuli were applied with 10-second rest interval to avoid the effects of post-activation depression, or decreased H-reflex amplitude due to previous Iα afferent activation. Three trials were measured and recorded, as well as the average value over these three recordings were used to calculate H<sub>max</sub>:M<sub>max</sub> ratio. Although participants’ position during the neural excitability assessments in the current study has not been used in previous studies, the measurements of the H<sub>max</sub>:M<sub>max</sub> ratio of the soleus muscle in various participant’s positions have been demonstrated to be reliable (ICC=0.75 to 0.97). A smaller H<sub>max</sub>:M<sub>max</sub> ratio is representative of a decrease in soleus alpha motoneuron pool excitability.
3.3.1.2  Efferent Alpha Motoneuronal Output

The V-wave is an electrophysiological variant of the H-reflex that has been shown to reflect the level of both spinal and supraspinal inputs to the motoneuron pool.\textsuperscript{244-247} The V-wave of the soleus muscle was examined to determine the level of efferent neural drive from spinal and/or supraspinal alpha motoneuron during a plantar flexion maximal voluntary isometric contraction (MVIC).\textsuperscript{244} The V-wave of the soleus muscle has been demonstrated to be reliable (ICC=0.86-0.92).\textsuperscript{248}

Participants were positioned exactly the same as for the spinal reflex excitability testing (Figure 3-1) and secured to the Biodex with a lap and thigh strap to limit auxiliary motions of the trunk and leg. Prior to eliciting V-wave, participant underwent peak torque assessment. Participants were asked to perform a series of
three trials of MVICs. The average of these trials was calculated and used to quantify peak torque. Following determination of participant’s peak torque, they were asked to perform an isometric plantar flexion contraction equivalent to 100% of their peak torque value using real-time visual feedback to match their torque output to 100% of their peak torque value.249 Once participants reached their target value for two seconds, a stimulus whose intensity is equivalent to 1.5 times that required to elicit maximal M-wave was applied to the tibial nerve (Figure 3-3).246 Three measurements of the soleus V-wave were recorded, and the average value over these three trials was used to quantify the maximal V-wave. Soleus V-wave was normalized to $M_{\text{max}}$ ($V: M_{\text{max}}$ ratio), reflecting the amount and frequency of efferent nerve impulses traveling in the alpha motoneuron.247 A smaller $V: M_{\text{max}}$ ratio is representative of a decrease in efferent neural drive to the soleus muscle. A minute rest was provided between V-wave recordings to limit the effects of fatigue on the measurement.

![M-response and V-wave diagram]

Figure 3-3. Schematic EMG Tracing of a Soleus V-wave and Muscle-reposes Signal
3.3.1.3 Corticospinal Excitability

Active motor threshold and cortical silent period (CSP) measured with TMS were used to assess corticospinal excitability to the soleus muscle. The MagStim (model BiStim; Magstim Company, Ltd., Wales, UK) was used to deliver a single magnetic pulse with a possible strength of 2.0 T. Before testing, patients were given a Lycra swim cap (Sprint Aquatics, Rothhammer International Inc. San Luis Obispo, CA) used to mark reference lines for the stimulation. The swim cap had a standard dot grid with two lines; one vertical line connected the nose to the occiput to separate the hemispheres sagittally and the other horizontal line connected the apexes of the ears bisecting the vertical line. The intersection of these two lines was the vertex of the skull and was placed half way between each landmark (Figure 3-4).

![Figure 3-4. A Lycra Swim Cap used for Corticospinal Excitability Testing](image)

During corticospinal excitability testing, participants were positioned exactly the same as during the V-wave testing, and a double cone coil (Magstim Company, Wales, UK)
was positioned over the vertex (Figure 3-5). Participants performed serial submaximal isometric plantar flexion contractions at 5% intensity of their MVIC in order to standardize volitional muscle contraction during active motor threshold and motor evoked potential (MEP) testing. The stimulator was set to produce a magnetic stimulus of 1.0 T. The investigator moved the coil anterior or posterior and laterally or medially, delivering a series of stimuli at each point on the grid until identifying the location where the largest peak-to-peak MEP was produced. The coil was fixed at this location for the remainder of testing.

Figure 3-5. Corticospinal Excitability Testing Set-up

Soleus AMT was established by using a protocol previously described for lower extremity corticomotor excitability. Soleus AMT was defined as the lowest TMS intensity required to evoke a measurable MEP of > 100μV amplitude in at least 4 of 8 trials.
Following determination of AMT, eight stimuli were delivered at 120% of AMT and MEP amplitudes were recorded for each trial. Soleus CSP was measured as the distance from the end of the MEP to a return of the mean EMG signal plus two times the standard deviation of the resting baseline (pre-stimulus) EMG signal (Figure 3-6). The EMG signals or other stimulation artifacts were visually examined, and the CSP was recorded in milliseconds. The CSP represents the integrity and excitability of inhibitory pathways between the motor cortex, thalamus, and basal ganglia, which may be mediated through gamma-aminobutyric acid-B receptors.253,254 A longer CSP indicates greater cortical inhibition to the soleus muscle.

![Figure 3-6. Schematic EMG Tracing of Cortical Silent Period (CSP).](image)
The CSP starts from the end of motor evoke potential (MEP) to a return to the signal exceeds two standard deviations above the resting baseline EMG signal.

### 3.3.2 Variability of Locomotor Patterns during Walking

Stride-to-stride variability of lower extremity motion patterns during walking
was examined using the nonlinear measure of the Approximate Entropy (ApEn). It has been suggested that gait variability analysis with nonlinear measures can provide useful information of the sensorimotor and neuromuscular mechanisms under both healthy and pathological conditions. \textsuperscript{197-199,255,256} Recent work examining sensorimotor and neuromuscular function in individuals with PAI during gait has suggested that a more constrained sensorimotor system may contribute to the major clinical symptoms of PAI. \textsuperscript{121,136}

Gait variability was assessed by examining the time series of lower extremity joint and trunk sagittal and frontal plane kinematics during walking. Participants were asked to walk on a motor-driven treadmill (Cambridge Model 3050, Quinton Instruments Inc., Seattle, MA) for three minutes at their selected speed (Figure 3-7) while kinematic data were captured using 12 Eagle digital cameras (Motion Analysis Corporation, Santa Rosa, CA) and Cortex 3.6.1 motion capture/processing software (Motion Analysis Corporation, Santa Rosa, CA). A self-selected speed was determined during an 8-min warm-up.\textsuperscript{257,258} The inclination of the treadmill was set to 0. Fifty-six retroreflective markers with double-side adhesive tape were placed on selected anatomical landmarks of the lower leg, the pelvis, the shoulder, and the neck (Figure 3-8). Markers were affixed bilaterally at: (1) iliac crest; (2) anterior superior iliac spine; (3) posterior superior iliac spine; (4) greater trochanter; (5) thigh clusters consisting of four lateral markers; (6) anterior distal thigh; (7) lateral femoral epicondy; (8) medial femoral epicondy; (9) patella; (10) tibial tuberosity; (11) anterior distal shank; (12) shank cluster consisting four lateral markers; (13) lateral malleolus; (14) medial malleolus; (15) anterior distal lower leg; (16) 1\textsuperscript{st} metatarsal
(MT) head; (17) top of 2nd MT head; (18) 5th MT base; (19) dorsal surface of navicular; (20) posterior aspect of calcaneus; and (21) acromioclavicular joints, as well as a single marker on the sacrum and C7. All gait data were sampled at 200 Hz. The sagittal plane kinematics at hip, knee, ankle, and trunk were processed in Visual 3D (C-Motion, Germantown, MD).

The ApEn for each gait data were calculated with a custom MATLAB file (Mathworks, Inc., Natick, MA). The ApEn quantifies irregularity of a kinematic time series and generates a number from 0 to 2. A value of ApEn closer to 0 indicates a more periodic and regular pattern, and its value closer to 2 indicates a more random and irregular pattern. It has been suggested that filtering the data may eliminate important information and provide a skewed view of inherent variability of the sensorimotor system. Therefore, the kinematic data were unfiltered for ApEn calculation to get a more accurate representation of the variability within the sensorimotor system. The ApEn mathematical algorithms have been previously described in detail. Each kinematic time series from the testing trials contains 36,000 data points. Input parameters for our ApEn calculation were (1) a series length (m) of 2 data points, (2) a tolerance widow (r) normalized to 0.2 times the standard deviation of individual time series, and (3) a lag value of 10.
**Figure 3-7. Treadmill Walking** (A: Experimental set-up, B: Visual 3D software for post processing, C: Cortex software for capturing 3D motion)

**Figure 3-8. Retroflective Markers Placement**
3.3.3 Postural Control Measures

3.3.3.1 Static Postural Control

Static postural control was assessed during a single-leg balance task with eyes-closed. It has been shown that measures of a single-leg balance with eyes-closed were consistently different between participants with and without PAI. A AMTI OR6 force platform (50cm × 50cm, Advanced Motion Technology, Inc., Watertown, MA) through National Instruments NI USB-6218 A/D converter (32-inputs, 16-bit, 250kS/s Isolated Multifunction I/O) (National Instruments, Austin, TX) integrated with Cortex 3.6.1 motion capture/processing software was used to record center of pressure (COP) trajectories in the anteroposterior (AP) and mediolateral (ML) directions at a sampling rate of 100Hz during 3, 20-seconds trials, separated by one minute of rest.

Participants were asked to stand in a barefoot single leg stance on the middle of the force plate and keep their hands on the chest while keeping their foot flat on the force platform (Figure 3-9). The non-stance leg was held at 45 degrees of knee flexion and 30 degrees of hip flexion. Participants were allowed three practice trials and then asked to perform three testing trials with their eyes-closed. Participants were instructed to stand for 20 seconds while COP data were collected. The trial was failed and repeated if (1) the non-testing limb makes contact on the force plate or the stance limb, (3) participants hop or take a step with the stance limb, and/or (4) they open eyes.

The COP trajectories in the AP and ML directions were calculated using Visual 3D. The COP velocity (COPV) (cm/s) and time-to-boundary (TTB) (sec) in
each direction were calculated with a custom MATLAB file using the method previously described.\textsuperscript{264} To calculate the TTB and COPV, the tested foot was placed in a rectangle denoted on the force plate to allow for separation of the AP and ML components of COP and so that the dimensions of the foot in the X and Y direction are known.\textsuperscript{189,265} The following TTB variables were reported: (1) mean of the TTB minima in the AP (mean TTB-AP) and ML (mean TTB-ML) directions as well as (2) standard deviation (SD) of TTB minima in the AP (SD of TTB-AP) and ML (SD of TTB-ML) directions.\textsuperscript{90,166} In addition to COP data, the amount of failed trials were recoded and compared between groups.

\textbf{Figure 3-9.} A Single-leg Postural Control Testing (A: Participant performing a static postural control task, B: Visual 3D software for post processing, C: Cortex software for capturing 3D motion)
3.3.3.2 Dynamic Postural Control

Dynamic postural control was assessed with the maximum anterior reach distance of the SEBT using a protocol previously recommended (Figure 3-10). The SEBT has been shown to have a good to excellent intra-tester, inter-tester, and test-retest reliability and validity as a functional test to identify dynamic postural control deficits. The anterior reach direction of the SEBT has consistently exhibited differences between individuals with PAI and healthy individuals and is the most predictive of ankle injury risk based on our previous work.

Participants established a stable base of support on the stance (testing) limb with the greater toe placed on the tape measure. While maintaining the base of support and keeping the hands on the hips, participants performed a series of single-limb squats and made an effort to: 1) reach maximally with the non-stance (non-testing) limb in the anterior direction; 2) touch lightly a point with the most distal portion of the toe along the tape measure on the ground, without shifting weight to the foot of the reaching limb or lifting the heel of the stance limb; and 3) return the reaching limb to the start position at the middle of the grid, resuming a stable bilateral stance. A trial was not considered complete and failed if the participant did not keep their hands on their hips, lost their balance, or lifted or shifted any part of the foot of the stance limb from the floor. Failed trials were recoded and compared between groups.

Participants were given four practice trials prior to completing three test trials. Excursion distances, in centimeters, were marked with ink on the tape measure from the point of the tape measure where the greater toe was placed to the
marked point of maximum reach. The average anterior maximum reach distance of three trials was normalized and reported as a percentage of the stance leg length of the participant.  

3.3.4 Mechanical Outcome Measures

3.3.4.1 Closed Chain Ankle Dorsiflexion Range of Motion

The weight-bearing lunge test (WBLT) was used to assess maximal ankle DF-ROM in a WB position (Figure 3-11-A). The WBLT has been shown to have an excellent reliability from previously published literature (ICC =0.97-0.98). Participants performed the WBLT as previously described. The testing limb was
positioned parallel over a measuring tape secured to the floor with the second toe, center of the heel, and knee perpendicular to a wall, while the non-testing limb was placed behind the testing limb on the floor. Participants were instructed to flex the knee of the testing limb to attempt to touch the wall while keeping the heel flat on the floor and the hands on the wall. The testing limb was progressed away from the wall and this movement was repeated until participants could no longer touch the wall with the knee while maintaining the heel flat. Participants were given three practice trials and then completed three testing trials. Distance from the great toe to the wall (cm) was reported.

3.3.4.2 Open Chain Active Ankle Dorsiflexion Range of Motion

Ankle DF-ROM in the NWB position (NWB-DF) was assessed using the sitting straight knee technique, which has demonstrated excellent reliability. Active DF-ROM was selected because we were interested in assessing the quantity of ankle DF-ROM participants with PAI can achieve by themselves, mimicking an open-kinetic position and limitations during the swing phase of gait they are likely to experience. Participants were seated on a treatment table with their knee fully extended with a bubble inclinometer (Fabrication Enterprises, Inc., White Plains New York, USA) attached over the fifth metatarsal using a Velcro strap (Figure 3-11-B). The thigh and lower leg were secured to the table by Velcro straps for stabilization. The ankle was in neutral (0°) off the end of the table. The participant was instructed to actively dorsiflex the ankle until reaching their perceived maximum, and three trials
were recorded in degrees. The mean of three measurements was used for analysis.

3.3.4.3 Ankle Subtalar Joint Laxity

The ankle-subtalar joint stability was assessed using a portable ankle arthrometer (Blue Bay Medical Inc., Navarre, FL) that is a highly reliable and valid instrument for assessing ankle ligamentous laxity.\textsuperscript{274,275} Total anterior-posterior (AP) displacement and inversion/eversion (I-E) motions were recorded using the method previously described (Figure 3-11-C).\textsuperscript{173,276} To record total AP displacement, the ankle was loaded with 125 N of force in the AP direction. An anterior load was applied first from the neutral position, followed by posterior load. The total AP displacement was measured in millimeters and defined as AP laxity. For I-E motions, the ankle was loaded to 4000 N/mm of inversion and eversion torque. Inversion load was applied first from the neutral position, followed by eversion loading. Total I-E motion was defined as I-E laxity and recorded in degrees. Each assessment began with the ankle positioned in 0° of flexion as confirmed by a digital goniometer in a custom LabVIEW program (version 7.1; National Instruments Corp, Austin, TX), which was the measurement reference point. During each trial, participants were instructed to relax and avoid contracting their muscles crossing the ankle joint. Three trials were recorded for each measurement direction. The following measures of the ankle-subtalar joint stability were reported: (1) anterior displacement, (2) posterior displacement, (3) total AP laxity, (4) inversion, (5) eversion, and (6) total I-E laxity.
3.4 Statistical Analysis

Using separate one-way ANOVAs, demographic variables were compared between groups. Because of the ordinal nature, self-reported instability and disability, ankle injury characteristics, and perceptual characteristics were compared using a separate independent samples Kruskal-Wallis test to verify group inclusion. An a priori alpha level was set at $P < 0.05$ using SPSS 21.0 (SPSS, Inc. Chicago, IL.) for Windows for all statistical tests.

Figure 3-11. Mechanical Outcome Measures (A: Weight bearing lunge test, B: Open-chain ankle dorsiflexion measure with a bubble goniometer, C: Ankle joint laxity assessment)
**AIM 1:** Based on analysis of the data using skewness and kurtosis tests, as well as a Kolmogorov-Smirnov Z test for normality, the following outcome variables were found not to be normally distributed ($P < 0.05$): $V$: $M_{\max}$ ratio; AMT; CSP; ApEn of the sagittal plane hip kinematics; COPV-AP and ML; mean TTB-ML; and SD of TTB-AP and ML. In order to examine the difference for failed trials during postural assessment and each outcome variable that was not normally distributed, a separate independent samples Kruskal-Wallis test was performed. In the event of statistical significance, a Mann-Whitney U test was used as *post-hoc* analysis.

For sensorimotor outcome variables that were found to be normally distributed ($H_{\max}$:$M_{\max}$ ratio, ApEn of the frontal plane hip kinematics, sagittal and frontal planes trunk, knee, and ankle kinematics, mean TTB-AP, and SEBT-A), one-way ANOVAs were performed to examine differences between groups. For each mechanical outcome variable, a separate ANCOVA was used to examine difference between groups. The covariate was sex because the sample size for male and female differed among the groups, and it has been suggested that sex difference may influence mechanical joint stability.²⁷⁶ Fisher’s LSD *post-hoc* testing was used in the event of statistical significance. Any corrections for multiple comparisons of sensorimotor and mechanical outcome measures on the alpha level were not performed in order to protect against type II errors.²⁷⁷

Cohen’s $d$ effect sizes using the means and pooled standard deviations were calculated, along with 95% confidence interval (CI) to determine the magnitude of differences in dependent variables between groups. The strength of effect sizes was interpreted as weak ($d < 0.40$), moderate ($0.40 \leq d < 0.80$), and strong ($d \geq 0.80$).²⁷⁸
AIM 2: In order to further the understanding of the sensorimotor or mechanical alterations associated with PAI by establishing which specific measures best differentiate between the PAI (RAS-PI, RAS, FAI, coper) and control groups, DFA was performed using dependent variables that were significantly different between the PAI and control groups. Because this was an exploratory analysis, dependent variables that approached statistical significance ($P < 0.07$) or produced large effect size ($d > 0.80$) in the PAI group compared to the coper or control group were also included in the DFA. The group variable was dichotomous, and significant factors were the dependent variables in the DFA. All significant factors were entered into the DFA to establish the best set of indicators of group membership. Standardized canonical discriminant function coefficients and a structural matrix were used to assess the contribution of each individual indicator on the determination of group memberships. The higher standardized canonical coefficients indicate that the variables with the high standardized coefficients have greater ability to differentiate groups. Any factors with a loading of 0.30 or greater in the structure matrix were considered to be important in the DFA.
Chapter 4

Results

4.1 Specific Aim 1: Five Groups Comparison

4.1.1 Group Demographics and Injury Characteristics

A total of 87 participants volunteered for the current study and were initially allocated to the five participant groups (RAS-PI = 24, RAS = 11, FAI = 12, Coper = 16, control = 24). Demographic characteristics and physical activity level did not differ among the groups (Table 4.1). The self-reported ankle instability and disability differed among the groups, with the RAS-PI and FAI groups scoring significantly higher on the AII and IdFAI and lower on the FAAM compared to the RAS, coper, and control groups ($P < 0.001$, Figure 4-1 and 4-2). Additional ankle injury characteristic information is provided in Table 4.1.

For perceptual characteristics, there were significant differences in the physical component summary, physical function, and bodily pain domain scale of the SF-36 ($P < 0.05$, Figure 4-2), as well as restless and isolation factors of the PRSII ($P < 0.05$, Table 4.2).
Table 4.1 Group demographic and ankle injury characteristic information as well as the ankle instability instrument (AI), identification of functional ankle instability (FAIM), foot and ankle ability measure (FAAM) Scores for five groups

<table>
<thead>
<tr>
<th>Mean (SD)</th>
<th>Posttraumatic Ankle Instability</th>
<th>Control (N = 24)</th>
<th>P-value (F_{4,86} or H_{4})</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RAS-PI (N = 24)</td>
<td>FAI (N = 11)</td>
<td>RAS (N = 12)</td>
</tr>
<tr>
<td>Sex</td>
<td>M: 14 M: 5</td>
<td>M: 4 M: 6</td>
<td>M: 6</td>
</tr>
<tr>
<td></td>
<td>F: 10 F: 6</td>
<td>F: 8 F: 10</td>
<td>F: 15</td>
</tr>
<tr>
<td>Age (years)</td>
<td>22.54 22.27</td>
<td>20.83 21.06</td>
<td>21.54</td>
</tr>
<tr>
<td></td>
<td>(4.05) (4.98)</td>
<td>(3.45) (3.30)</td>
<td>(0.694)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>171.56 169.68</td>
<td>165.76 167.76</td>
<td>166.82</td>
</tr>
<tr>
<td></td>
<td>(8.83) (9.62)</td>
<td>(6.54) (11.57)</td>
<td>(7.82) (1.260)</td>
</tr>
<tr>
<td>Body Mass (kg)</td>
<td>76.38 74.35</td>
<td>65.67 73.00</td>
<td>67.28</td>
</tr>
<tr>
<td></td>
<td>(15.06) (22.55)</td>
<td>(11.77) (17.92)</td>
<td>(13.49) (1.508)</td>
</tr>
<tr>
<td>Physical Activity Level (day/wk)</td>
<td>3.96 3.91</td>
<td>4.08 3.63</td>
<td>3.88</td>
</tr>
<tr>
<td></td>
<td>(2.10) (1.70)</td>
<td>(2.15) (1.45)</td>
<td>(1.39) (0.161)</td>
</tr>
<tr>
<td>Physical Activity Level (hour/day)</td>
<td>1.43 1.05</td>
<td>1.46 1.11</td>
<td>1.03</td>
</tr>
<tr>
<td></td>
<td>(0.89) (0.52)</td>
<td>(1.01) (0.56)</td>
<td>(0.45) (1.080)</td>
</tr>
<tr>
<td>All</td>
<td>5.96† 2.82</td>
<td>5.75 2.19‖</td>
<td>0.00</td>
</tr>
<tr>
<td></td>
<td>(1.43) (1.08)</td>
<td>(1.48) (1.11)</td>
<td>(0.00) (75.328)</td>
</tr>
<tr>
<td>IdFAI</td>
<td>18.85† 5.91</td>
<td>15.50† 4.13‖</td>
<td>0.00</td>
</tr>
<tr>
<td></td>
<td>(3.53) (2.81)</td>
<td>(2.71) (3.93)</td>
<td>(0.00) (77.299)</td>
</tr>
<tr>
<td># of ankle sprain</td>
<td>3.79† 3.10†</td>
<td>1.00‖ 1.00‖</td>
<td>0.00</td>
</tr>
<tr>
<td>Time since last LAS (month)</td>
<td>35.54 67.64</td>
<td>51.50 37.31</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>(30.47) (63.79)</td>
<td>(34.27) (25.27)</td>
<td>-</td>
</tr>
<tr>
<td># of giving-way (last 6 months)</td>
<td>9.17† 0.27</td>
<td>6.92 0.06</td>
<td>0.00</td>
</tr>
<tr>
<td></td>
<td>(19.81) (0.47)</td>
<td>(6.57) (0.25)</td>
<td>(0.00) (75.255)</td>
</tr>
<tr>
<td>Modified Physical Activity</td>
<td>Y: 8† Y: 0</td>
<td>Y: 3† Y: 0</td>
<td>Y: 0</td>
</tr>
<tr>
<td></td>
<td>N: 16 N: 9</td>
<td>N: 16 N: 24</td>
<td>N: 24</td>
</tr>
<tr>
<td>Feel Risk Re-injury</td>
<td>Y: 8† Y: 4</td>
<td>Y: 0 Y: 0</td>
<td>Y: 0</td>
</tr>
<tr>
<td></td>
<td>N: 8 N: 8</td>
<td>N: 16 N: 24</td>
<td>N: 24</td>
</tr>
<tr>
<td>Environmental Concern</td>
<td>Y: 9† Y: 2†</td>
<td>Y: 4† Y: 1</td>
<td>Y: 0</td>
</tr>
<tr>
<td></td>
<td>N: 15 N: 9</td>
<td>N: 16 N: 24</td>
<td>N: 24</td>
</tr>
<tr>
<td>FAAM-ADL (%)</td>
<td>90.00† 97.82</td>
<td>90.95† 99.48</td>
<td>99.95</td>
</tr>
<tr>
<td></td>
<td>(8.68) (2.83)</td>
<td>(8.42) (0.98)</td>
<td>(0.24) (55.444)</td>
</tr>
<tr>
<td>FAAM-S (%)</td>
<td>79.08† 94.95†</td>
<td>87.47† 98.49</td>
<td>99.61</td>
</tr>
<tr>
<td></td>
<td>(11.57) (5.48)</td>
<td>(10.34) (3.36)</td>
<td>(1.92) (60.983)</td>
</tr>
</tbody>
</table>

† Significant differences compared to the RAS, coper, and control groups (p < 0.05)

^ Significant differences compared to the FAI, coper, and control groups (p < 0.05)

‡ Significant differences compared to the coper and control groups (p < 0.05)

‖ Significant difference compared to the control group (p < 0.05),

ADL = Activities of daily living; RAS-PI = Recurrent ankle sprain with perceived instability; RAS = Recurrent ankle sprain; FAI = Functional ankle instability
Figure 4-1. Ankle Injury Characteristics Information for Five Groups

* Significant differences compared to the RAS, coper, and control groups (p < 0.05)
^ Significant differences compared to the FAI, coper, and control groups (p < 0.05)

Figure 4-2. Perceptual Information for Five Groups

* Significant differences compared to the RAS, coper, and/or control groups (p < 0.05)
† Significant differences compared to the FAI, RAS, coper, and control groups (p < 0.05)
∥ Significant differences compared to the control group (p < 0.05)
Table 4.2 Perceptual characteristic information for five groups

<table>
<thead>
<tr>
<th>Mean (±SD)</th>
<th>Posttraumatic Ankle Instability</th>
<th>Control (N = 21)</th>
<th>p-value (H₄)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RAS-PI (N = 21)</td>
<td>RAS (N = 11)</td>
<td>FAI (N = 12)</td>
<td>Coper (N = 16)</td>
</tr>
<tr>
<td>Tampa Scale</td>
<td>Kinesiophobia</td>
<td>Physical component</td>
<td>Physical function</td>
</tr>
<tr>
<td>32.50</td>
<td>(4.74)</td>
<td>54.50*</td>
<td>55.70*</td>
</tr>
<tr>
<td>Kinesiophobia</td>
<td></td>
<td>(3.88)</td>
<td>(4.08)</td>
</tr>
<tr>
<td></td>
<td>Physical component</td>
<td>56.80</td>
<td>(4.96)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>52.81*</td>
<td>(3.71)</td>
</tr>
<tr>
<td></td>
<td>Physical function</td>
<td>56.20</td>
<td>(2.74)</td>
</tr>
<tr>
<td></td>
<td>Role-physical</td>
<td>28.88</td>
<td>(5.07)</td>
</tr>
<tr>
<td></td>
<td>Bodily pain</td>
<td>0.228</td>
<td>(5.63)</td>
</tr>
<tr>
<td></td>
<td>General health</td>
<td>0.017</td>
<td>(12.01)</td>
</tr>
<tr>
<td></td>
<td>Vitality</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Social functioning</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Role-emotional</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mental health</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Devastation</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Reorganization</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Feeling-Cheated</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Restlessness</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Isolation</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Significant differences compared to the RAS, coper, and/or control groups (p < 0.05)

^ Significant differences compared to the FAI, coper, and control groups (p < 0.05)

‖ Significant difference compared to the control group (p < 0.05)

Norm-based measures have population mean of 50 and am SD of 10.

PCS = Physical component summary; MCS = Mental component summary, RAS-PI = Recurrent ankle sprain with perceived instability; RAS = Recurrent ankle sprain; FAI = Functional ankle instability.
4.1.2 Neural Excitability Outcome Measures

Spinal reflex excitability (H_max:M_max ratio) of the soleus was significantly different among the groups (F_{4,86} = 2.643, P = 0.039, Figure 4-3). Group means and standard deviations for neural excitability outcome measures are reported in Table 4.3, and corresponding effect sizes are found in Figure 4-5 to 4-14. Post-hoc analyses revealed that the RAS-PI group had lower H_max:M_max ratio compared to the RAS (P = 0.004), coper (P = 0.048), and control groups (P = 0.043). However, there was no difference in H:M ratio between the RAS-PI and FAI groups (P = 0.471). These findings were supported by effect sizes for H_max:M_max ratio that were moderate between the RAS-PI and control groups (d = -0.63, 95% CIs: -1.14, -0.003, Figure 4-5) and large between the RAS-PI and RAS groups (d = -1.06, 95% CIs: -1.79, -0.28, Figure 4-8). No differences in H_max:M_max ratio were observed among the FAI, RAS, coper, control groups (p > 0.05). However, large effect size for H_max:M_max ratio was noted between the RAS and FAI groups (d = 0.88, 95% CIs: 0.003, 1.71, Figure 4-11).

V: M_max ratio did not differ among the groups (H_4 = 9.069, P = 0.059, Figure 4-3). However, group differences in V: M_max ratio approached to significant. Moderate to large effect sizes were found for V: M_max ratio between the RAS-PI and ankle sprain coper groups (d = -0.79, 95% CIs: -1.42, -0.11, Figure 4-6) as well as between the coper and control group (d = 0.91, 95% CIs: 0.23, 1.56, Figure 4-14) respectively. This may indicate that ankle sprain copers had greater V: M_max ratio compared to participants with RAS-PI and healthy controls.

Corticospinal excitability variables were obtained from 69 out of 87 participants (RAS: n = 19, RAS: n = 10, FAI: n = 11, Coper: n = 9, control: n = 20). Eleven
participants were excluded from TMS testing, and we could not identify AMT of the soleus from seven participants. Therefore, a total of 18 participants were excluded from the analysis. No significant group differences were observed for AMT ($H_4 = 0.2778, P = 0.596$) and CSP ($H_4 = 3.338, P = 0.503$) for the soleus.

**Figure 4-3. Neural Excitability Outcome Measures for Five Groups**
*Significant differences compared to the RAS, coper, and/or control groups ($p < 0.05$)
|| Moderate to large effect sizes compared to the control group ($d > 0.79$)
Table 4.3 Group means and standard deviation for neural excitability outcome measures for five groups

<table>
<thead>
<tr>
<th></th>
<th>Mean ± SD (95% CIs)</th>
<th>Posttraumatic Ankle Instability</th>
<th>Control</th>
<th>P-value (F_{4,86} or H_4)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>RAS-PI</td>
<td>RAS</td>
<td>FAI</td>
</tr>
<tr>
<td>H:M ratio</td>
<td>0.39±0.19 ††</td>
<td>0.61±0.21</td>
<td>0.44±0.15</td>
<td>0.52±0.25</td>
</tr>
<tr>
<td></td>
<td>(0.31, 0.48)</td>
<td>(0.46, 0.75)</td>
<td>(0.35, 0.54)</td>
<td>(0.39, 0.65)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>P-values</td>
<td></td>
<td>D-values</td>
</tr>
<tr>
<td>V:M ratio</td>
<td>0.22±0.16</td>
<td>0.34±0.26</td>
<td>0.26±0.26</td>
<td>0.39±0.28 ††</td>
</tr>
<tr>
<td></td>
<td>(0.15, 0.29)</td>
<td>(0.17, 0.51)</td>
<td>(0.10, 0.43)</td>
<td>(0.24, 0.54)</td>
</tr>
<tr>
<td>TMS</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AMT</td>
<td>42.29±13.40</td>
<td>39.70±7.60</td>
<td>36.82±6.82</td>
<td>45.11±16.49</td>
</tr>
<tr>
<td></td>
<td>(35.70, 48.62)</td>
<td>(34.26, 45.14)</td>
<td>(32.23, 41.40)</td>
<td>(32.44, 37.79)</td>
</tr>
<tr>
<td>CSP</td>
<td>53.73±15.88</td>
<td>53.50±20.81</td>
<td>44.42±19.68</td>
<td>48.02±19.03</td>
</tr>
<tr>
<td></td>
<td>(44.94, 62.52)</td>
<td>(31.66, 75.34)</td>
<td>(26.23, 62.62)</td>
<td>(28.05, 67.99)</td>
</tr>
</tbody>
</table>

† Indicates significant differences compared to the RAS, coper, and control groups (p < 0.05)
†† Indicates a large Cohen’s d effect size was observed compared to the control groups (d > 0.80)

RAS-PI = Recurrent ankle sprain with perceived instability; RAS = Recurrent ankle sprain; FAI = Functional ankle instability; AMT = Active motor threshold; SICI = Cortical silent period; TMS = Transcranial magnetic stimulation

4.1.3 Postural Control Outcome Measures

For static postural control, there were statistically significant differences in the COPV-AP (H_4 = 14.574, P = 0.006) and COPV-ML (H_4 = 10.542, P = 0.032) among the groups (Figure 4-4 and Table 4.4). Post-hoc and effect size analysis revealed that participants with RAS-PI demonstrated larger COPV-AP and COPV-ML compared to ankle sprain copers (COPV-AP: U_4 = 71.50, z = -3.327, P = 0.001, d = 0.86, 95% CIs: 0.18, 1.50, COPV-ML: U_4 = 112.00, z = -2.209, P = 0.027, d = 0.62, 95% CIs: -0.04, 1.25) (Figure 4-6) and healthy controls (COPV-AP: U_4 = 153.50, z = -2.774, P = 0.006, d = 0.75, 95% CIs: 0.15, 1.31, COPV-ML: U_4 = 145.50, z = -2.938, P = 0.003, d = 0.66, 95% CIs: 0.07, 1.23) (Figure 4-5).

For the TTB measures of static postural control, no differences were observed.
among the groups ($P > 0.05$, Table 4.4). However, effect size analysis revealed that the RAS-PI group had lower mean TTB-ML ($d = -0.77$, 95% CIs: -1.34, -0.17) and SD of TTB-ML ($d = -0.82$, 95% CIs: -1.39, -0.21) compared to the control group (Figure 4-5). The RAS-PI group had lower mean TTB-AP compared to the ankle sprain coper group ($d = -0.89$, 95% CIs: -1.54, -0.21, Figure 4-6). There was no difference in the amount of failed trials during static postural control assessment ($H_4 = 2.553$, $P = 0.635$).

For dynamic postural control assessment, normalized reaching distance of the SEBT-A did not differ among the groups ($F_{4,86} = 0.672$, $P = 0.613$, Table 4.4). Small to moderate effect sizes were observed for %MAXD of the SEBT-A (Figure 4-5 to 4-14). No group differences were found in the amount of failed trial during the SEBT-A ($H_4 = 6.520$, $P = 0.164$).

**Figure 4-4. Static Postural Control Outcome Measures for Five Groups**

*Significant differences compared to the coper and control groups ($p < 0.05$)¶
¶ Moderate to large effect sizes compared to the control group ($d > 0.75$)
### Table 4.4 Group means and standard deviation for postural control outcome measures for five groups

<table>
<thead>
<tr>
<th>Mean ± SD (95% CIs)</th>
<th>Posttraumatic Ankle Instability</th>
<th>Control</th>
<th>P-value (F_{4,86} or H_4)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RAS-PI</td>
<td>RAS</td>
<td>FAI</td>
</tr>
<tr>
<td>COPV (cm/s)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AP</td>
<td>4.51±1.43* (3.90, 5.11)</td>
<td>3.99±0.65 (3.56, 4.43)</td>
<td>4.01±0.90 (3.44, 4.58)</td>
</tr>
<tr>
<td>ML</td>
<td>6.36±3.71* (4.79, 7.92)</td>
<td>4.83±2.06 (3.45, 6.21)</td>
<td>4.92±1.64 (3.88, 5.96)</td>
</tr>
<tr>
<td>Mean TTB (s)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AP</td>
<td>3.18±0.86* (2.82, 3.54)</td>
<td>3.33±0.99 (2.66, 3.99)</td>
<td>3.40±0.81 (2.88, 3.92)</td>
</tr>
<tr>
<td>ML</td>
<td>1.28±0.52 (1.06, 1.07)</td>
<td>2.78±4.10 (0.03, 5.54)</td>
<td>1.54±0.53 (1.20, 1.88)</td>
</tr>
<tr>
<td>SD TTB (s)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AP</td>
<td>3.47±1.26 (2.94, 4.00)</td>
<td>3.30±1.30 (2.43, 4.17)</td>
<td>4.02±1.62 (2.99, 5.05)</td>
</tr>
<tr>
<td>ML</td>
<td>1.41±0.52* (1.19, 1.63)</td>
<td>2.73±3.71 (0.24, 5.22)</td>
<td>1.68±0.55 (1.33, 2.03)</td>
</tr>
<tr>
<td>Failed Trials</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Static Postural</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>4.67±6.53 (3.73±4.36)</td>
<td>1.75±1.96 (1.06±3.89)</td>
<td>4.06±3.89 (3.75±4.28)</td>
</tr>
<tr>
<td>SEBT-A</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>%MA</td>
<td>67.38±6.17 (64.87, 69.99)</td>
<td>69.28±7.55 (64.21, 74.35)</td>
<td>67.90±7.37 (63.22, 72.59)</td>
</tr>
<tr>
<td>%MAXD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Failed Trials</td>
<td>0.46±0.66 (0.36±0.50)</td>
<td>0.08±0.29 (0.38±0.62)</td>
<td>0.17±0.48 (0.38±0.62)</td>
</tr>
</tbody>
</table>

* Indicates a significant difference among groups (p<0.05)
# Indicates significant differences compared to the coper and control groups (p < 0.05)
\* Indicates a moderate or large Cohen’s d effect size was observed compared to the control groups (d > 0.75)

**RAS-PI** = Recurrent ankle sprain with perceived instability; **RAS** = Recurrent ankle sprain; **FAI** = Functional ankle instability; **COPV** = Center of pressure velocity; **AP** = Anteroposterior; **ML** = Mediolateral; **TTB** = Time to boundary, **SEBT-A** = Anterior research direction of the Star Excursion Balance Test; **%MAXD** = Normalized reach distance by participant’s stance leg

### 4.1.4 Variability of Locomotor Patterns during Walking

No significant group differences were noted for the self-selected walking speed ($F_{4,86} = 0.706, P = 0.590$) (Table 4.5). There were no differences in any ApEn values among the groups ($P > 0.05$, Table 4.5). However, effect size analysis revealed that the RAS group demonstrated less ApEn of the frontal plane ankle kinematics compared to
the FAI group ($d = -0.91$, 95% CIs: -1.73, -0.02, Figure 4-11), and the ankle sprain cope group exhibited less ApEn of the frontal plane ankle kinematics compared to the control group ($d = -0.67$, 95% CIs: -1.30, -0.001, Figure 4-14).

Table 4.5 Group means and standard deviation for approximate entropy values for five groups

<table>
<thead>
<tr>
<th>Mean ± SD (95% CIs)</th>
<th>Posttraumatic Ankle Instability</th>
<th>Control</th>
<th>$P$-value ($F_{4,56}$ or $H_4$)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RAS-PI</td>
<td>RAS</td>
<td>FAI</td>
</tr>
<tr>
<td><strong>Trunk</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sagittal</td>
<td>1.01±0.25</td>
<td>1.00±0.31</td>
<td>1.03±0.35</td>
</tr>
<tr>
<td>(0.90, 1.11)</td>
<td>(0.79, 1.21)</td>
<td>(0.81, 1.25)</td>
<td>(0.83, 1.07)</td>
</tr>
<tr>
<td>Frontal</td>
<td>0.82±0.16</td>
<td>0.86±0.25</td>
<td>0.79±0.15</td>
</tr>
<tr>
<td>(0.75, 0.90)</td>
<td>(0.69, 1.03)</td>
<td>(0.69, 0.88)</td>
<td>(0.73, 0.88)</td>
</tr>
<tr>
<td><strong>Hip</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sagittal</td>
<td>0.23±0.06</td>
<td>0.24±0.05</td>
<td>0.21±0.04</td>
</tr>
<tr>
<td>(0.20, 0.25)</td>
<td>(0.20, 0.28)</td>
<td>(0.20, 0.24)</td>
<td>(0.20, 0.24)</td>
</tr>
<tr>
<td>Frontal</td>
<td>0.55±0.12</td>
<td>0.55±0.09</td>
<td>0.52±0.20</td>
</tr>
<tr>
<td>(0.50, 0.60)</td>
<td>(0.49, 0.62)</td>
<td>(0.39, 0.64)</td>
<td>(0.47, 0.55)</td>
</tr>
<tr>
<td><strong>Knee</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sagittal</td>
<td>0.32±0.03</td>
<td>0.30±0.06</td>
<td>0.30±0.03</td>
</tr>
<tr>
<td>(0.30, 0.33)</td>
<td>(0.28, 0.37)</td>
<td>(0.28, 0.32)</td>
<td>(0.32, 0.04)</td>
</tr>
<tr>
<td>Frontal</td>
<td>0.79±0.24</td>
<td>0.80±0.35</td>
<td>0.79±0.29</td>
</tr>
<tr>
<td>(0.69, 0.89)</td>
<td>(0.56, 1.03)</td>
<td>(0.61, 0.98)</td>
<td>(0.58, 0.86)</td>
</tr>
<tr>
<td><strong>Ankle</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sagittal</td>
<td>0.59±0.10</td>
<td>0.56±0.09</td>
<td>0.56±0.12</td>
</tr>
<tr>
<td>(0.55, 0.63)</td>
<td>(0.50, 0.62)</td>
<td>(0.48, 0.63)</td>
<td>(0.49, 0.60)</td>
</tr>
<tr>
<td>Frontal</td>
<td>1.03±0.26</td>
<td>0.95±0.24</td>
<td>1.15±0.19</td>
</tr>
<tr>
<td>(0.92, 1.14)</td>
<td>(1.03, 1.27)</td>
<td>(1.03, 1.27)</td>
<td>(1.01, 1.22)</td>
</tr>
<tr>
<td>Walking speed (km/h)</td>
<td>4.29±0.89</td>
<td>4.14±0.79</td>
<td>4.40±0.80</td>
</tr>
</tbody>
</table>

**RAS-PI** = Recurrent ankle sprain with perceived instability; **RAS** = Recurrent ankle sprain; **FAI** = Functional ankle instability

† Indicates a large Cohen’s $d$ effect size was observed compared to the FAI group ($d = -0.91$)

* Indicates a moderate Cohen’s $d$ effect size was observed compared to the control group ($d = -0.67$)

### 4.1.5 Mechanical Outcome Measures

The ANCOVA models demonstrated no significant group difference in the
WBLT, NWB-DF, as well as the ankle joint laxity measures after controlling for the variance contributed by sex \((P > 0.05, \text{Table 4.6})\). The range of effect sizes for mechanical outcome variables were small to large, with large 95% CIs crossing zero (Figure 4-5 to 4-14).

<table>
<thead>
<tr>
<th>Mean ± SD (95% CIs)</th>
<th>Posttraumatic Ankle Instability</th>
<th>Control</th>
<th>(P)-value ((F_{4,86}))</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RAS-PI</td>
<td>RAS</td>
<td>FAI</td>
</tr>
<tr>
<td><strong>WBLT (cm)</strong></td>
<td>12.79±3.49 (11.32, 14.26)</td>
<td>10.28±4.06 (7.55, 13.02)</td>
<td>11.27±5.23 (7.95, 14.59)</td>
</tr>
<tr>
<td><strong>NWB-DF (°)</strong></td>
<td>14.10±4.52 (12.19, 16.01)</td>
<td>16.03±4.32 (13.13, 18.93)</td>
<td>14.95±4.31 (12.21, 17.68)</td>
</tr>
<tr>
<td></td>
<td>Ankle Joint Laxity</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Anterior (mm)</strong></td>
<td>11.80±3.70 (10.24, 13.37)</td>
<td>11.41±2.81 (9.53, 13.30)</td>
<td>11.68±3.69 (9.33, 14.02)</td>
</tr>
<tr>
<td></td>
<td>Posterior (mm)</td>
<td>9.17±3.25 (7.80, 10.55)</td>
<td>8.54±2.30 (6.99, 10.09)</td>
</tr>
<tr>
<td><strong>AP total (mm)</strong></td>
<td>20.92±5.93 (18.41, 23.42)</td>
<td>19.93±4.15 (17.15, 22.73)</td>
<td>20.11±5.12 (16.86, 23.36)</td>
</tr>
<tr>
<td><strong>Inversion (°)</strong></td>
<td>37.70±10.61 (33.21, 42.18)</td>
<td>37.14±6.02 (33.09, 41.18)</td>
<td>36.46±10.01 (30.10, 42.82)</td>
</tr>
<tr>
<td><strong>Eversion (°)</strong></td>
<td>22.00±5.94 (19.50, 24.51)</td>
<td>20.85±3.28 (18.64, 23.05)</td>
<td>26.82±8.51 (20.88, 31.69)</td>
</tr>
<tr>
<td><strong>I-E total (°)</strong></td>
<td>59.65±14.20 (53.66, 65.65)</td>
<td>58.88±7.92 (53.56, 64.20)</td>
<td>59.36±11.52 (52.04, 66.68)</td>
</tr>
</tbody>
</table>

**RAS-PI** = Recurrent ankle sprain with perceived instability; **RAS** = Recurrent ankle sprain; **FAI** = Functional ankle instability; **WBLT** = Weight bearing lunge test, **NWB-DF** = Non-weight bearing dorsiflexion **AP** = Anteroposterior; **I-E** = Inversion-Eversion.
Figure 4-5. Effect Sizes for each Outcome Measures (RAS-PI vs. Control)

- H:M [0.63 (-1.19, -0.003)]
- V:M [0.22 (-0.35, 0.78)]
- AMT [-0.02 (-0.65, 0.60)]
- CSP [0.46 (-0.29, 1.17)]
- COPV-AP [0.75 (0.15, 1.31)]
- COPV-ML [0.66 (0.07, 1.23)]
- TTB-mean AP [-0.50 (-1.07, 0.08)]
- TTB-mean ML [-0.77 (-1.34, -0.17)]
- TTB-SD AP [-0.40 (-0.96, 0.18)]
- TTB-SD ML [0.82 (-1.39, -0.21)]
- ApEn Trunk sagittal [-0.25 (-0.81, 0.33)]
- ApEn Hip sagittal [-0.06 (-0.63, 0.51)]
- ApEn Knee sagittal [-0.03 (-0.59, 0.54)]
- ApEn Ankle sagittal [0.41 (-0.17, 0.97)]
- ApEn Trunk Frontal [-0.20 (-0.76, 0.37)]
- ApEn Hip Frontal [0.09 (-0.47, 0.66)]
- ApEn Knee Frontal [0.01 (-0.55, 0.58)]
- ApEn Ankle Frontal [-0.34 (-0.91, 0.23)]
- SEBT-A [-0.04 (-0.60, 0.53)]
- WBLT [0.57 (-0.01, 1.14)]
- NWB-DF [-0.02 (-0.58, 0.55)]
- Laxity-A [-0.05 (-0.61, 0.52)]
- Laxity-P [0.14 (-0.43, 0.70)]
- Laxity-AP total [0.02 (-0.54, 0.59)]
- Laxity-I [0.25 (-0.33, 0.81)]
- Laxity-E [-0.34 (-0.90, 0.24)]
- Laxity-IE total [0.10 (-0.46, 0.67)]
Figure 4-6. Effect Sizes for each Outcome Measures (RAS-PI vs. Coper)

- H:M [-0.59 (-1.23, 0.07)]
- VM [-0.79 (-1.42, -0.11)]
- AMT [-0.20 (-0.99, 0.60)]
- CSP [0.34 (-0.62, 1.28)]
- COPV-AP [0.86 (0.18, 1.50)]
- COPV-ML [0.62 (-0.04, 1.25)]
- TTB-mean AP [0.89 (-1.54, -0.21)]
- TTB-mean ML [-0.57 (-1.20, 0.09)]
- TTB-SD AP [-0.62 (-1.26, 0.04)]
- TTB-SD ML [-0.50 (-1.13, 0.15)]
- ApEn Trunk sagittal [0.26 (-0.38, 0.89)]
- ApEn Hip sagittal [0.20 (-0.44, 0.83)]
- ApEn Kace sagittal [0.51 (-0.15, 1.14)]
- ApEn Ankle sagittal [0.48 (-0.17, 1.11)]
- ApEn Trunk Frontal [0.10 (-0.53, 0.739)]
- ApEn Hip Frontal [0.37 (-0.28, 1.00)]
- ApEn Kace Frontal [0.28 (-0.37, 0.91)]
- ApEn Ankle Frontal [0.37 (-0.28, 0.99)]
- SEBT-A [-0.52 (-1.15, 0.14)]
- WBLT [-0.01 (-0.64, 0.62)]
- NWB-DF [-0.29 (-0.92, 0.35)]
- Laxity-A [-0.04 (-0.67, 0.59)]
- Laxity-P [0.09 (-0.54, 0.72)]
- Laxity-AP total [0.02 (-0.61, 0.65)]
- Laxity-I [-0.32 (-0.95, 0.33)]
- Laxity-E [-0.23 (-0.86, 0.41)]
- Laxity-IE total [-0.32 (-0.95, 0.32)]
Figure 4-7. Effect Sizes for each Outcome Measures (RAS-PI vs. FAI)

- H:M [-0.28 (-0.97, 0.42)]
- V:M [-0.20 (-0.89, 0.50)]
- AMT [0.46 (-0.30, 1.20)]
- CSP [0.54 (-0.39, 1.43)]
- COPV-AP [0.39 (-0.32, 1.08)]
- COPV-ML [0.45 (-0.26, 1.14)]
- TTB-mean AP [-0.26 (-0.95, 0.44)]
- TTB-mean ML [-0.49 (-1.18, 0.22)]
- TTB-SD AP [-0.39 (-1.08, 0.31)]
- TTB-SD ML [-0.51 (-1.20, 0.20)]
- ApEn Trunk sagittal [-0.07 (-0.77, 0.61)]
- ApEn Hip sagittal [0.31 (-0.39, 1.00)]
- ApEn Knee sagittal [0.40 (-0.30, 1.09)]
- ApEn Ankle sagittal [0.30 (-0.40, 0.996)]
- ApEn Trunk Frontal [-0.22 (-0.48, 0.91)]
- ApEn Hip Frontal [-0.22 (-0.48, 0.91)]
- ApEn Knee Frontal [-0.01 (-0.70, 0.68)]
- ApEn Ankle Frontal [-0.48 (-1.17, 0.23)]
- SEBT-A [-0.08 (-0.77, 0.62)]
- WBLT [0.37 (-0.34, 1.06)]
- NWB DF [0.19 (0.88, 0.51)]
- Laxity-A [0.03 (-0.66, 0.73)]
- Laxity-P [0.25 (-0.45, 0.94)]
- Laxity-AP total [0.14 (-0.55, 0.83)]
- Laxity-I [0.12 (-0.58, 0.81)]
- Laxity-E [-0.62 (-1.32, 0.10)]
- Laxity-IE total [0.02 (-0.67, 0.71)]
Figure 4-10. Effect Sizes for each Outcome Measures (RAS vs. Coper)

<table>
<thead>
<tr>
<th>Measure</th>
<th>Effect Size (Confidence Interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>H:M</td>
<td>[0.36 (-0.43, 1.12)]</td>
</tr>
<tr>
<td>V:M</td>
<td>[-0.18 (-0.95, 0.59)]</td>
</tr>
<tr>
<td>AMT</td>
<td>[-0.43 (-1.32, 0.50)]</td>
</tr>
<tr>
<td>CSP</td>
<td>[0.27 (-0.88, 1.39)]</td>
</tr>
<tr>
<td>COPV-AP</td>
<td>[0.77 (0.05, 1.54)]</td>
</tr>
<tr>
<td>COPV-ML</td>
<td>[0.20 (-0.57, 0.97)]</td>
</tr>
<tr>
<td>TTB-mean AP</td>
<td>[-0.68 (-1.45, 0.13)]</td>
</tr>
<tr>
<td>TTB-mean ML</td>
<td>[0.47 (-0.32, 1.24)]</td>
</tr>
<tr>
<td>TTB-SD AP</td>
<td>[-0.72 (-1.49, 0.09)]</td>
</tr>
<tr>
<td>TTB-SD ML</td>
<td>[0.46 (-0.33, 1.22)]</td>
</tr>
<tr>
<td>ApEn Trunk sagittal</td>
<td>[0.21 (-0.57, 0.97)]</td>
</tr>
<tr>
<td>ApEn Hip sagittal</td>
<td>[0.48 (-0.32, 1.24)]</td>
</tr>
<tr>
<td>ApEn Knee sagittal</td>
<td>[0.54 (-0.26, 1.30)]</td>
</tr>
<tr>
<td>ApEn Ankle sagittal</td>
<td>[0.21 (-0.57, 0.97)]</td>
</tr>
<tr>
<td>ApEn Trunk Frontal</td>
<td>[0.27 (-0.51, 1.03)]</td>
</tr>
<tr>
<td>ApEn Hip Frontal</td>
<td>[0.50 (-0.28, 1.26)]</td>
</tr>
<tr>
<td>ApEn Knee Frontal</td>
<td>[0.25 (-0.53, 1.01)]</td>
</tr>
<tr>
<td>ApEn Ankle Frontal</td>
<td>[0.11 (-0.66, 0.88)]</td>
</tr>
<tr>
<td>SEBT-A</td>
<td>[0.18 (-0.64, 1.00)]</td>
</tr>
<tr>
<td>WBLT</td>
<td>[-0.74 (-1.51, 0.07)]</td>
</tr>
<tr>
<td>NWB-DF</td>
<td>[0.10 (-0.67, 0.86)]</td>
</tr>
<tr>
<td>Laxity-A</td>
<td>[-0.17 (-0.93, 0.61)]</td>
</tr>
<tr>
<td>Laxity-P</td>
<td>[-0.12 (-0.88, 0.65)]</td>
</tr>
<tr>
<td>Laxity-AP total</td>
<td>[-0.18 (-0.94, 0.60)]</td>
</tr>
<tr>
<td>Laxity-I</td>
<td>[-0.43 (-1.20, 0.35)]</td>
</tr>
<tr>
<td>Laxity-E</td>
<td>[-0.45 (-1.21, 0.34)]</td>
</tr>
<tr>
<td>Laxity-IE total</td>
<td>[-0.42 (-1.18, 0.37)]</td>
</tr>
</tbody>
</table>
Figure 4.11. Effect Sizes for each Outcome Measures (RAS vs. FAI)
Figure 4-12. Effect Sizes for each Outcome Measures (FAI vs. Control)

- H/M [-0.39 (-1.08, 0.32)]
- VM [0.37 (-0.34, 1.06)]
- AMT [-0.60 (-1.33, 0.17)]
- CSP [-0.05 (-0.95, 0.85)]
- COPV-AP [0.44 (-0.27, 1.13)]
- COPV-ML [0.28 (-0.42, 0.97)]
- TTB-mean AP [-0.29 (-0.98, 0.41)]
- TTB-mean ML [-0.32 (-1.01, 0.38)]
- TTB-SD AP [-0.11 (-0.80, 0.58)]
- TTB-SD ML [-0.43 (-1.12, 0.28)]
- ApEn Trunk sagittal [-0.14 (-0.83, 0.56)]
- ApEn Hip sagittal [-0.46 (-1.15, 0.25)]
- ApEn Knee sagittal [-0.38 (-1.07, 0.32)]
- ApEn Ankle sagittal [0.09 (-0.61, 0.78)]
- ApEn Trunk Frontal [-0.38 (-1.07, 0.33)]
- ApEn Hip Frontal [-0.11 (-0.81, 0.58)]
- ApEn Knee Frontal [0.02 (-0.67, 0.71)]
- ApEn Ankle Frontal [0.13 (-0.57, 0.82)]
- SEBT-A [0.04 (-0.65, 0.73)]
- WBLT [0.12 (-0.58, 0.81)]
- NWB-DF [0.15 (-0.55, 0.84)]
- Laxity-A [-0.08 (-0.77, 0.61)]
- Laxity-P [-0.14 (-0.84, 0.55)]
- Laxity-AP total [-0.13 (-0.82, 0.56)]
- Laxity-I [0.13 (-0.56, 0.82)]
- Laxity-E [0.21 (-0.49, 0.90)]
- Laxity-IE total [0.09 (-0.61, 0.78)]
Figure 4-13. Effect Sizes for each Outcome Measures (FAI vs. Coper)

- H: M [-0.37 (-1.11, 0.40)]
- V: M [-0.48 (-1.22, 0.29)]
- AMT [-0.68 (-1.56, 0.25)]
- CSP [0.19 (-1.26, 0.92)]
- COPV-AP [0.67 (-0.11, 1.42)]
- COPV-ML [0.32 (-0.45, 1.06)]
- TTB-mean AP [-0.65 (-1.40, 0.13)]
- TTB-mean ML [-0.02 (-0.77, 0.73)]
- TTB-SD AP [-0.19 (-0.93, 0.57)]
- TTB-SD ML [0.08 (-0.67, 0.82)]
- ApEn Trunk sagittal [-0.25 (-0.83, 0.56)]
- ApEn Hip sagittal [-0.15 (-0.90, 0.60)]
- ApEn Knee sagittal [0.15 (-0.60, 0.90)]
- ApEn Ankle sagittal [0.15 (-0.60, 0.90)]
- ApEn Trunk Frontal [-0.13 (-0.87, 0.63)]
- ApEn Hip Frontal [0.04 (-0.71, 0.79)]
- ApEn Knee Frontal [0.26 (-0.50, 1.01)]
- ApEn Ankle Frontal [0.74 (-0.05, 1.49)]
- SEBT-A [0.40 (-1.14, 0.37)]
- WBLT [-0.38 (-1.13, 0.38)]
- NWB-DF [-0.12 (-0.86, 0.63)]
- Laxity-A [-0.08 (-0.82, 0.67)]
- Laxity-P [-0.16 (-0.91, 0.59)]
- Laxity-AP total [-0.13 (-0.88, 0.62)]
- Laxity-I [-0.45 (-1.19, 0.32)]
- Laxity-E [0.37 (-0.40, 1.11)]
- Laxity-IE total [-0.36 (-1.10, 0.41)]
4.2 Specific Aim 1: Exploratory Three Groups Comparisons

In this current study, PAI was initially subdivided into four groups based on the number of ankle sprains (a single ankle or two or more ankle sprains), the number of giving-way episodes in the ankle, as well as the presence of self-reported instability and disability (Table 3.1). While there were some relation emerging between the five groups based on giving-way and self-reported symptoms, we did not found many differences in sensorimotor outcome measures within these subgroups based on the number of previous ankle sprains. Additionally, self-reported functional levels and perceptual outcome measures did not differ between the RAS-PI and FAI or between the RAS and copers. These findings in the current study indicate that the presence of self-reported instability and repeated episodes of “giving-way” may be more important factors, but the factor of the number of ankle sprains may not be influential. Based on these findings, all participants with RAS-PI and FAI were combined and classified as the PAI group. Participants initially categorized as RAS and ankle sprain copers were combined into the ankle instability coper group. Therefore, as the exploratory aim, we examined the selected same sensorimotor and mechanical outcomes between the PAI, ankle instability copers, and control groups.

4.2.1 Group Demographics and Injury Characteristics

When participants were classified into the more “traditional” three groups (PAI, ankle instability coper, and control), the distribution of participants was as follows: PAI = 36, Coper = 27, Controls = 24. Demographic characteristics and physical activity level
did not differ among the groups (Table 4.7). However, the PAI group scored significantly higher on the AII and IdFAI and lower on the FAAM compared to the ankle instability coper and control groups ($P < 0.001$, Figure 4-15 and 4-16). Ankle injury characteristic information of three groups is provided in Table 4.7.

**Table 4.7 Group demographic and ankle injury characteristic information as well as the Ankle Instability Instrument (AII), Identification of Functional Ankle Instability (IdFAI), Foot and Ankle Ability Measure (FAAM) Scores for three groups**

<table>
<thead>
<tr>
<th>Mean ± SD</th>
<th>PAI (n = 36)</th>
<th>Coper (n = 27)</th>
<th>Control (n = 24)</th>
<th>$P$-value (F$_{2,86}$ or H$_2$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>M: 18</td>
<td>M: 11</td>
<td>M: 9</td>
<td>-</td>
</tr>
<tr>
<td>Age (years)</td>
<td>21.97±3.50</td>
<td>21.56±4.10</td>
<td>21.54±3.30</td>
<td>0.600 (0.514)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>169.62±8.51</td>
<td>168.54±10.67</td>
<td>166.82±7.82</td>
<td>0.867 (0.142)</td>
</tr>
<tr>
<td>Body Mass (kg)</td>
<td>72.81±14.79</td>
<td>73.55±19.53</td>
<td>67.28±13.49</td>
<td>0.505 (0.689)</td>
</tr>
<tr>
<td>Physical Activity Level (day/wk)</td>
<td>4.00±2.08</td>
<td>3.74±1.53</td>
<td>3.88±1.39</td>
<td>0.884 (0.169)</td>
</tr>
<tr>
<td>Physical Activity Level (hour/day)</td>
<td>1.44±0.92</td>
<td>1.08±0.54</td>
<td>1.03±0.45</td>
<td>0.052 (3.69)</td>
</tr>
<tr>
<td>AII</td>
<td>5.89±1.43†</td>
<td>2.44±1.12#</td>
<td>0.00±0.00</td>
<td>&lt;0.001* (74.943)</td>
</tr>
<tr>
<td>IdFAI</td>
<td>17.56±3.56†</td>
<td>4.85±3.57†</td>
<td>0.00±0.00</td>
<td>&lt;0.001* (75.651)</td>
</tr>
<tr>
<td># of LAS</td>
<td>2.86±2.26#</td>
<td>1.85±1.20#</td>
<td>0.00±0.00</td>
<td>&lt;0.001* (56.662)</td>
</tr>
<tr>
<td>Time since last LAS (month)</td>
<td>41.91±32.72</td>
<td>49.67±46.52</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td># of giving-way (last 6 months)</td>
<td>9.11±17.71#</td>
<td>0.15±0.36</td>
<td>0.00 (0.00)</td>
<td>&lt;0.001* (74.874)</td>
</tr>
<tr>
<td>Modified Physical Activity</td>
<td>Y: 11†</td>
<td>Y: 0</td>
<td>Y: 0</td>
<td>0.001* (17.634)</td>
</tr>
<tr>
<td>Feel Risk Re-injury</td>
<td>Y: 20#</td>
<td>Y: 3</td>
<td>Y: 0</td>
<td>&lt;0.001* (27.264)</td>
</tr>
<tr>
<td>Environmental Concern</td>
<td>Y: 13†</td>
<td>Y: 3</td>
<td>Y: 0</td>
<td>0.004* (13.734)</td>
</tr>
<tr>
<td>FAAM-ADL(%)</td>
<td>90.32±8.49†</td>
<td>98.80±2.08</td>
<td>99.95±0.24</td>
<td>&lt;0.001* (52.771)</td>
</tr>
<tr>
<td>FAAM-S (%)</td>
<td>81.88±11.73#</td>
<td>97.05±4.60</td>
<td>99.61±1.92</td>
<td>&lt;0.001* (55.711)</td>
</tr>
</tbody>
</table>

* Indicates significant differences among groups (p<0.05)
† Indicates significant differences compared to the coper and control groups (p < 0.05)
# Indicates significant difference compared to the control groups (p < 0.05)

ADL = Activities of daily living; LAS = lateral ankle sprain; PAI = Posttraumatic ankle instability
Figure 4-15. Ankle Injury Characteristics Information for Three Groups
*Significant differences compared to the ankle instability coper and control groups (p < 0.05)
^ Significant differences compared to the control groups (p < 0.05)

Figure 4-16. Perceptual Information for Three Groups
*Significant differences compared to the ankle instability coper and control groups (p < 0.05)
^ Significant differences compared to the control groups (p < 0.05)
For perceptual characteristics, there were significant differences in the physical component summary, physical function, bodily pain domain, vitality, and social functioning scales of the SF-36 (P < 0.05, Figure 4-16), as well as restless and isolation factors of the PRSII (P < 0.05, Table 4.9). Group means and standard deviations for perceptual characteristic information are reported in Table 4-8.

Table 4.8 Perceptual characteristic information for three groups

<table>
<thead>
<tr>
<th></th>
<th>Mean ± SD</th>
<th>PAI (n = 36)</th>
<th>Coper (n = 27)</th>
<th>Control (n = 24)</th>
<th>P-value (F2,8 or H2)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Tampa Scale Kinesiophobia</strong></td>
<td>Physical Component Summary</td>
<td>53.93±4.27#</td>
<td>56.44±3.80</td>
<td>56.81±2.74</td>
<td>0.002* (12.105)</td>
</tr>
<tr>
<td>Physical function</td>
<td>55.19±3.00#</td>
<td>55.31±8.05</td>
<td>57.01±0.43</td>
<td>0.001* (13.236)</td>
<td></td>
</tr>
<tr>
<td>Role-physical</td>
<td>54.04±6.71</td>
<td>55.42±2.98</td>
<td>55.91±1.43</td>
<td>0.582 (1.083)</td>
<td></td>
</tr>
<tr>
<td>Bodily pain</td>
<td>55.76±4.89#</td>
<td>58.91±6.94</td>
<td>59.05±4.27</td>
<td>0.003* (11.574)</td>
<td></td>
</tr>
<tr>
<td>General health</td>
<td>53.19±8.11#</td>
<td>57.81±5.25</td>
<td>57.55±5.23</td>
<td>0.038 (6.536)</td>
<td></td>
</tr>
<tr>
<td>MCS</td>
<td>50.55±4.27</td>
<td>53.31±6.33</td>
<td>53.66±4.24</td>
<td>0.095 (4.711)</td>
<td></td>
</tr>
<tr>
<td>Vitality</td>
<td>50.52±7.53#</td>
<td>55.69±6.69</td>
<td>54.89±6.13</td>
<td>0.031* (6.923)</td>
<td></td>
</tr>
<tr>
<td>Social functioning</td>
<td>53.50±5.78#</td>
<td>55.46±6.69</td>
<td>56.43±2.42</td>
<td>0.034 (6.768)</td>
<td></td>
</tr>
<tr>
<td>Role-emotional</td>
<td>51.50±9.47</td>
<td>55.30±0.00</td>
<td>55.30±0.00</td>
<td>0.085 (4.921)</td>
<td></td>
</tr>
<tr>
<td>Mental health</td>
<td>51.71±5.39</td>
<td>53.56±7.54</td>
<td>53.20±6.21</td>
<td>0.304 (2.379)</td>
<td></td>
</tr>
<tr>
<td>Devastation</td>
<td>5.42±1.70</td>
<td>5.26±2.03</td>
<td>5.13±1.75</td>
<td>0.588 (1.063)</td>
<td></td>
</tr>
<tr>
<td>Reorganization</td>
<td>10.47±2.47</td>
<td>10.07±3.21</td>
<td>9.92±3.89</td>
<td>0.956 (0.091)</td>
<td></td>
</tr>
<tr>
<td>Feeling-Cheated</td>
<td>5.39±1.76</td>
<td>4.89±1.82</td>
<td>5.21±12.04</td>
<td>0.225 (2.983)</td>
<td></td>
</tr>
<tr>
<td>Restlessness</td>
<td>6.33±2.64#</td>
<td>4.81±1.82</td>
<td>4.88±1.94</td>
<td>0.002* (12.048)</td>
<td></td>
</tr>
<tr>
<td>Isolation</td>
<td>4.672±1.06†</td>
<td>4.37±1.28</td>
<td>4.50±1.25</td>
<td>0.029* (7.074)</td>
<td></td>
</tr>
</tbody>
</table>

*Indicates significant differences among groups (p<0.05)
# Indicates significant differences compared to the coper and control groups (p < 0.05)
† Indicates significant difference compared to the control groups (p < 0.05)
‖ Indicates significant difference compared to the coper group
PAI = Posttraumatic ankle instability; MCS = Mental component summary
4.2.2 Neural Excitability Outcome Measures

Group differences in spinal reflex excitability of the soleus were observed between the PAI, coper, and control groups (F_{2,86} = 4.473, P = 0.014, Table 4-9 and Figure 4-17). Post-hoc testing illustrates that the PAI demonstrated lower H_{max}:M_{max} ratio compared to the coper group (P = 0.005). The differences in H_{max}:M_{max} ratio between the PAI and control groups approached statistical significance (P = 0.057), while a moderate effect size indicating that the PAI group had less soleus excitability at the spinal level (d = -0.56, 95% CIs: -1.07, -0.02, Figure 4-19).

There were significant differences in V: M_{max} ratio of the soleus among the three groups (H₂ = 8.962, P = 0.011, Table 4.9). Post-hoc and effect size analysis revealed that ankle sprain copers demonstrated greater V: M_{max} ratio compared to participants with PAI (U₂ = 334.50, z = -2.105, P = 0.035, d = -0.59, 95% CIs: -1.09, -0.07, Figure 4-20) and healthy controls (U₂ = 178.00, z = -2.756, P = 0.006, d = 0.81, 95% CIs: 0.22, 1.36, Figure 4-21). No differences in V:M ratio were noted between the PAI and control groups ((U₂ = 342.50, z = -1.351, P = 0.177, d = 0.27, 95% CIs: -0.26, 0.78, Figure 4-19).

For corticospinal excitability variables, we excluded 11 participants for TMS testing and could not obtain AMT of the soleus from seven participants. Therefore, 69 out of 81 participants were included in the analysis (PAI = 30, Coper = 19, control = 20) for the soleus. No significant group differences were observed for AMT (H₂ = 0.459, P = 0.795) and CSP (H₂ = 0.475, P = 0.788, Table 4.9).
Figure 4-17. Neural Excitability Outcome Measures for Three Groups

*Significant differences compared to the coper group (p < 0.05)
Table 4-9. Group means and standard deviation for neural excitability outcome measures for three groups

<table>
<thead>
<tr>
<th>Mean ± SD (95% CIs)</th>
<th>PAI (n = 36)</th>
<th>Coper (n = 27)</th>
<th>Control (n = 24)</th>
<th>P-value (F_{2.86} or H_{2})</th>
</tr>
</thead>
<tbody>
<tr>
<td>H\textsubscript{max}:M\textsubscript{max} ratio</td>
<td>0.41±0.18$^#$ (0.35, 0.47)</td>
<td>0.56±0.23 (0.46, 0.65)</td>
<td>0.51±0.18 (0.43, 0.59)</td>
<td>0.014$^*$ (4.473)</td>
</tr>
<tr>
<td>V: M\textsubscript{max} ratio</td>
<td>0.24±0.20$^#$ (0.17, 0.30)</td>
<td>0.37±0.26 (0.27, 0.47)</td>
<td>0.18±0.19$^#$ (0.11, 0.26)</td>
<td>0.011$^*$ (8.931)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th># of participants analyzed</th>
<th>n = 30</th>
<th>n = 19</th>
<th>n = 20</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>TMS</td>
<td>AMT</td>
<td>40.20±11.59 (35.87, 44.53)</td>
<td>42.26±12.55 (36.22, 48.31)</td>
<td>42.45±10.5 (37.54, 47.36)</td>
</tr>
<tr>
<td></td>
<td>CSP</td>
<td>50.77±17.27 (43.11, 58.43)</td>
<td>50.76±19.23 (38.54, 62.98)</td>
<td>45.46±20.14 (34.30, 56.61)</td>
</tr>
</tbody>
</table>

*Indicates significant difference among groups (p<0.05)
$^\#$ Indicates significant difference compared to the coper group (p < 0.05)

PAI = Posttraumatic ankle instability, AMT = Active motor threshold; CSP = Cortical silent period; TMS = Transcranial magnetic stimulation

4.2.3 Postural Control Outcome Measures

For static postural control, there were statistically significant differences in COPV-AP ($H_{2} = 9.212, P = 0.010$) and COPV-ML ($H_{2} = 8.962, P = 0.011$) among the groups (Table 4-10 and Figure 4-18). Post-hoc and effect size analysis revealed that participants with PAI demonstrated worse postural control (larger COPV-AP) compared to ankle sprain copers ($U_{2} = 308.00, z = -2.472, P = 0.013, d = 0.60, 95\%\ CIs: 0.08, 1.10$, Figure 4-20) and healthy controls ($U_{2} = 259.50, z = -2.603, P = 0.009, d = 0.62, 95\%\ CIs: 0.08, 1.14$, Figure 4-19). Participants with PAI also showed larger COPV-ML compared to healthy controls ($U_{2} = 257.50, z = -2.633, P = 0.008, d = 0.53, 95\%\ CIs: -0.01, 1.04$, Figure 4-21). No difference was observed in either COPV-AP or ML between the coper and control groups ($P > 0.05$, Figure 4-18).

For the TTB measures of static postural control, only SD of TTB-ML differed
among the groups ($H_2 = 6.416, P = 0.040$). The PAI group had less SD of TTB-ML compared to the control group ($U_2 = 279.00, z = -2.309, P = 0.021, d = -0.74, 95\% \text{ CIs: } -1.26, -0.19, \text{ Figure 4-19}$); however, no difference was noted between the coper and control groups ($U_2 = 252.00, z = -1.359, P = 0.174, d = 0.02, 95\% \text{ CIs: } -0.53, 0.57, \text{ Figure 4-21}$). There were no differences in the other TTB measures between the PAI, coper, and control groups ($P > 0.05$, Table 4.10). However, effect size analysis revealed that the RAS-PI group had lower mean TTB mean-ML ($d = -0.64, 95\% \text{ CIs: } -1.15, -0.09$) compared to the control group (Figure 4-19). Finally, there was no difference in the amount of failed trials during static postural control assessment between the groups ($H_2 = 0.275, P = 0.871$).

For dynamic postural control assessment, normalized reaching distance of the SEBT-A did not differ among the groups ($F_{2,86} = 1.248, P = 0.292$, Table 4.10). Small to moderate effect sizes were observed for %MAXD of the SEBT-A (Figure 4-19 to 4-21). No group differences were found in the amount of failed trials during the SEBT-A ($H_2 = 2.780, P = 0.249$).
**Figure 4-18. Static Postural Control Outcome Measures for Three Groups**

*Significant differences compared to the ankle instability coper and control groups (p < 0.05)*

^ Significant differences compared to the control groups (p < 0.05)
Table 4.10 Group means and standard deviation for postural control outcome measures for three groups

<table>
<thead>
<tr>
<th></th>
<th>Mean ± SD (95% CIs)</th>
<th>PAI</th>
<th>Coper</th>
<th>Control</th>
<th>p-value (F&lt;sub&gt;2,80&lt;/sub&gt; or H&lt;sub&gt;2&lt;/sub&gt;)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>COPV (cm/s)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AP</td>
<td>4.34±1.28*</td>
<td>3.69±0.70</td>
<td>3.65±1.04</td>
<td>0.010*</td>
<td></td>
</tr>
<tr>
<td>(3.91, 4.78)</td>
<td></td>
<td>(3.42, 3.97)</td>
<td>(3.33, 3.98)</td>
<td>(9.212)</td>
<td></td>
</tr>
<tr>
<td>ML</td>
<td>5.88±3.22†</td>
<td>4.92±1.64</td>
<td>4.44±1.72</td>
<td>0.011*</td>
<td></td>
</tr>
<tr>
<td>(4.79, 6.97)</td>
<td></td>
<td>(4.11, 5.21)</td>
<td>(3.72, 5.17)</td>
<td>(8.962)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>TTB (s)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AP</td>
<td>3.25±0.84</td>
<td>3.72±0.81</td>
<td>3.75±1.36</td>
<td>0.117</td>
<td></td>
</tr>
<tr>
<td>(2.97, 3.54)</td>
<td></td>
<td>(3.32, 4.13)</td>
<td>(3.18, 4.32)</td>
<td>(2.205)</td>
<td></td>
</tr>
<tr>
<td>ML</td>
<td>1.37±0.53</td>
<td>2.05±2.63</td>
<td>1.73±0.64</td>
<td>0.069</td>
<td></td>
</tr>
<tr>
<td>(1.19, 1.55)</td>
<td></td>
<td>(1.01, 3.09)</td>
<td>(1.46, 2.00)</td>
<td>(5.338)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>SD TTB (s)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AP</td>
<td>3.65±1.39</td>
<td>3.90±1.46</td>
<td>4.28±2.54</td>
<td>0.586</td>
<td></td>
</tr>
<tr>
<td>(3.18, 4.12)</td>
<td></td>
<td>(3.32, 4.48)</td>
<td>(3.20, 5.35)</td>
<td>(1.068)</td>
<td></td>
</tr>
<tr>
<td>ML</td>
<td>1.50±0.54†</td>
<td>2.09±2.38</td>
<td>2.05±0.98</td>
<td>0.040*</td>
<td></td>
</tr>
<tr>
<td>(1.32, 1.68)</td>
<td></td>
<td>(1.14, 3.03)</td>
<td>(1.64, 2.47)</td>
<td>(6.416)</td>
<td></td>
</tr>
<tr>
<td>Failed Trials</td>
<td>3.69±5.58</td>
<td>3.93±4.01</td>
<td>3.75±4.28</td>
<td>0.871 (0.275)</td>
<td></td>
</tr>
<tr>
<td>%MAXD</td>
<td>67.56±6.49</td>
<td>69.95±6.22</td>
<td>67.61±6.71</td>
<td>0.292</td>
<td></td>
</tr>
<tr>
<td>(65.36, 69.75)</td>
<td></td>
<td>(67.49, 72.41)</td>
<td>(64.78, 70.44)</td>
<td>(1.248)</td>
<td></td>
</tr>
<tr>
<td>Failed Trials</td>
<td>0.33±0.59</td>
<td>0.37±0.56</td>
<td>0.17±0.48</td>
<td>0.249 (2.780)</td>
<td></td>
</tr>
</tbody>
</table>

* Indicates significant differences among groups (p<0.05)
# Indicates significant differences compared to the coper and control groups (p < 0.05)
† Indicates significant difference compared to the control groups (p < 0.05)
PAI = Posttraumatic ankle instability, COPV = Center of pressure velocity; AP = Anteroposterior; ML = Mediolateral; TTB = Time to boundary, SEBT-A = Anterior research direction of the Star Excursion Balance Test; %MAXD = Normalized reach distance by participant’s stance leg

4.2.4 Variability of Locomotor Patterns during Walking

No significant differences between groups were noted for the self-selected walking speed (F<sub>2,86</sub> = 1.356, P = 0.263, Table 4.11, and Figure 4-18). For movement pattern variability during walking, group differences existed in ApEn of the frontal plane ankle kinematics (F<sub>2,86</sub> = 3.365, P = 0.039). The ankle instability coper group demonstrated decreased variability (less ApEn) of the frontal plane ankle kinematics compared to the PAI (P = 0.049, d = 0.49, 95% CIs: -0.02, 0.99) and control groups (P =
0.016, \( d = -0.64, \) 95% CIs: -1.19, -0.107); while no difference was observed between the PAI and control groups (\( P = 0.498, d = -0.20, \) 95% CIs: -0.71, 0.32). There were no differences in any other ApEn values among the groups (\( P > 0.05, \) Table 4.11).

![Graph showing PAI and control groups](image)

**Figure 4.19. Frontal Plane Ankle Kinematic Variability**

*Significant differences compared to the coper group (p < 0.05)*
Table 4.11 Group means and standard deviation for approximate entropy values for three groups

<table>
<thead>
<tr>
<th>Mean ± SD (95% CIs)</th>
<th>PAI</th>
<th>Coper</th>
<th>Control</th>
<th>P-value ( F_{2,86} ) or ( H^2 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trunk</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sagittal</td>
<td>1.01±0.28</td>
<td>0.97±0.26</td>
<td>1.07±0.25</td>
<td>0.405</td>
</tr>
<tr>
<td></td>
<td>(0.92, 1.11)</td>
<td>(0.87, 1.07)</td>
<td>(0.96, 1.18)</td>
<td>(0.913)</td>
</tr>
<tr>
<td>Frontal</td>
<td>0.81±0.16</td>
<td>0.83±0.19</td>
<td>0.86±0.20</td>
<td>0.612</td>
</tr>
<tr>
<td></td>
<td>(0.76, 0.86)</td>
<td>(0.75, 0.90)</td>
<td>(0.77, 0.94)</td>
<td>(0.493)</td>
</tr>
<tr>
<td>Frontal</td>
<td>0.54±0.15</td>
<td>0.55±0.09</td>
<td>0.54±0.15</td>
<td>0.956</td>
</tr>
<tr>
<td></td>
<td>(0.49, 0.59)</td>
<td>(0.49, 0.56)</td>
<td>(0.47, 0.60)</td>
<td>(0.045)</td>
</tr>
<tr>
<td>Frontal</td>
<td>0.31±0.03</td>
<td>0.31±0.05</td>
<td>0.32±0.04</td>
<td>0.757</td>
</tr>
<tr>
<td></td>
<td>(0.30, 0.32)</td>
<td>(0.29, 0.33)</td>
<td>(0.30, 0.33)</td>
<td>(0.280)</td>
</tr>
<tr>
<td>Frontal</td>
<td>0.79±0.25</td>
<td>0.75±0.30</td>
<td>0.79±0.28</td>
<td>0.835</td>
</tr>
<tr>
<td></td>
<td>(0.70, 0.88)</td>
<td>(0.63, 0.87)</td>
<td>(0.67, 0.91)</td>
<td>(0.180)</td>
</tr>
<tr>
<td>Frontal</td>
<td>0.58±0.11</td>
<td>0.55±0.10</td>
<td>0.55±0.11</td>
<td>0.402</td>
</tr>
<tr>
<td></td>
<td>(0.54, 0.62)</td>
<td>(0.51, 0.59)</td>
<td>(0.50, 0.59)</td>
<td>(0.921)</td>
</tr>
<tr>
<td>Ankle</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sagittal</td>
<td>1.07±0.24</td>
<td>0.93±0.32*</td>
<td>1.12±0.25</td>
<td>0.039*</td>
</tr>
<tr>
<td></td>
<td>(0.99, 1.15)</td>
<td>(0.81, 1.06)</td>
<td>(1.01, 1.22)</td>
<td>(3.365)</td>
</tr>
<tr>
<td>Frontal</td>
<td>4.33±0.85</td>
<td>4.05±0.72</td>
<td>4.38±0.75</td>
<td>0.263(1.356)</td>
</tr>
</tbody>
</table>

* Indicates significant differences among groups (p<0.05)
# Indicates significant differences compared to the PAI and control groups (p < 0.05)
PAI = Posttraumatic ankle instability

4.2.5 Mechanical Outcome Measures

The ANCOVA models demonstrated a non-significant group difference in the WBLT, DF-ROM in the NWB position, and the ankle joint laxity measures after controlling for the variance contributed by sex \( P > 0.05 \), Table 4.12). The range of effect sizes for mechanical outcome variables were small to large, with large 95% CIs crossing zero (Figure 4-19 to 4-21).
Table 4.12 Group means and standard deviation for mechanical outcome measures for three groups

<table>
<thead>
<tr>
<th>Mean ± SD (95% CIs)</th>
<th>PAI</th>
<th>Coper</th>
<th>Control</th>
<th>P-value (F_{2,86})</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBLT (cm)</td>
<td>12.28±4.13</td>
<td>11.79±3.60</td>
<td>10.80±3.44</td>
<td>0.353 (1.054)</td>
</tr>
<tr>
<td></td>
<td>(10.88, 13.68)</td>
<td>(10.37, 13.21)</td>
<td>(9.34, 12.25)</td>
<td></td>
</tr>
<tr>
<td>NWB-DF (°)</td>
<td>14.38±4.41</td>
<td>15.74±4.94</td>
<td>14.18±5.53</td>
<td>0.458 (0.788)</td>
</tr>
<tr>
<td></td>
<td>(12.89, 15.87)</td>
<td>(13.78, 17.70)</td>
<td>(11.84, 16.52)</td>
<td></td>
</tr>
<tr>
<td>Anterior (mm)</td>
<td>11.76±3.64</td>
<td>11.74±3.20</td>
<td>11.99±3.80</td>
<td>0.971 (0.029)</td>
</tr>
<tr>
<td></td>
<td>(10.53, 12.99)</td>
<td>(10.47, 13.01)</td>
<td>(10.38, 13.59)</td>
<td></td>
</tr>
<tr>
<td>Posterior (mm)</td>
<td>8.93±2.86</td>
<td>8.74±2.78</td>
<td>8.78±2.52</td>
<td>0.897 (0.106)</td>
</tr>
<tr>
<td></td>
<td>(7.96, 9.89)</td>
<td>(7.64, 9.84)</td>
<td>(7.71, 9.84)</td>
<td></td>
</tr>
<tr>
<td>AP total (mm)</td>
<td>20.65±5.61</td>
<td>20.46±4.81</td>
<td>20.80±5.19</td>
<td>0.967 (0.033)</td>
</tr>
<tr>
<td></td>
<td>(18.75, 22.55)</td>
<td>(18.55, 22.36)</td>
<td>(18.61, 22.99)</td>
<td></td>
</tr>
<tr>
<td>Inversion (°)</td>
<td>37.28±10.29</td>
<td>39.46±9.06</td>
<td>35.00±11.40</td>
<td>0.246 (1.425)</td>
</tr>
<tr>
<td></td>
<td>(33.80, 40.76)</td>
<td>(35.87, 43.04)</td>
<td>(30.18, 39.81)</td>
<td></td>
</tr>
<tr>
<td>Eversion (°)</td>
<td>23.43±7.08</td>
<td>22.40±5.86</td>
<td>24.52±8.62</td>
<td>0.545 (0.612)</td>
</tr>
<tr>
<td></td>
<td>(21.03, 25.83)</td>
<td>(20.09, 24.72)</td>
<td>(20.88, 28.16)</td>
<td></td>
</tr>
<tr>
<td>I-E total (°)</td>
<td>59.55±13.20</td>
<td>62.17±13.26</td>
<td>57.91±19.07</td>
<td>0.524 (0.651)</td>
</tr>
<tr>
<td></td>
<td>(55.09, 64.02)</td>
<td>(56.92, 67.41)</td>
<td>(49.86, 65.97)</td>
<td></td>
</tr>
</tbody>
</table>

**PAI** = Posttraumatic ankle instability; **WBLT** = Weight bearing lunge test, **NWB-DF** = Non-weight bearing dorsiflexion, **AP** = Anteroposterior; **I-E** = Inversion-Eversion
Figure 4-19. Effect Sizes for each Outcome Measures (PAI vs. Control)
Figure 4-20. Effect Sizes for each Outcome Measures (PAI vs. Coper)
Figure 4-21. Effect Sizes for each Outcome Measures (Coper vs. Control)

- H:M [0.21 (-0.34, 0.76)]
- V:M [0.81 (0.22, 1.36)]
- AMT [-0.02 (-0.64, 0.61)]
- CSP [0.27 (-0.51, 1.02)]
- COPV-AP [0.06 (-0.49, 0.561)]
- COPV-ML [0.14 (-0.42, 0.69)]
- TTB-mean AP [-0.02 (-0.57, 0.53)]
- TTB-mean ML [0.16 (-0.39, 0.71)]
- TTB-SD AP [-0.19 (-0.73, 0.37)]
- TTB-SD ML [0.02 (-0.53, 0.57)]
- ApEn Trunk sagittal [-0.39 (-0.94, 0.17)]
- ApEn Hip sagittal [-0.10 (-0.64, 0.46)]
- ApEn Knee sagittal [-0.18 (-0.73, 0.37)]
- ApEn Ankle sagittal [0.01 (-0.54, 0.56)]
- ApEn Trunk Frontal [-0.15 (-0.70, 0.40)]
- ApEn Hip Frontal [-0.06 (-0.61, 0.49)]
- ApEn Knee Frontal [-0.12 (-0.67, 0.43)]
- ApEn Ankle Frontal [-0.64 (-1.19, -0.07)]
- SEBT-A [0.36 (-0.20, 0.91)]
- WBLT [0.28 (-0.28, 0.83)]
- NWB-DF [0.30 (-0.26, 0.84)]
- Laxity-A [-0.07 (-0.62, 0.48)]
- Laxity-P [-0.01 (-0.56, 0.51)]
- Laxity-AP total [-0.07 (-0.62, 0.48)]
- Laxity-I [0.44 (-0.13, 0.98)]
- Laxity-E [-0.36 (-0.90, 0.20)]
- Laxity-IE total [0.26 (-0.30, 0.81)]
4.3 Specific Aim 2: Discriminant Functional Analysis

4.3.1 Five Homogenous Group Analysis

Three dependent variables (\(H_{\text{max}}:M_{\text{max}}\) ratio, COPV-AP, and COPV-ML) were significantly different among the groups. Group difference in \(V: M_{\text{max}}\) ratio approached statistical significance (\(P = 0.059\)). Large effect sizes were observed for four outcome measures (TTB mean-AP and SD of TTB-ML) compared to the coper or control group. Therefore, six significant factors were entered into the DFA to assess the ability of these factors to best differentiate participants by groups (RAS-PI, RAS, FAI, coper, and healthy).

The overall DFA model showed a significant classification among the groups (Wilk’s \(\lambda = 0.578\), \(\chi^2_{24} = 44.194\), \(P = 0.007\), canonical correlation = 0.484) and accounted for 23.43% of the variance in the significant factors. Examination of the standardized canonical discriminant function coefficients and structure matrix indicated that \(H_{\text{max}}:M_{\text{max}}\) ratio, COPV-AP, COPV-ML and SD of TTB-ML strongly contributed to this DFA model.

The DFA model correctly classified 45.83% of participants with RAS-PI and 54.17% of healthy controls. The DFA data identifying the variables most related to the PAI group membership is provided in Table 4.13. Overall, the DFA model correctly classified group membership in 44.83% of the total cases.
### Table 4.13 Discriminant functional analysis classification results for five groups

<table>
<thead>
<tr>
<th>Group</th>
<th>RAS-PI</th>
<th>RAS</th>
<th>FAI</th>
<th>Coper</th>
<th>Control</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>RAS-PI</td>
<td>11</td>
<td>0</td>
<td>6</td>
<td>3</td>
<td>4</td>
<td>24</td>
</tr>
<tr>
<td>RAS</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>11</td>
</tr>
<tr>
<td>FAI</td>
<td>4</td>
<td>0</td>
<td>3</td>
<td>3</td>
<td>2</td>
<td>12</td>
</tr>
<tr>
<td>Coper</td>
<td>1</td>
<td>2</td>
<td>7</td>
<td>4</td>
<td>16</td>
<td>24</td>
</tr>
<tr>
<td>Control</td>
<td>4</td>
<td>1</td>
<td>2</td>
<td>4</td>
<td>13</td>
<td>24</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>22</strong></td>
<td><strong>8</strong></td>
<td><strong>14</strong></td>
<td><strong>18</strong></td>
<td><strong>25</strong></td>
<td><strong>87</strong></td>
</tr>
</tbody>
</table>

Percentage of participants correctly classified:
- **RAS-PI**: 45.83%
- **RAS**: 18.18%
- **FAI**: 33.33%
- **Coper**: 6.25%
- **Control**: 16.67%

Overall, 44.83% of participants were correctly classified.

**RAS-PI** = Recurrent ankle sprain with perceived instability; **RAS** = Recurrent ankle sprain; **FAI** = Functional ankle instability

### 4.3.2 Three Traditional Group Analysis

Six dependent variables (\(H_{\text{max}}:M_{\text{max}}\) ratio, \(V: M_{\text{max}}\) ratio, COPV-AP and ML, SD of TTB-ML, and ApEn of the frontal plane ankle kinematics) were significantly different among the groups. Group difference in mean TTB-ML approached statistical significance (\(p = 0.069\)). Therefore, a total of seven significant factors were entered into the DFA to assess the ability of these factors to best differentiate participants by groups (PAI, coper, and healthy).

The overall DFA model showed a significant classification among the groups (Wilk’s \(\lambda = 0.542, \chi^2_{14} = 49.683, P < 0.001\), canonical correlation = 0.563) and accounted for 31.70% of the variance in the significant factors. Examination of the standardized canonical discriminant function coefficients and structure matrix indicated that \(H_{\text{max}}:M_{\text{max}}\)
ratio, \( V: M_{\text{max}} \) ratio, COPV-AP, COPV-ML, mean TTB-ML, and SD of TTB-ML strongly contributed to this DFA model.

The resulting DFA model correctly classified 63.89\% of participants with PAI, 62.96\% of ankle sprain copers, and 66.67\% of healthy controls. The DFA data identifying the variables most related to the PAI group membership is provided in Table 4.14. Overall, the DFA model correctly classified group membership 64.37\% of the total cases.

Table 4.14 Discriminant functional analysis classification results for three groups

<table>
<thead>
<tr>
<th>Number of participants correctly classified</th>
<th>Predicted Group Membership</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>PAI</td>
<td>23</td>
<td>35</td>
</tr>
<tr>
<td>Coper</td>
<td>7</td>
<td>28</td>
</tr>
<tr>
<td>Control</td>
<td>5</td>
<td>24</td>
</tr>
<tr>
<td>Total</td>
<td>35</td>
<td>87</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Percentage of participants correctly classified</th>
<th>PAI</th>
<th>Coper</th>
<th>Control</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>PAI</td>
<td>63.89</td>
<td>22.22</td>
<td>13.89</td>
<td>100</td>
</tr>
<tr>
<td>Coper</td>
<td>25.93</td>
<td>62.96</td>
<td>11.11</td>
<td>100</td>
</tr>
<tr>
<td>Control</td>
<td>20.83</td>
<td>12.50</td>
<td>66.67</td>
<td>100</td>
</tr>
</tbody>
</table>

Overall, 64.37\% of participants were correctly classified.

PAI = Posttraumatic ankle instability
Chapter 5

Discussion

5.1 Specific Aim 1: Five Groups Comparison

The current study proposed four homogenous subgroups of PAI (RAS-PI, RAS, FAI, and ankle sprain coper) to facilitate the identification of and intervention for specific sources of self-reported instability and disability in patients with PAI. In this study, the presence of self-reported (perceived) ankle instability was confirmed in the RAS-PI and FAI groups with scoring higher on the AII and IdFAI and reported larger number of repeated episodes of giving-way compared to those with RAS, copers, and healthy controls. Additionally, the RAS-PI group reported a larger number of recurrent ankle sprains compared with the FAI, coper, and control groups, but not compared with the RAS group. No ankle sprain copers or participants with RAS reported that they have modified the level of physical activity due to ankle injury. Based on ankle injury characteristic information indicating the severity of ankle instability, participants in this current study fell within more homogenous subgroups of PAI.

Investigators using self-reported foot and ankle disability questionnaires have
consistently reported that perceived disability is present in individuals with PAI.\cite{Z99-281} In the current study, participants with RAS-PI, RAS, and FAI demonstrated self-reported disability as assessed with the FAAM-ADL and FAAM-S. The RAS-PI had the lowest scores on the FAAM measures of the five groups. While the RAS and FAI group scored less on the FAAM-S compared to the coper and control groups, there were no differences between the RAS and FAI groups. On the FAAM-ADL, the FAI scored lower than the RAS, coper and control groups, whereas no differences were observed between the RAS, coper, and control groups. There were no differences in the FAAM scores either between the RAS-PI and FAI groups or between the coper and control groups. All of the factors of perceived ankle instability, repeated episodes of giving-way, and recurrent ankle sprains may have a strong relation with self-assessed functional limitations during physical activities; however, the number of ankle sprains participants have experienced may be less associated with self-assessed disability during ADL.

When health related quality of life was assessed by the SF-36, lower scores of the physical dimensions of health were observed in participants with RAS-PI and FAI groups compared to the RAS, coper, and control groups. The results of this study support the evidence that FAI was associated with lower health-related quality of life along the physical dimension but not the mental dimension of the SF-36.\cite{9} Mean scores on the SF-36 of both RAS-PI and FAI groups (50-56) in our study were similar to the mean scores previous authors found (51-55).\cite{9} Lastly, we assessed participants’ psychological responses to PAI using the Tampa Scale for Kinesiophobia and the PRSII. While no group differences were noted in the Tampa Scale for Kinesiophobia, we found that participants with RAS-PI and FAI had heightened feelings of restlessness and isolation.
measured with the PRSII. Overall, these findings from self-reported questionnaires illustrate that the presence of the perception of instability and repeated episodes of “giving-way” associated with PAI may limit self-assessed function, decrease health-related quality of life, and alter psychological response to injury. Therefore, the presence of self-reported instability and repeated episodes of “giving-way” may be important factors that contribute to the development of PAI compared to the number of ankle sprains.

5.1.1 Neural Excitability Alterations

The current investigation found that participants with RAS-PI had decreased $H_{max}:M_{max}$ ratio of the soleus compared to participants with RAS, ankle sprain copers, and healthy controls. While the FAI group did not exhibit a difference in $H_{max}:M_{max}$ ratio compared to the other four groups, effect size calculations revealed the FAI group may have a lower $H_{max}:M_{max}$ ratio compared to the RAS group ($d = 0.88$). The $H_{max}:M_{max}$ ratio is an estimate of the overall excitability of the alpha motoneurons through the Ia afferents reflex pathway. These findings illustrate that the presence of perceived ankle instability and episodes of “giving-way” may be significantly associated with decreased spinal reflex excitability in the soleus. An earlier work examining the effect of PAI on spinal reflex excitability measures while prone observed a decrease in $H_{max}:M_{max}$ ratio in the involved limb of participants with PAI compared to their non-involved limb as well as in the matched-involved limb of those without PAI.

Authors of two studies have presented results of $H_{max}:M_{max}$ ratio data that conflict with that of McVey et al. and our current study. Although Sefton et al. found
altered pre- and postsynaptic levels of H-reflex modulation in the soleus in participants with PAI, these authors reported no difference in $H_{\text{max}}:M_{\text{max}}$ ratio between participants with and without PAI. The authors obtained $H_{\text{max}}:M_{\text{max}}$ ratio in double- and single-legged stance while we assessed the spinal reflex excitability in the seated position with 90° of hip flexion, knee flexion, and ankle dorsiflexion. The spinal reflex excitability of the soleus is highly influenced by changes in body positions.\textsuperscript{283}

Recent investigation demonstrated that percent change of $H_{\text{max}}:M_{\text{max}}$ ratio in the soleus measured during rest to double-and single-legged stance was smaller in participants with PAI compared to healthy controls.\textsuperscript{282} Although Sefton et al.\textsuperscript{13,144} did not measure spinal reflex excitability of the soleus during sitting, it is possible that the H-reflex in the soleus was more inhibited in healthy controls in the double- or single-legged stance compared to the seated position, making small difference in $H_{\text{max}}:M_{\text{max}}$ ratio between participants with and without PAI. Therefore, the conflicting results of $H_{\text{max}}:M_{\text{max}}$ ratio may be explained by the larger level of spinal reflex modulation in healthy controls and the smaller level of spinal reflex modulation during a positional transition in participants with PAI.

Spinal reflex inhibition of the soleus observed in participants with RAS-PI and FAI in this current study was likely a protective mechanism to reduce “giving-way” episodes by avoiding a position of ankle plantar flexion and inversion. A combined subtalar joint adduction and inversion plus an increase in a talocrural joint plantar flexion before the foot contact with ground has been suggested as the possible mechanism to cause an ankle sprain because the position of the rearfoot is inherently unstable.\textsuperscript{69} The soleus is one of the most powerful plantar flexors that produce approximately 80% of the
total plantar flexion torque at the ankle with the gastrocnemius. The soleus also acts via the Achilles tendon as an invertor at the subtalar joint because the Achilles tendon passes slightly medial to the subtalar joint and produce an inversion moment at the subtalar joint. Increased soleus activation may predispose the ankle to injury by positioning the joint in an unstable open-packed position. Klykken et al. reported facilitated spinal reflex excitability in the injured soleus of patients with an acute ankle sprain. Although increased spinal reflex excitability in the injured soleus could be a part of the recovery process, the authors speculated that the observed soleus facilitation possibly contribute to recurrent ankle sprains.

We observed increased spinal reflex excitability of the soleus in participants with RAS that had no self-reported instability and repeated episodes of “giving-way” compared to those with RAS-PI and FAI. The findings of our study may partially support their speculations. However, the strong relation between the presence of perceived instability/giving-way and decreased spinal excitability of the soleus indicates that the CNS more likely inhibits the soleus alpha motoneurons reflexively at the spinal level to prevent placing the ankle in an unstable position, possibly in an attempt to reduce the “giving-way” sensation. Furthermore, it has been documented that postural anxiety and fear of instability or falling decreased H-reflex amplitude. Based on ankle injury characteristic and perceptual information in the current study, the presence of PAI (especially RAS-PI and FAI) influenced psychological responses to this ankle pathology. Therefore, it is possible that psychological responses to repeated episodes of “giving-way” inhibit spinal reflex excitability in the soleus. However, caution should be taken that experimental conditions, such as participant’s position, may influence levels of
spinal excitability of the soleus. While spinal reflex excitability of the soleus was assessed in the seated position in this study, the relation between postural anxiety or fear of instability and levels of spinal reflex excitability was investigated in a standing position by the researchers. Future studies should investigate the relation between psychological responses to PAI and spinal reflex excitability in the standing position.

We acknowledge that retrospective design does not permit a causal link between PAI and the identified alterations in spinal reflex excitability. Therefore, it remains unknown whether altered neural excitability observed in this current study is a consequence to protect the ankle or predisposes individuals with PAI to their self-reported pathology. Clearly long-term prospective investigations are needed to explore the time course of the spinal and intracortical excitability changes after an initial lateral ankle sprain.

We did not find statistically significant differences in AMT and CSP associated with the soleus between the groups, which does not support our hypotheses. The results of this study reveal that supraspinal changes in sensorimotor functions associated with PAI may not influence soleus excitability. A limited number of investigations have assessed corticospinal excitability in patients with this ankle pathology. Researchers have documented increased resting motor threshold (RMT) in the fibularis longus of individuals with PAI, suggesting that corticospinal neurons require a greater magnetic stimulation to be excited. It is important to note that the functional roles in stabilizing the ankle joint are different between the fibularis longus and soleus. The fibularis longus eccentrically controls ankle inversion. Therefore, the effect of PAI on corticospinal excitability may depend on the functional roles of stabilizing muscles. The potential
adaptation to the chronic nature of joint injury has been documented in previously published work in which increased MEP amplitudes in knee musculature were observed in patients with chronic anterior knee pain. The authors suggested that chronic knee pain may influence central and supraspinal changes in sensorimotor control. The primarily and significant symptoms of our participants with PAI were perception of instability and “giving-way sensation, but not perceived chronic pain. Thus, it is speculated that lack of group differences in corticospinal excitability measures may be attributed to no association between the presence of PAI and perceived chronic pain. However, it is important to note that the level of perceived pain of the involved ankle was not quantified at the time of testing in the current investigation.

We found that differences in V:M ratio in the soleus among the five groups trended towards statistical significance with moderate effect sizes between the RAS-PI and ankle sprain coper groups and between the RAS and control groups, as well as a large effect size between the coper and control groups. The coper and RAS groups demonstrated a larger V:M_max ratio compared to the RAS-PI or control groups. A larger V:M_max represents an increase in descending volitional neural drive to the soleus muscle. Therefore, these findings indicate that volitional excitability of the soleus was likely increased in the coper and RAS group compared to the RAS-PI and control groups. The coper group demonstrated a similar level of spinal reflex excitability to the control group. Taking these findings together, increased V: M_max in the coper group may suggest that the supraspinal modulation serves to enhance volitional neural drive in descending pathways from higher motor centers to the soleus. Contrary to our hypothesis, there was no difference in V: M_max ratio between the RAS-PI and control groups. We observed less
H_{max}: M_{max} ratio in the RAS-PI group compared to the control group. Theoretically, suppressed alpha motoneuron pool excitability due to altered peripheral inputs results in a decrease in V: M_{max} ratio.\textsuperscript{244} The lack of decrease in V: M_{max} ratio in the soleus of participants with RAS-PI may be due to altered supraspinal drive. However, we did not find differences in AMT and CSP in the soleus between the groups. While the selected corticospinal excitability measures in this study provide overall information regarding global changes in the supraspinal pathway, we are unaware if suprapsinal changes in intracortical pathway were associated with PAI. Therefore, in order to identify more specific local changes in corticospinal functions, further investigation is needed to examine the association between the PAI and intracortical excitability using paired-pulse TMS paradigms, such as short-interval intracrotical inhibition and intracortical facilitation.

5.1.2 Contributions of Altered Neural Excitability to Postural Control

It has been proposed that deficits in neural excitability following joint injury may be one of multiple contributing factors to neuromuscular dysfunction\textsuperscript{289,290} that alter maintenance of postural control,\textsuperscript{90} gait,\textsuperscript{121,291} and jump-landing performance.\textsuperscript{30,163} In the current study, participants with RAS-PI and FAI demonstrated increased COPV and decreased TTB values compared to ankle sprain copers and healthy controls. The lower TTB and larger COPV values are representative of postural impairments as the individual has less time and fewer movement solutions to make postural corrections and maintain postural stability in a single-limb due to high COPV.\textsuperscript{90} The results of our study indicate that participants with RAS-PI and FAI had worse postural control compared to ankle
sprain copers and healthy controls. These findings are consistent with previous findings that participants with PAI exhibited static postural control impairments\[13,90,166,174\]. However, the specific neurophysiological mechanisms of these impairments remain unclear. The soleus takes a key role in controlling the postural sway movements of the lower limb over the base of support during the standing.\[237,284\] We speculate that decreased spinal reflex excitability in the soleus of participants with PAI may alter feedback neural controls, possibly contributing to static postural control impairments observed in those with PAI.

It has been suggested that mechanoreceptors located within the lateral ligamentous complex at the ankle joint are damaged following an acute initial lateral ankle sprain.\[15\] Loss of the afferent sources following the ankle sprain lead to proprioceptive deficits that alter feedback strategies within the neuromuscular control system, which are proposed as the primary source of postural control impairments associated with PAI.\[292\] This idea has been supported by evidence of impaired postural control following deafferentation of the lateral ankle ligaments\[293\] and cutaneous receptors.\[294\] The alterations in peripheral afferent inputs have been shown to influence the gamma motor neuron.\[295,296\] A lack of peripheral afferent inputs from the mechanoreceptors and cutaneous receptors could chronically suppress gamma activation and desensitize the muscle spindle,\[112\] which may indirectly affect muscle activation by altering sensory signals propagated to the CNS.\[297\]

While the gamma loop dysfunction and inhibition of alpha motoneurons has been observed in the fibularis longus of patients with PAI,\[113,123\] the level of spinal reflex excitability and dynamic muscle activation of the fibularis longus were not correlated
with each other. We do not know whether the suppressed gamma activation and desensitized muscle spindle as well as the relation between levels of gamma activation and alpha motoneuronal pool excitability were present in the soleus of participants with PAI. However, decreased $H_{\text{max}}:M_{\text{max}}$ ratio in the soleus of those with PAI indicates that altered afferent inputs arising from an unstable ankle lead to a decreased efferent motor drive to the soleus, ultimately altering feedback strategies to control fine movement and postural sway. Therefore, altered feedback neural control to the soleus may be driving the altered static postural control impairments observed in this study.

Postural control requires all the afferent, efferent, and central integration and processing components to control functions of the muscle around the ankle in order to maintain balance. It has been proposed that postural control impairments may be associated with a change in feed-forward motor control, as evidenced by altered neuromuscular and movement patterns in the lower extremity before landing as well as during gait initiation and unplanned gait termination. Suppressed gamma and alpha motoneuron activations in stabilizing muscles surrounding the ankle may make the supraspinal motor center offset these inhibitions. Recent investigations reported decreased H-reflex modulations in the soleus of participants with PAI compared to healthy controls during positional changes from lying to standing. In a more challenging postural control task, modulation of the H-reflex is required to make less reflexive efferent responses and allow the supraspinal motor center to control postural sway. It is possible that the diminished ability to suppress spinal excitability of the soleus associated with PAI results from inactivating spinal inhibitory neurons. Decreased H-reflex modulation in the soleus has been demonstrated to associate with altered
postural control.\textsuperscript{283,299} It is important to note that we did not assess H-reflex of the soleus in a standing position. Therefore, further investigation is needed to test this hypothesis.

Participants with RAS-PI and FAI had impaired static postural control (increased COPV values and decreased TTB values) relative to ankle sprain copers. The current results are in agreement with previously published work suggesting that copers could develop successful compensatory strategies in order to improve postural control.\textsuperscript{174} Ankle sprain copers may have a greater number of movement solutions available to maintain balance.\textsuperscript{156} We found higher spinal reflex excitability of the soleus in copers compared to the PAI groups, possibly providing a window of opportunity within which copers can benefit from increased availability of alpha motoneuron pool availability. The coper group also demonstrated increased V: M\textsubscript{max} ratio compared to the PAI and control groups. These findings revealed that the supraspinal motor centers may be allowed to recruit more motor neurons and produce movement corrections in order to maintain an upright posture. These CNS adaptations appear to improve postural control in the coper group.

While the primary motor cortex serves a vital role for adjusting postural sway movements and performing coordinated movements,\textsuperscript{283,300} optimal postural control also requires activation of subcortical areas, such as cerebellum.\textsuperscript{301,302} Therefore, further investigations are needed to determine the effects of PAI on subcortical areas.

\subsection*{5.1.3 Variability of Locomotor Patterns during Walking}

The effect of PAI on movement variability during walking was examined with non-linear measure, ApEn. We found group differences only in ApEn of frontal plane ankle kinematics. The RAS and coper groups appear to have less variability in ankle
motions during self-selected walking compared to the FAI and control groups. Using the “optimal movement variability” theoretical model, decreased gait variability observed in the RAS and coper groups may make the sensorimotor system more constrained, rigid, and very repeatable. According to this model, healthy state is associated with an optimal amount of movement variability that provides flexibility, adaptability, and ability to respond to perturbation and changes in environmental demands. The RAS and coper groups decreased gait variability at the ankle joint compared to the control group. This locking-down variability at the ankle joint may be an effort of the sensorimotor system to minimize ankle giving-way by avoiding risker positions and eliminating extra movements; therefore, perhaps ankle sprain copers and recurrent ankle sprainers are “more careful” while walking. However, there were no differences in gait variability between the RAS and coper groups. We do not know why some individuals with a previous history of ankle sprain and decreased gait variability will suffer recurrent ankle sprains and while other individuals do not. It is possible that this constraint on the sensorimotor system observed in the RAS group decreases ability to respond to the environmental changes, possibly predisposing to recurrent ankle sprains.

We reported no differences in any movement variability during gait among the RAS-PI, FAI, and control groups. To our knowledge, this is the first study to examine stride-to-stride variability during walking using ApEn. Therefore, comparison of our data to previous studies is limited. Researches have shown that individuals with ACL reconstruction increased stride-to-stride variability at the knee joint compared to healthy controls, suggesting that musculoskeletal pathologies are associated with altered movement variability and influence the organization of the sensorimotor system. In
contrast, previous investigators reported that no difference in stride-to-stride variability of knee motion was observed between the degenerative limb of patients with unilateral knee OA and the limb of the healthy controls. Interestingly, the authors found increased variability of knee motion in the uninvolved limb of patients with unilateral knee OA compared to their degenerative limb and the tested leg of the matched control, which may be a compensatory mechanism for functional impairments on the degenerative limb. We did not analyze stride-to-stride variability in the uninvolved limb because patients with previous history of bilateral ankle sprains were included in this study. Examining movement variability in uninvolved side may provide insight into the underlying mechanism of PAI. Future investigation should incorporate bilateral examination of movement variability in patients with unilateral PAI to determine the extent that PAI has on the sensorimotor function and understand the mechanism of bilateral PAI.

Previous authors using linear analysis, such as coefficient of variation and principal component analyses, have demonstrated that individuals with PAI appear to have greater movement variability at the ankle and less variability at the knee and hip during jump landing tasks compared to controls. This assumes that increases in the amount of variability in movement during functional tasks equate with increased instability. In our study, movement variability was assessed during walking with self-selected speeds. Changing the demands of the task affects the variability of movement solutions the sensorimotor system can use. These findings reveal that a more complex task may challenge the sensorimotor system and decrease the ability of individuals with PAI to control variability and stability. Furthermore, linear variability analysis provides information regarding the amount or magnitude of variability, while
nonlinear variability analysis determines whether a chaotic structure and complexity are present in movement by quantifying the structure or organization of the variability and assessing how movements changes over time.\textsuperscript{177} We did not examine the effect of PAI on the amount of movement variability during gait using linear analysis. Further research is needed to fully understand the interactions of ankle pathology, movement variability, and risk of injury.

**5.1.4 Mechanical Outcome Measures**

Ankle joint laxity measures did not differ among the groups, supporting our hypothesis. This is consistent with previous investigations suggesting the presence of PAI does not have an association with mechanical ankle laxity.\textsuperscript{41,306} However, conflicting results were shown in early work that have reported ankle-subtalar joint complex laxity, specifically in the inversion and anterior directions\textsuperscript{307} in participants with PAI. Ultrasonography evidence has shown increased talocrual joint laxity with greater elongation of the anterior talofibular ligament of participants with PAI and ankle sprain copers compared to healthy control. Although the reason for these inconsistent findings are unclear, taken together, all cases of PAI cannot be explained by the mechanical ankle laxity.\textsuperscript{308} Individuals who have a previous history of ankle sprain may experience a lingering feeling of joint instability with repeated episodes of ankle “giving-way” without contributions from mechanical ankle laxity.

We did not observe differences in WBLT and NW-DF among the groups. A positional fault of the talus in the ankle of participants with PAI has been identified in radiographic evidence,\textsuperscript{309} which is theorized as a contributing factor that impairs
arthrokinematics and decreases ankle DF-ROM. While we did not assess the positional fault of the talus, our results indicate that the potential anatomical changes associated with ankle instability may not manifest in a decrease in ankle DF-ROM between the groups. The findings of ankle DF-ROM are in agreement with a previous study that used similar DF-ROM testing and did not find differences between previously injured ankles and the healthy contralateral ankle; yet, the amount of posterior talar glide was reduced in the injured ankle. In contrast, previous investigators have reported reductions of DF-ROM during the WBLT.

The availability of ankle DF-ROM is influenced by multiple factors, including gastrocnemius-soleus complex tightness, impaired athrokinematics, and hypermobility of other joints. If restricted DF-ROM is identified in patients with PAI, it is necessary to recognize which factors limit ankle DF-ROM. Furthermore, decreased DF-ROM was observed during gait in participants with PAI compared to healthy controls, indicating that the presence of PAI more likely influences ankle dorsiflexion during more functional tasks. This supports that self-reported ankle instability with repeated episodes of ankle “giving-way” is attributed to sensorimotor dysfunction at both the spinal and supraspinal levels regardless of mechanical restrictions or deficits. Sensorimotor alterations may manifest as altered movement organization during functional tasks in individuals with PAI. Further investigation should consider if restricted ankle DF-ROM during functional tasks are due to sensorimotor alterations rather than mechanical impairments in the ankle.

5.1.5 Dynamic Postural Control

The SEBT is a clinician-generated assessment tool to assess dynamic postural
control. Interestingly, the SEBT-A revealed no differences among the groups.
Contrasting findings were reported in previous work that reported shorter reach distances in participants with PAI compared to healthy controls. It has been shown that restricted ankle DF-ROM is associated with decreased performance on the SEBT. We did not find any group differences with the WBLT or NWB-DF measures. Therefore, it is possible that the lack of group differences in ankle DF-ROM may be the primary reason that we did not find differences in the SEBT-A performance between the groups. During the SEBT-A, the sensorimotor system utilizes various options within the involved degrees of freedom to maintain balance and achieve maximal reaches. If one of the options within the degrees of freedom is not available because of the presence of PAI, other movement solutions may be utilized by the sensorimotor system. Sefton et al. reported no difference in SEBT performance between participants with and without PAI and suggested the variability of the self-assessed disability in participants with PAI may account for the lack of difference in the SEBT. While we observed lower FAAM scores in the PAI groups compared to the control group, the three PAI subgroups means of the FAAM-ADL (90.05% to 97.82%) and FAAM-S (78.7% to 94.95%) were higher than what typically is reported. For instance, Hoch et al. reported the PAI group means of 80.8% and 58.1% for the FAAM-ADL and FAAM-S, respectively. We did not find differences in physical activity levels between the five groups, and participants with PAI we recruited for this study were young adults and moderately physical active. Therefore, it is possible that those with PAI have developed ways to improved SEBT-A performance, by utilizing other options within degrees of freedom available with the sensorimotor system. We are unaware which options
participants with PAI utilized. Researchers have observed that participants with PAI utilized more of “proximal strategies” during the SEBT-A.\textsuperscript{167} Future work should consider the global functions in the sensorimotor systems to assess the effect of PAI on dynamic balance measure.

5.2 Specific Aim 1: Exploratory Three Traditional Groups Comparison

In the primary aim 1, we subgrouped PAI into four categories based on the number of ankle sprains (a single ankle sprain or two or more ankle sprains), the number of repeated episodes of ankle giving-way, as well as the presence of self-assessed instability questionnaire scores. Examining the selected outcome measures between these four groups and comparing with a group with no history of ankle sprain provided important direction toward elucidating the underlying mechanism of PAI. However, self-reported disability during ADL and perceptual outcome measures did not differ between the RAS-PI and FAI or between the RAS and copers. The number of acute lateral ankle sprain incidents may be independent of the level of self-reported disability and ankle instability. To our knowledge, this was the first investigation of this size to consider the number of acute ankle sprains as a differentiating factor for patient categorization. Wikstrom et al.\textsuperscript{12} reported patient-generated outcome measures exhibited the greatest ability to discriminate between ankle instability copers and participants with PAI. The authors also suggested that perception of instability is likely the most serious symptoms of PAI.\textsuperscript{12} Therefore, based on the presence of self-reported instability questionnaire
scores and the number of repeated episodes of “giving-way,” we combined participants with RAS-PI and FAI into the PAI group as well as participants initially categorized as RAS and ankle sprain copers into the ankle instability coper group.

Differences between the more “traditional” three groups were observed in neural excitability and static postural control outcome measures. Additionally, differences in the variability of the frontal plane ankle kinematics during walking become much more glaring. With the three group categorization, the perception of ankle instability and giving-way had a stronger relation with self-assessed functional limitations, psychological responses to injury, and altered sensorimotor functions. Therefore, the presence of self-reported instability and repeated episodes of “giving-way” may be more important components to determine group membership, than the number of acute ankle sprains suffered by a patient.

It should be acknowledged that the more traditional three group classifications do not represent a true homogenous cohort of participants. The original definition of ankle sprain coper is an individual who has a previous history of one lateral ankle sprain, but returns to high-level activities without recurrent injury, functional impairments, and/or the development of perceptive instability and repetitive episodes of giving way. However, the number of acute ankle sprains suffered by participants in the coper group (mean = 1.85 ± 1.20) did not differ greatly from those in the PAI group (mean = 2.86 ± 2.62). Some of participants in the coper group had recurrent ankle sprains, but returned to previous physical activity levels without any other complications such as self-reported disability and instability. Therefore, it is possible that recurrent ankle sprainers have successfully developed strategies to cope perceived instability and repeated episodes of
ankle giving-way; yet, the coping strategies employed are not enough to prevent recurrent ankle sprains incidents, but are successful at reducing the perceived instability and actual giving-way. In light of this, perhaps additional work is needed to differentiate “ankle instability” copers and “ankle sprain” copers.

5.3 Specific Aim 2: Discriminate Functional Analysis

Multiple sensorimotor and mechanical measurements were used to investigate individual factors that could manifest differently in PAI, copers, and healthy control participants. Perhaps more interesting was the DFA used to determine the optimal combination of the selected outcome measures in this current study that could define and identify members of each participant group. Our study revealed a combination of six sensorimotor variables (\(H_{\text{max}}:M_{\text{max}}\) ratio, COPV-AP and-ML, V: \(M_{\text{max}}\) ratio, TTB mean-AP, and SD of TTB-ML) could correctly classify only 45.83% of participants with RAS-PI. Specifically, static postural control (COPV-AP, COPV-ML, and SD of TTB-ML) and spinal excitability measure (\(H_{\text{max}}:M_{\text{max}}\) ratio) were found to be the most influential components of classification. However, in our original design with five patient groups, these selected outcome measures could correctly classify less than 45% of the combined three subgroups of PAI.

When participants were classified into the more “traditional” three groups, the overall classification in the DFA model was improved. This result supports our speculation that the presence of self-reported instability and repeated episodes of “giving-way” may be more important components for group classification, than the number of ankle sprains. This is consistent with Hiller et al.\(^{34}\), suggesting the need to add perceived
instability into the model of defining PAI. This three group DFA model included a similar five sensorimotor variables (H_{max}^\text{max}: M_{max}^\text{max} ratio, V: M_{max}^\text{max} ratio, COPV-AP and ML, and SD of TTB-ML) to the original grouping, as well as could correctly classify 63.89% of participants with PAI, 62.96% of ankle sprain copers, and 66.67% of healthy controls. Specifically, H_{max}^\text{max}: M_{max}^\text{max} ratio, V: M_{max}^\text{max} ratio, COPV-AP, COPV-ML, mean TTB-ML, and SD of TTB-ML strongly contributed to this classification model.

The DFA findings in the current study partially support previous investigation of Sefton et al.\textsuperscript{13} in which a combination of static postural control and spinal reflex excitability measures could correctly classify over 86% of participants with PAI. Both their and our investigations indicate that static postural control and neural excitability measures may be most able to detect sensorimotor dysfunction in participants with PAI. Of these sensorimotor variables, static postural control measures most influenced the PAI classification. Therefore, static postural control and neural excitability measures possibly represent the targeted area for modification and management of PAI through therapeutic interventions.

However, it should be noted that only 62.96% of ankle instability copers were correctly classified. Approximately 47% of the variance observed in the coper group membership remains unexplained. Wikstrom et al.\textsuperscript{12} identified some sensorimotor outcome measures that were able to predict which individuals are more and less likely to develop PAI after an initial lateral ankle sprain. These sensorimotor outcome measures included the dynamic postural stability index obtained during a single-legged hop stabilization test that is a more complex and dynamic task than sensorimotor assessment tools used in this study. It is possible that examining sensorimotor outcome measures
during more dynamic and complex tasks would improve the classification model for copers and help to understand the relation between PAI and sensorimotor function.

5.4 Limitations

This study was not without limitations. The primary limitation is the small number of participants in the RAS (n = 11) and FAI (n = 12) groups. *Post hoc* power analyses showed that all our non-significant findings were associated with low to moderate statistical power (observed powers = 0.07-0.71), increasing the risk of a type II error. Additionally, low to moderate statistical power levels were observed in all our non-significant results from three groups comparisons (observed powers = 0.05-0.588). However, some of the non-significant differences had small effect sizes with associated 95% CIs crossing zero, indicating that these relation simply may not be clinically significant. Some of the non-significant differences were associated with moderate to large effect sizes, indicating that these relations are likely associated with a moderate or large clinical difference. In cases of moderate effect sizes with 95% CI that crossed zero, these relations may be associated with statistical error and strengthened with an expanded sample size. Nonetheless, it is possible that a larger numbers of participants are needed to confirm the findings of the current study.

A methodological issue in our neural excitability testing could complicate the interpretation of the findings. We assessed neural excitability in the seated position with 90° of hip flexion, knee flexion, and ankle dorsiflexion. The H-reflex and AMT in the soleus depends on changes in body positions and the type of task. Additionally, it has been suggested that $H_{\text{max}}: M_{\text{max}}$ ratios obtained during rest do not adequately reflect
neuromuscular function during functional tasks. Therefore, interpretations of the association of neural excitability and postural control should be made with caution. Future investigation should consider how best to conduct these neural excitability assessments during functional tasks.

This study included only the soleus muscle because it has a significant role in maintenance of upright stance. The tibialis anterior and fibularis longus muscles are also vital for ankle stabilization. Further investigation is needed to determine the effect of PAI on intracrotical excitability of other ankle joint stabilizers.

Our participants walked on a motorized treadmill instead of over-ground for movement variability assessment. Previous investigations reported that treadmill walking can influence lower extremity kinematics and variability measures compared to over-ground walking. However, it has been documented that familiarization trials can generalize kinematics to over-ground walking. A large number of continuous data points are required to calculate ApEn of the lower extremity kinematics. Furthermore, speed can influence kinematic variability during walking and over-ground walking does not warrant a constant speed for a long period of time. Therefore, the motorized treadmill was used to eliminate the confounding effect of speed.

Retroflective markers were secured to the skin to calculate joint kinematics, which can induce measurement errors in assessing the true joint motions due to skin motion artifact. We calculated joint centers from the 3D trajectories of markers placed over areas without soft tissue movement to minimize this error.

Lastly, ankle sprain copers returned to previous physical activity levels without any other complications such as self-reported disability and instability. However, we did
not ask participants whether they were using ankle tape or brace to assist in improving ankle stability and to compensate “giving-way” sensation or not. It is possible that use of ankle tape or brace is associated with the coping mechanisms following an ankle sprain, and some participants in the coper group experience perceived instability without an ankle tape or brace. Therefore, future study should consider information regarding use of ankle tape or brace during the screening process.

5.5 Clinical Implications and Future Perspectives

The information from this current study may help clinicians and researchers to develop a better understanding of PAI. Differentiating patients based on self-reported instability with repeated episodes of ankle “giving-way” had strong associations with altered neural excitability and impaired static postural control. Furthermore, these sensorimotor measures provided insight into how ankle instability or sprain copers have successfully developed strategies within the sensorimotor system to cope with perceived instability and repeated episodes of ankle giving-way. These altered sensorimotor functions associated with PAI may be targets for clinical interventions, and it is critical to explore how interventions and rehabilitation protocols affect sensorimotor system function.

Static postural control impairments have been shown to be related to a decreased in spinal reflex excitability and inability to modulate segmental spinal reflex.\textsuperscript{289,320} It has been reported that static postural control was improved after H-reflex training.\textsuperscript{321} Therefore, treatment and rehabilitation of PAI should focus on manipulating the spinal reflex excitability. Because we observed increased $H_{\text{max}} : M_{\text{max}}$ and $V : M_{\text{max}}$ ratios in
ankle instability copers compared to participants with PAI, therapeutic interventions that can increase increased H-reflex and V-wave in the soleus is likely effective to manage PAI. It has been documented that a lower intensity transcutaneous electrical stimulation (TENS) may be effective at increasing H-reflex in the soleus muscle.\(^{322,323}\) In addition to TENS, previous studies demonstrated that spinal reflex excitability can be trained and improved with reflex conditioning protocols.\(^{221-223}\) Thompson et al.\(^ {223}\) demonstrated that H-reflex operant conditioning protocols with visual feedback could modulate the soleus H-reflex in healthy individuals during standing and waking and induced plasticity in the spinal cord, which leads to improvements in motor function. However, the effect of H-reflex operant conditioning protocols with visual feedback on spinal reflexive excitability of the soleus in patients with PAI is unknown. In order to potentially target the spinal reflex excitability, it may be beneficial for future research to determine if H-reflex operant conditioning protocols have an effect on the spinal reflex pathways that are influential to motor function following ankle sprains.

The results of the current investigation indicate static postural control impairments may be associated with altered feedback and feed-forward controls in the sensorimotor system. Therefore, comprehensive sensorimotor evaluation should be included in rehabilitation programs for managing this ankle pathology. Ross et al.\(^ {324}\) reported that participants with PAI demonstrated significant improvements in static postural stability following feedback balance training with stochastic resonance stimulation that transmits subsensory electrical Gaussian white noise into the body. The error-based balance training program developed by McKeon et al.\(^ {325}\) has been shown to improve the ability of patients to cope with changes in demand tasks during excursion of...
movement goals. Lastly, Rozzi et al. reported significant improvement in the sensorimotor functions in patients with PAI following balance training with visual feedback. Visual feedback during functional tasks influence supraspinal motor control through addressing impaired movement abilities. Therefore, clinicians may consider visual feedback during sensorimotor retraining to focus on the quality of the movement goal execution.

Lastly, the DFA model included only the laboratory-generated measures that capture changes within the sensorimotor system. It has been recommended to use all of the patient-, clinician, and-laboratory (PCL)-generated outcome measures in order to assess how altered sensorimotor functions associated with PAI lead to self-reported limitations and restrictions. Specially, the patient-generated outcome measures provide valuable information on how sensorimotor dysfunctions observed in patients with PAI alter self-reported instability and disability, quality of life, and psychological responses to their ankle pathology. The patient-generated outcome measures also capture improvements, help determine when patients should progress, and assess effectiveness of treatments targeting sensorimotor dysfunctions on self-reported limitations and restrictions. Identifying which of the specific patient-generated measures is the most influential may help clinicians to make a decision when a patient can progress and whether the patient has overcome the continuum of disability associated with PAI. Therefore, further analysis should include the patient-generated outcome measures in the DFA to assess how self-reported outcome measures assessing patient-reported limitations and psychological responses to injury play a vital role in group classification.
5.6 Conclusion

In conclusion, alterations in neural excitability and static postural control were strongly associated with the major symptoms that can differentiate PAI and ankle instability cope groups, including perceived instability and repeated episodes of ankle "giving-way." Neural excitability and static postural control measures were shown to be the most influential factors to classify group membership. These results suggest that future investigations should consider focusing on altered neural excitability and static postural control impairments in developing an understanding of the relation between PAI and sensorimotor dysfunction. Clinically, targeting these changes in neural excitability and postural control may benefit patients with PAI to develop strategies to cope with their ankle pathology. Long-term prospective investigations are necessary to explore the time course of the neural excitability and postural control changes after an initial lateral ankle sprain to develop more effective prevention and rehabilitation interventions in managing PAI.
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Appendix A

IRB Informed Consent

ADULT RESEARCH SUBJECT INFORMATION AND CONSENT FORM
SENSORIMOTOR AND MECHANICAL FACTORS CONTRIBUTING TO POSTTRAUMATIC ANKLE INSTABILITY
Principal Investigator: Phillip Grable, Ph.D., ATC
Other Staff (identified by role): Massachusetts General, MS, ATC, Co-Investigator
Samantha Benner, ATC, Co-Investigator
Abbey Thomas, PhD, ATC, Co-Investigator

Contact Phone number(s): (419) 530-2691

What you should know about this research study:
- We give you this consent/authorization form so that you may read about the purpose, risks, and benefits of this research study. All information in this form will be communicated to you verbally by the research staff as well.
- Routine clinical care is based upon the best-known treatment and is provided with the main goal of helping the individual patient. The main goal of research studies is to gain knowledge that may help future patients.
- We cannot promise that this research will benefit you. Just like routine care, this research can have side effects that can be serious or minor.
- You have the right to refuse to take part in this research, or agree to take part now and change your mind later.
- If you decide to take part in this research or not, or if you decide to take part now but change your mind later, your decision will not affect your routine care.
- Please review this form carefully. Ask any questions before you make a decision about whether or not you want to take part in this research. If you decide to take part in this research, you may ask any additional questions at any time.
- Your participation in this research is voluntary.

PURPOSE (WHY THIS RESEARCH IS BEING DONE)
You are being asked to take part in a research study examining Star Excursion Balance Test (SEBT) performance, brain function, how the brain and spinal cord control the lower leg muscles, locomotor patterns during walking, static postural control, ankle joint stability, and ankle dorsiflexion range of motion (DF-ROM). Posttraumatic ankle instability (PAI), which is characterized by the presence of repeated episodes of giving-way feeling and repetitive ankle sprains, is common after an initial acute lateral ankle
sprain in physically active populations, leading to decreased activity levels, decreased quality of life, limited occupational involvement, and an early onset of degenerative pathology in the ankle. Therefore, PAI is a significant public health problem, and there is an increased need to better understand the underlying mechanisms that develop PAI. The purpose of the study is to identify specific sensorimotor and mechanical factors that would characterize homogenous groups of participants with PAI established based on the presence of self-reported impairment, perception of instability, and/ or recurrent ankle sprain.

You were selected as someone who may want to take part in this study because you have met following criteria:

You will be in the PAI group if you:
- Would like to voluntarily participate in this study
- Between the ages 18 and 45 years
- Have previous history of at least one significant ankle sprain that causes pain, swelling, and temporary loss of function
- Have at least 2 episodes of feeling unstable or “giving way” in the past 12 months
- Have no significant injury to the ankle in the past 3 months
- No history of any musculoskeletal and neurovascular injury in the lower extremity other than the ankle in the previous two years
- No previous fractures or surgery in the lower extremity
- Are free of balance or vestibular dysfunction
- Have no history of concussion in the previous 5 months
- Have no history of low back pain in the previous 12 months
- Answer “yes” to the question, “Do you have a history of ankle sprain?” on the Ankle Instability Instrument (AII)
- Have no history of heart disease
- Do not have metal implants anywhere in the head, neck, or shoulders (excluding dental work)
- Have no personal or familial history of seizures or epilepsy
- Do not have dental foreign objects or cochlear implants
- Do not have any implanted brain stimulators, aneurysm clips, implanted medication pumps, intra-cardiac lines, or cardiac pacemakers
- Have no history of or is currently abusing illicit drugs or alcohol or is currently withdrawing from any substance
- Are not taking any medication that may lower seizure threshold (including, but not limited to, tricyclic antidepressants, neuroleptic agents, Baccot, and Tramadol)
- Have no history of serious head injury or increased intracranial pressure; and 9) may be pregnant.
Further, you will be in the following subgroups of posttraumatic Ai if you have met following criteria:

<table>
<thead>
<tr>
<th></th>
<th># of previous ankle sprains</th>
<th>Repeated episodes of “giving-way”</th>
<th>FAAM Score</th>
<th>All</th>
<th>dF/AI score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Posttraumatic Ai: RAS-PI</td>
<td>2</td>
<td>At least two episodes in previous 12 months</td>
<td>ADL: &lt; 60%</td>
<td>&lt; 3</td>
<td>&lt; 10</td>
</tr>
<tr>
<td>Posttraumatic Ai: RAS</td>
<td>2</td>
<td>No</td>
<td>ADL: 60%</td>
<td>&lt; 3</td>
<td>&lt; 10</td>
</tr>
<tr>
<td>Posttraumatic Ai: FAI</td>
<td>1</td>
<td>At least two episodes in previous 12 months</td>
<td>ADL: &lt; 80%</td>
<td>&lt; 3</td>
<td>&lt; 10</td>
</tr>
<tr>
<td>Posttraumatic Ai: Coper</td>
<td>1</td>
<td>No</td>
<td>ADL: 80%</td>
<td>&lt; 3</td>
<td>&lt; 10</td>
</tr>
</tbody>
</table>

Ai=Ankle Instability; RAS-PI=Recurrence Ankle Sprain with Perceptual Instability; FAI=Functional Ankle Instability; FAAM=Foot and Ankle Ability Measure; All=Ankle Instability Instrument; dF/AI=Identification of Functional Ankle Instability; ADL=Activities Daily Living

You will be in the control (healthy) group if you:
- Would like to voluntarily participate in this study
- Between the ages 18 and 45 years
- Are free of balance or vestibular dysfunction
- Have no history of concussion in the previous 6 months
- Have no history of any self-reported musculoskeletal and neurovascular injury and disorder in the lower extremity
- Have no history of surgery in the lower extremity
- Have no history of low back pain in the previous 12 months
- Have no history of heart disease
- Do not have any metal implants anywhere in the head, neck, or shoulders (excluding dental work)
- Have no personal or familial history of seizures or epilepsy
- Do not have ocular foreign objects or cochlear implants
- Do not have any implanted brain stimulators, aneurysm clips, implanted medication pumps, intracardiac lines, or cardiac pacemakers
- Have no history of or is currently abusing illicit drugs or alcohol or is currently withdrawing from any substance
- Are not taking any medication that may lower seizure threshold (including, but not limited to, tricyclic antidepressants, neuroleptic agents, Bactroban, and Tramadol)
- Have no history of serious head injury or increased intracranial pressure; and 5) may be pregnant.
- Have a score of = 103% on the FADI and the FADI Sport Subscale.
- Answer no to the question, “Do you have a history of ankle sprain?” on the All
- Report a score of 100% on the Foot and Ankle Ability Measure (FAAM), and 100 on the FAAM Sport Subscale.
- Report a score of 0 on the Identification of Functional Ankle Instability (dF/AI).

We will be enrolling a total of 120 participants. This research study will be conducted in the Musculoskeletal Health and Movement Science research laboratory that is a collection of three adjacent lab spaces: the Athletic Training Research Laboratory (Room: 1406A), Joint Injury and Muscle Activation Laboratory (Room: 1408), and Motion Analysis Lab (Room: 1412) in the Health Sciences and Human Services building at the University of Toledo.
DESCRIPTION OF THE RESEARCH PROCEDURES AND DURATION OF YOUR INVOLVEMENT

If you decide to take part in this study, you will be asked to complete two testing sessions. Each testing session will take approximately 2 hours. At the beginning of the session, your pre-participation screening will be conducted.

After reading and signing the informed consent, you will be asked to complete a health history questionnaire, exclusion criteria screening sheet, an ankle function questionnaire, called the Foot and Ankle Ability Measure (FAAM) including daily activity and sport sections, the Ankle Instability Instrument Questionnaire, the Identification of Functional Ankle Instability, the Short-form 36, Global Physical Activity Questionnaire, Tampa Scale of Kinesiophobia, and Psychological/Response to Sport Injury Inventory to allow us to better understand your history of the lower extremity injury, your self-reported functions, and your quality of life. Following completion of questionnaire, your leg length, foot length and width, height, and weight will be assessed. The following measurements will then be taken in randomized order:

- Static postural control
- Ankle joint laxity
- Neural excitability

Static Postural Control Testing

Static postural control will be assessed by balancing barefoot on a forceplate. You will be asked to place your hands on hips and hold the opposite leg at approximately 45 degrees of knee flexion (bending knee) while keeping the test foot flat on the forceplate. Three practice trials are given and three testing trials will be recorded, with eyes closed for the testing leg. Failed trials will be repeated until six successful trials are recorded for data analysis.

Star Excursion Balance Test (SEBT)

The SEBT will be performed in the anterior (ANT), posteromedial (PM), and posterolateral (PL) directions. For the ANT reach, you will stand with your toes at the middle of the grid and reach out with the opposite foot to tap as far as possible along the tap mark without raising the test foot. For PM and PL directions, the heel will be at the middle of the grid and you will reach back as far as possible in each direction to tap the measuring tape. You will be given instruction and then perform four practice trials, followed by three test trials in each direction for a total of nine successful trials.

Ankle Joint Stability Testing

Ankle joint stability will be assessed by placing the ankle in an ankle arthrometer and securely fastening the footplate and clamps. You will lie down and try to keep your leg muscles relaxed while your ankle is gently glided and turned inside the device. The examiner will begin with the ankle in a neutral position than test anterior to posterior displacement first. Anterior loading will be applied first followed by posterior loading. Next, an inversion to eversion load will be applied. Inversion will be applied from neutral first followed to eversion. You will remain relaxed to avoid calf contraction for this entire process.

Ankle DP-ROM Testing

We will test how far you are able to comfortably move your ankle. You will be first asked to point your toes by moving your ankle joint toward your head as far as you feel comfortable. We will measure this in a standing position and while you are lying on your back.

Brain and Spinal Cord Function Testing

Three different measures will be performed to assess how your brain and spinal cord control your lower leg muscles (the soleus and tibialis longus muscles).

1. Spinal reflex exotitibility testing
This testing provides an estimate of how well nerves in the lower leg are functioning. You will be asked to sit on a table and to relax your musculature. Two electromyography (EMG) electrodes (stickers) will be placed over your lower leg muscles (the fibularis longus and the soleus) on the testing leg and the medial malleolus on the non-testing leg. These electrodes do not do anything to you; they simply record your muscle activity. The areas of the EMG electrodes will be shaved, scraped with fine sandpaper, and cleaned with isopropyl alcohol wipes. An electrode that provides a stimulus will be taped in the back side of your knee. Several reflex measurements will be taken while you are lying down:

- These measurements include a brief (1-millisecond) electrical stimulus.
- The intensity of this stimulus will vary depending on the reflex being elicited.
- You will feel the stimuli similar to static electricity felt as you touch a doorknob after walking across a carpet.

2. V-wave testing

   This testing provides information how spinal cord and central nervous system control the lower leg muscles during activity. You will be asked to sit in a chair that resembles a car seat. You will have a seat belt applied so that you do not move as you are contracting your leg muscles as hard as you can. You will be asked move your ankle like you are pushing down on a gas pedal as hard as you can and hold it for five seconds. While you are flexing the ankle, the electrical stimulus will be delivered to back side of your knee. This stimulus feels similar to a static electric shock that you could get from walking across a carpet in a dry room and then touching a doorknob, although the voltage is low. You will be asked to perform this at least three times for the test leg. You will be provided 1 minute of rest between each repetition.

3. Intracortical excitability testing

   This testing provides us important information regarding how your brain is sending messages to muscles in your legs. You will be asked to sit in the same chair as above with your arms crossed at your chest. We will position a coil over your head and adjust the position of the coil until it is in the correct spot. We will ask you to wear a swim cap and ear plugs. A brief magnetic shock will then be produced which will sound like a “click.” You may feel a brief muscular contraction in the muscles of your leg or thigh. You will be asked to flex certain leg muscles at a small to moderate intensity while we provide a series of brief magnetic stimuli to your head. For all TMS procedures listed below, you will be seated comfortably in a chair and stickers (electrodes) will be placed on the skin overlying the muscles of your legs. These electrodes record the activity of your muscles. Next, a coil will be placed on your head. The coil will be held close to your scalp while a magnetic pulse is delivered. The magnetic pulse will make your thigh muscles contract. So that we can make sure we place the coil in the same place every time we will ask you to wear a swim cap during the experiment. Detail magnetic stimulation procedures are listed below.

   Motor Threshold Determination

   For this test, you will sit quietly in a chair while the researcher places the coil over your optimal stimulating point. Sets of 10 stimuli will be delivered. The intensity of the stimulus will be varied up and down with each set until the researchers find the lowest intensity possible that makes your muscle contract 3 out of 10 times during a set. You may be asked to lightly (20%) contract your thigh muscle during this test. This process will take approximately 20 minutes.

   Single Pulse Testing

   The data collected during this test are used to normalize the rest of the data collected. Your lower leg muscle contractions during this test will help the researchers to interpret the data collected during your thigh muscle contractions in the other tests. The researcher will place the coil over your optimal stimulating point. Sets of 10 stimuli will be delivered. The intensity of the stimulus will be...
This testing provides an estimate of how well nerves in the lower leg are functioning. You will be asked to lie on a table and to relax your musculature. Two electromyography (EMG) electrodes (stingers) will be placed over your lower leg muscles (the tibialis anterior and the soleus) on the testing leg and the medial malleolus on the non-testing leg. These electrodes do not do anything to you; they simply record your muscle activity. The areas of the EMG electrodes will be shaved, scraped with fine sandpaper, and cleaned with isopropyl alcohol wipe. An electrode that provides a stimulus will be taped in the back side of you knee. Several reflex measurements will be taken while you are lying down:

- These measurements include a brief (1-millisecond) electrical stimulus.
- The intensity of this stimulus will vary depending on the reflex being elicited.
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Motor Threshold Determination

For this test, you will sit quietly in a chair while the researcher places the coil over your optimal stimulating point. Sets of 10 stimuli will be delivered. The intensity of the stimulus will be varied up and down with each set until the researchers find the lowest intensity possible that makes your muscle contract 5 out of 10 times during a set. You may be asked to lightly (25%) contract your thigh muscle during this test. This process will take approximately 20 minutes.

Single Pulse Testing

The data collected during this test are used to normalize the rest of the data collected. Your lower leg muscle contractions during this test help the researchers to interpret the data collected during your thigh muscle contractions in the other tests. The researcher will place the coil over your optimal stimulating point. Sets of 10 stimuli will be delivered. The intensity of the stimulus will be...
COST TO YOU FOR TAKING PART IN THIS STUDY
You are not directly responsible for making any type of payment to take part in this study. However, you are responsible for providing your own means of transportation to and from the Health Science and Human Services Building at The University of Toledo. You will not be compensated for gas for travel or any other expense to participate in this study. You will receive a two-day parking permit for participation in this study by the investigators if you do not have it.

PAYMENT OR OTHER COMPENSATION TO YOU FOR TAKING PART IN THIS RESEARCH
If you decide to take part in this research you will not receive any compensation including money, free treatment, free medications, or free transportation.

PAYMENT OR OTHER COMPENSATION TO THE RESEARCH SITE
The University of Toledo is receiving money or other benefits from the sponsor of this research as reimbursement for conducting the research.

ALTERNATIVE(S) TO TAKING PART IN THIS RESEARCH
There is no alternative to taking part in this research. Exclusion from the study, however, will not affect the quality of care you may receive at the sports medicine/physical therapy facility, doctor's office, or other medical facilities.

CONFIDENTIALITY - (USE AND DISCLOSURE OF YOUR PROTECTED HEALTH INFORMATION)
By agreeing to take part in this research study, you give to The University of Toledo (UT), the Principal Investigator and all personnel associated with this research study your permission to use or disclose information that can be identified with you that we obtain in connection with this study. We will use this information for the purpose of conducting the research study as described in the research consent/authorization form.

The information that we will use or disclose includes the consent forms with your signature, your height, body weight, information from pre-participation screen questionnaire and assessment, and data from all outcome measures. The information will be stored in locked cabinet and computer secured by anti-virus software and password which research team can only access. We may use this information ourselves, or we may disclose or provide access to the information to Dr. Gibble, Phillip, Principal Investigator; Sam Bowker, Co-Investigator, Masafumi Terada, Co-Investigator, and Dr. Abbey Thomas, Co-Investigator as part of the research study. Under some circumstances, the Institutional Review Board and Research and Sponsored Programs of the University of Toledo may review your information for compliance audits. Your protected health information when required by law, such as in response to judicial orders.

The researchers will make every effort to prevent anyone who is not on the research team from knowing that you provided this information, or what that information is. The consent forms with signatures will be kept separate from responses, which will not include names and which will be presented to others only when combined with other responses. Although we will make every effort to protect your confidentiality, there is a low risk that this might be breached.

Under some circumstances, the Institutional Review Board, or the Research and Sponsored Programs of the University of Toledo may review your information for compliance audits. If you receive any payments for taking part in this study, your personal information and limited information about this study will be given to The University of Toledo’s accounts payable department as necessary to process payment to you. We may also disclose your protected health information when required by law, such as in response to judicial orders.
The University of Toledo is required by law to protect the privacy of your health information, and to use or disclose the information we obtain about you in connection with this research study only as authorized by you in this form. There is a possibility that the information we disclose may be re-disclosed by the persons we give it to, and no longer protected. However, we will encourage any person who receives your information from us to continue to protect and not re-disclose the information.

Except as noted in the above paragraph, your permission for us to use or disclose your protected health information as described in this section is voluntary. However, you will not be allowed to participate in the research study unless you give us your permission to use or disclose your protected health information by signing this document.

A more complete statement of University of Toledo's Privacy Practices is set forth in its Joint Notice of Privacy Practices. If you have not already received this Notice, a member of the research team will provide this to you. If you have any further questions concerning privacy, you may contact the University of Toledo's Privacy Officer at 419-383-3413.

**IN THE EVENT OF A RESEARCH-RELATED INJURY**

In the event of injury resulting from your taking part in this study, treatment can be obtained at a health care facility of your choice. You should understand that the costs of such treatment will be your responsibility. Financial compensation is not available through The University of Toledo or The University of Toledo Medical Center. By signing this form you are not giving up any of your legal rights as a research subject.

In the event of an injury, contact Phillip Gribble, PhD, ATC (419) 530-2691.

**VOLUNTARY PARTICIPATION**

Taking part in this study is voluntary. You may refuse to participate or discontinue participation at any time without penalty or a loss of benefits to which you are otherwise entitled. If you decide not to participate or to discontinue participation, your decision will not affect your course grades and evaluations as well as your future relations with the University of Toledo or The University of Toledo Medical Center.

**NEW FINDINGS**

You will be notified of new information that might change your decision to be in this study if any becomes available.

**OTHER IMPORTANT INFORMATION**

There is no additional information.

**ADDITIONAL ELEMENTS**

There are no additional elements to the study.

*Continued On Next Page*
OFFER TO ANSWER QUESTIONS
Before you sign this form, please ask any questions on any aspect of this study that is unclear to you. You may take as much time as necessary to think it over. If you have questions regarding the research at any time before, during or after the study, you may contact Phillip Gribble, PhD, ATC (419) 530-2591.

If you have questions beyond those answered by the research team or your rights as a research subject or research-related injuries, please feel free to contact the Chairperson of the University of Toledo Biomedical Institutional Review Board at 419-383-6796.

SIGNATURE SECTION (Please read carefully)
YOU ARE MAKING A DECISION WHETHER OR NOT TO PARTICIPATE IN THIS RESEARCH STUDY. YOUR SIGNATURE INDICATES THAT YOU HAVE READ THE INFORMATION PROVIDED ABOVE, YOU HAVE HAD ALL YOUR QUESTIONS ANSWERED, AND YOU HAVE DECIDED TO TAKE PART IN THIS RESEARCH.

BY SIGNING THIS DOCUMENT YOU AUTHORIZE US TO USE OR DISCLOSE YOUR PROTECTED HEALTH INFORMATION AS DESCRIBED IN THIS FORM.

The date you sign this document to enroll in this study, that is, today's date, MUST fall between the dates indicated on the approval stamp affixed to the bottom of each page. These dates indicate that this form is valid when you enroll in the study but do not reflect how long you may participate in the study. Each page of this Consent/Authorization Form is stamped to indicate the form's validity as approved by the UT Biomedical Institutional Review Board (IRB).

| Name of Subject (please print) | Signature of Subject or Person Authorized to Consent | Date |
| Relationship to the Subject (Healthcare Power of Attorney authority or Legal Guardian) | Time | a.m. p.m. |
| Name of Person Obtaining Consent (please print) | Signature of Person Obtaining Consent | Date |
| Name of Witness to Consent Process (when required by ICH Guidelines) (please print) | Signature of Witness to Consent Process (when required by ICH Guidelines) | Date |

YOU WILL BE GIVEN A SIGNED COPY OF THIS FORM TO KEEP.
## Appendix B

### Ankle Instability Instrument

<table>
<thead>
<tr>
<th>Instructions</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>This form will be used to categorize your ankle instability. A separate form</td>
<td></td>
<td></td>
</tr>
<tr>
<td>should be used for the right and left ankles. Please fill out the form</td>
<td></td>
<td></td>
</tr>
<tr>
<td>completely. If you have any questions, please ask the administrator of the</td>
<td></td>
<td></td>
</tr>
<tr>
<td>survey. Thank you for your participation.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Have you ever sprained an ankle?</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>2. Have you ever seen a doctor for an ankle sprain?</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>If yes,</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2a. How did the doctor categorize your most serious ankle sprain?</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>☐ Mild (grade 1) ☐ Moderate (grade 2) ☐ Severe (grade 3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Did you ever use a device (such as crutches) because you could not bear</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>weight due to an ankle sprain?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>If yes,</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3a. In the most serious case, how long did you need to use the device?</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>☐ 1–3 days ☐ 4–7 days ☐ 1–2 weeks ☐ 2–3 weeks ☐ &gt;3 weeks</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Have you ever experienced a sensation of your ankle “giving way”?</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>If yes,</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4a. When was the last time your ankle “gave way”?</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>☐ &lt;1 month ☐ 1–6 months ago ☐ 6–12 months ago ☐ 1–2 years ago ☐ &gt;2 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Does your ankle ever feel unstable while walking on a flat surface?</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>6. Does your ankle ever feel unstable while walking on uneven ground?</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>7. Does your ankle ever feel unstable during recreational or sport activity?</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>☐ Yes ☐ No ☐ N/A</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8. Does your ankle ever feel unstable while going up stairs?</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>9. Does your ankle ever feel unstable while going down stairs?</td>
<td>☐</td>
<td>☐</td>
</tr>
</tbody>
</table>
Appendix C

Identification of Functional Ankle Instability

<table>
<thead>
<tr>
<th>IDENTIFICATION OF FUNCTIONAL ANKLE INSTABILITY (6{FAI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Instructions: This form will be used to categorize your ankle stability status. A separate form should be used for the right and left ankles. Please fill out the form completely and if you have any questions, please ask the administrator. Thank you for your participation.</td>
</tr>
<tr>
<td>-------------------------------------------------------</td>
</tr>
<tr>
<td>Please carefully read the following statement:</td>
</tr>
<tr>
<td>&quot;Giving way&quot; is described as a temporary uncontrollable sensation of instability or rolling over of one's ankle.</td>
</tr>
<tr>
<td>-------------------------------------------------------</td>
</tr>
<tr>
<td>I am completing this form for my RIGHT/LEFT ankle (circle one).</td>
</tr>
<tr>
<td>1.) Approximately how many times have you sprained your ankle? ________</td>
</tr>
<tr>
<td>2.) When was the last time you sprained your ankle?</td>
</tr>
<tr>
<td>□ Never □ &gt; 2 years □ 1-2 years □ 6-12 months □ 1-6 months □ &lt; 1 month</td>
</tr>
<tr>
<td>3.) If you have seen an athletic trainer, physician, or healthcare provider how did he/she categorize your most serious ankle sprain?</td>
</tr>
<tr>
<td>□ Have not seen someone □ Mild (Grade I) □ Moderate (Grade II) □ Severe (Grade III)</td>
</tr>
<tr>
<td>4.) If you have ever used crutches, or other device, due to an ankle sprain how long did you use it?</td>
</tr>
<tr>
<td>□ Never used a device □ 1-3 days □ 4-7 days □ 1-2 weeks □ 2-3 weeks □ &gt; 3 weeks</td>
</tr>
<tr>
<td>5.) When was the last time you had &quot;giving way&quot; in your ankle?</td>
</tr>
<tr>
<td>□ Never □ &gt; 2 years □ 1-2 years □ 6-12 months □ 1-6 months □ &lt; 1 month</td>
</tr>
<tr>
<td>6.) How often does the &quot;giving way&quot; sensation occur in your ankle?</td>
</tr>
<tr>
<td>□ Never □ Once a year □ Once a month □ Once a week □ Once a day</td>
</tr>
<tr>
<td>7.) Typically when you start to roll over (or &quot;twist&quot;) on your ankle can you stop it?</td>
</tr>
<tr>
<td>□ Never rolled over □ Immediately □ Sometimes □ Unable to stop it</td>
</tr>
<tr>
<td>8.) Following a typical incident of your ankle rolling over, how soon does it return to &quot;normal&quot;?</td>
</tr>
<tr>
<td>□ Never rolled over □ Immediately □ &lt; 1 day □ 1-2 days □ &gt; 2 days</td>
</tr>
<tr>
<td>9.) During &quot;Activities of Daily Life&quot; how often does your ankle feel UNSTABLE?</td>
</tr>
<tr>
<td>□ Never □ Once a year □ Once a month □ Once a week □ Once a day</td>
</tr>
<tr>
<td>10.) During &quot;Sport/or recreational activities&quot; how often does your ankle feel UNSTABLE?</td>
</tr>
<tr>
<td>□ Never □ Once a year □ Once a month □ Once a week □ Once a day</td>
</tr>
</tbody>
</table>

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IDENTIFICATION OF FUNCTIONAL ANKLE INSTABILITY (IdFAI)

Instructions: This form will be used to categorize your ankle stability status. A separate form should be used for the right and left ankles. Please fill out the form completely and if you have any questions, please ask the administrator. Thank you for your participation.

Please carefully read the following statement:
"Giving way" is described as a temporary uncontrollable sensation of instability or rolling over of one's ankle.

I am completing this form for my RIGHT/LEFT ankle (circle one).

1.) Approximately how many times have you sprained your ankle? _________

2.) When was the last time you sprained your ankle?
- Never
- > 2 years
- 1-2 years
- 6-12 months
- 1-6 months
- < 1 month

3.) If you have seen an athletic trainer, physician, or healthcare provider how did he/she categorize your most serious ankle sprain?
- Have not seen someone
- Mild (Grade I)
- Moderate (Grade II)
- Severe (Grade III)

4.) If you have ever used crutches, or other device, due to an ankle sprain how long did you use it?
- Never used a device
- 1-3 days
- 4-7 days
- 1-2 weeks
- 2-3 weeks
- >3 weeks

5.) When was the last time you had "giving way" in your ankle?
- Never
- > 2 years
- 1-2 years
- 6-12 months
- 1-6 months
- < 1 month

6.) How often does the "giving way" sensation occur in your ankle?
- Never
- Once a year
- Once a month
- Once a week
- Once a day

7.) Typically when you start to roll over (or 'twist') on your ankle can you stop it?
- Never rolled over
- Immediately
- Sometimes
- Unable to stop it

8.) Following a typical incident of your ankle rolling over, how soon does it return to normal?
- Never rolled over
- Immediately
- < 1 day
- 1-2 days
- > 2 days

9.) During "Activities of daily life" how often does your ankle feel UNSTABLE?
- Never
- Once a year
- Once a month
- Once a week
- Once a day

10.) During "Sport/or recreational activities" how often does your ankle feel UNSTABLE?
- Never
- Once a year
- Once a month
- Once a week
- Once a day

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## Appendix D

### Foot and Ankle Ability Measure

<table>
<thead>
<tr>
<th>Activity</th>
<th>No Difficulty</th>
<th>Slight Difficulty</th>
<th>Moderate Difficulty</th>
<th>Extreme Difficulty</th>
<th>Unable to do</th>
<th>N/A</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standing</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Walking on even ground</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Walking on even ground without shoes</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Walking up hills</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Walking down hills</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Going up stairs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Going down stairs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Walking on uneven ground</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stepping up and down curbs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Squatting</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coming up on your toes</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Walking initially</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Walking 5 minutes or less</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Walking approximately 10 minutes</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Walking 15 minutes or greater</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Foot and Ankle Ability Measure (FAAM)
Activities of Daily Living Subscale

Because of your foot and ankle how much difficulty do you have with:

<table>
<thead>
<tr>
<th>No Difficulty at all</th>
<th>Slight Difficulty</th>
<th>Moderate Difficulty</th>
<th>Extreme Difficulty</th>
<th>Unable to do</th>
<th>N/A</th>
</tr>
</thead>
<tbody>
<tr>
<td>Home responsibilities</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Activities of daily living</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Personal care</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Light to moderate work (standing, walking)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heavy work</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(push/pulling, climbing, carrying)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recreational activities</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

How would you rate your current level of function during your usual activities of daily living from 0 to 100 with 100 being your level of function prior to your foot or ankle problem and 0 being the inability to perform any of your usual daily activities.

___ ___ ___. 0 %

**Foot and Ankle Ability Measure (FAAM) Sports Subscale**

Because of your foot and ankle how much difficulty do you have with:

<table>
<thead>
<tr>
<th>Activity</th>
<th>No Difficulty at all</th>
<th>Slight Difficulty</th>
<th>Moderate Difficulty</th>
<th>Extreme Difficulty</th>
<th>Unable to do</th>
<th>N/A</th>
</tr>
</thead>
<tbody>
<tr>
<td>Running</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Jumping</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Landing</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Starting and stopping quickly</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Cutting/lateral Movements</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Ability to perform Activity with your Normal technique</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Ability to participate In your desired sport As long as you like</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
</tbody>
</table>

How would you rate your current level of function during your sports related activities from 0 to 100 with 100 being your level of function prior to your foot or ankle problem and 0 being the inability to perform any of your usual daily activities?

___ ___ 0%

Overall, how would you rate your current level of function?

- □ Normal
- □ Nearly Normal
- □ Abnormal
- □ Severely Abnormal
Appendix E

Health History Questionnaire

Participant #____________

Name: ________________________________________

Age: ____________
Height: ____________
Weight: ____________

Sex: M F

1. How many hours and days do you participate in physical activities? :________

2. Which foot do you kick a ball with?: Right_______ Left_______

3. Have you sprained your ankle?: Yes No
   If Yes, which have you sprained, RIGHT or LEFT ankle? _________
   How many times have you sprained your ankle? _________
   When was the most recent? _________

4. Have you ever experienced more than 2 repeated episodes of your ankle “giving way” in the past 12 months? and how many? Yes _______ No _______
   a. How many repeated episodes of “giving-way” have you experienced following an initial ankle sprain _________
   b. When was the last time your ankle “gave way”? ___<1 month ___1-6 months ago ___ 6-12 months ago ___1-2 years ago ___>2 years
   c. _________

5. Have you modified your activity and occupational involvement due to ankle injury? Yes_______ No_______
   If yes, please provide more detail information:__________________________________________
6. Do you feel that you risk injury when playing your sport?  Yes No

7. Are you concerned about environmental conditions such as a wet playing field, a hard court or the type of gym floor when involved in your sport?  Yes No

8. Have you had a concussion in the past twelve months?  Yes No
   If yes, explain: ______________________________________
   ______________________________________
   ______________________________________

9. Have you ever experienced a head injury beside concussion?  Yes No
   If Yes, what was the injury?  ______________________
   When was the most recent?  ______________________

10. Have you ever suffered from a significant back injury causing you to interrupt your sports activity?  Yes No
    If Yes, when was the most recent incident?  ______________________
    What was the cause of the back injury/pain?  ______________________

11. Have you ever suffered from a fracture to any part of your leg, knee, ankle, hip, back, thigh, or foot?  Yes No
    If Yes, when did the fracture occur?  ______________________
    Which bone(s) was fractured?  ______________________

12. Have you ever suffered from a significant hip/thigh injury causing you to interrupt your sports activity?  Yes No
    a) If Yes, when was the most recent incident?  ______________________
    What injuries have you experienced?  ______________________
    b) Did the injury require surgery?  Yes No
    If yes, when was the surgery?  ______________________

13. Have you ever suffered from a significant knee injury causing you to interrupt your sports activity?  Yes No
    a) If Yes, when was the most recent incident?  ______________________
    What injuries have you experienced?  ______________________
    b) Did the injury require surgery?  Yes No
    If yes, when was the surgery?  ______________________

14. Have you ever suffered from a significant lower leg injury causing you to interrupt your sports activity?  Yes No
    a) If Yes, when was the most recent incident?  ______________________
    What injuries have you experienced?  ______________________
b) Did the injury require surgery? Yes  No
If yes, when was the surgery? ______________________

15. Have you ever suffered from a significant ankle/foot injury (other than ankle sprains) causing you to interrupt your sports activity? Yes  No
   a) If Yes, when was the most recent incident? __________________
      What injuries have you experienced? ____________________

   b) Did the injury require surgery? Yes  No
      If yes, when was the surgery? ______________________

16. Do you suffer from vertigo, or any other neurological disorders?: Yes____ No____

   If Yes, explain:________________________________________________________
   ______________________________________________________________________

17. Are you currently suffering from the effects of a cold or flu?: Yes____ No____
Appendix F

Short Form 36

<table>
<thead>
<tr>
<th>Question</th>
<th>SF36 Survey</th>
</tr>
</thead>
</table>
| 1. In general, would you say your health is: | 1. Excellent  
2. Very Good  
3. Good  
4. Fair  
5. Poor |
| 2. Compared to one year ago, how would you rate your health in general now? | 1. Much better now than one year ago  
2. Somewhat better now than one year ago  
3. About the same as one year ago  
4. Somewhat worse now than one year ago  
5. Much worse than one year ago |
| The following items (question 3 to 12) are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much? |  |
| 3. Vigorous activities, such as running, lifting heavy objects, participating in strenuous sports. | 1. Yes, limited a lot  
2. Yes, limited a little  
3. No, not limited at all |
| 4. Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling or playing golf. | 1. Yes, limited a lot  
2. Yes, limited a little  
3. No, not limited at all |
| 5. Lifting or carrying groceries. | 1. Yes, limited a lot  
2. Yes, limited a little  
3. No, not limited at all |
| 6. Climbing several flights of stairs. | 1. Yes, limited a lot  
2. Yes, limited a little  
3. No, not limited at all |
| 7. Climbing one flight of stairs. | 1. Yes, limited a lot  
2. Yes, limited a little  
3. No, not limited at all |
| 8. Bending, kneeling, or stooping. | 1. Yes, limited a lot  
2. Yes, limited a little  
3. No, not limited at all |
| 9. Walking more than a mile. | 1. Yes, limited a lot  
2. Yes, limited a little  
3. No, not limited at all |
| 10. Walking several blocks. | 1. Yes, limited a lot  
2. Yes, limited a little  
3. No, not limited at all |
| 11. Walking one block. | 1. Yes, limited a lot  
2. Yes, limited a little  
3. No, not limited at all |
| 12. Bathing or dressing yourself. | 1. Yes, limited a lot  
2. Yes, limited a little  
3. No, not limited at all |
| During the past 4 weeks, have you had any of the following problems (question 13-16) with your work or other regular daily activities as a result of your physical health? |  |
| 13. Cut down the amount of time you spent on work or other activities. | 1. Yes  
2. No |
| 14. Accomplished less than you would like. | 1. Yes  
2. No |

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15. Were limited in the kind of work or other activities.
   1. Yes
   2. No

16. Had difficulty performing the work or other activities (for example, it took extra effort).
   1. Yes
   2. No

During the past 4 weeks, have you had any of the following problems (Question 17-19) with your work or other regular daily activities as a result of any EMOTIONAL PROBLEMS (such as feeling depressed or anxious)?

17. Cut down the amount of time you spent on work or other activities.
   1. Yes
   2. No

18. Accomplished less than you would like.
   1. Yes
   2. No

19. Didn't do work or other activities as carefully as usual.
   1. Yes
   2. No

20. During the past 4 weeks, to what extent has your physical health OR emotional problems interfered with your normal social activities with family/friends, neighbors, or groups?
   1. Not at all
   2. Slightly
   3. Moderately
   4. Quite a bit
   5. Extremely

21. How much bodily pain have you had during the past 4 weeks?
   1. None
   2. Very mild
   3. Mild
   4. Moderate
   5. Severe
   6. Very severe

22. During the past 4 weeks how much did pain interfere with your normal work (including both work outside the home and housework)?
   1. Not at all
   2. A little bit
   3. Modestly
   4. Quite a bit
   5. Extremely

These questions (Question 23-31) are about how you feel and how things have been with you during the past 4 weeks. For each question, please give the one answer that comes closest to the way you have been feeling.

How much of the time during the past 4 weeks...

23. Did you feel full of pep?
   1. All of the time
   2. Most of the time
   3. A good bit of the time
   4. Some of the time
   5. A little of the time
   6. None of the time

24. Have you been a very nervous person?
   1. All of the time
   2. Most of the time
   3. A good bit of the time
   4. Some of the time
   5. A little of the time
   6. None of the time

25. Have you felt so down in the dumps that nothing could cheer you up?
   1. All of the time
   2. Most of the time
   3. A good bit of the time
   4. Some of the time
   5. A little of the time
   6. None of the time

26. Have you felt calm and peaceful?
   1. All of the time
   2. Most of the time
   3. A good bit of the time
   4. Some of the time
   5. A little of the time
   6. None of the time

Assigned Version Date: 06/05/2013
27. Did you have a lot of energy?
   1. All of the time
   2. Most of the time
   3. A good bit of the time
   4. Some of the time
   5. A little of the time
   6. None of the time

28. Have you felt downhearted and blue?
   1. All of the time
   2. Most of the time
   3. A good bit of the time
   4. Some of the time
   5. A little of the time
   6. None of the time

29. Did you feel worn out?
   1. All of the time
   2. Most of the time
   3. A good bit of the time
   4. Some of the time
   5. A little of the time
   6. None of the time

30. Have you been a happy person?
   1. All of the time
   2. Most of the time
   3. A good bit of the time
   4. Some of the time
   5. A little of the time
   6. None of the time

31. Did you feel tired?
   1. All of the time
   2. Most of the time
   3. A good bit of the time
   4. Some of the time
   5. A little of the time
   6. None of the time

32. During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting with friends, relatives, etc.)?
   1. All of the time
   2. Most of the time
   3. Some of the time
   4. A little of the time
   5. None of the time

How true or false is the following statement? (Question 33-36)?

33. I seem to get sick a little easier than other people.
   1. Definitely true
   2. Mostly true
   3. Don't know
   4. Mostly false
   5. Definitely false

34. I am as healthy as anybody I know.
   1. Definitely true
   2. Mostly true
   3. Don't know
   4. Mostly false
   5. Definitely false

35. I expect my health to get worse.
   1. Definitely true
   2. Mostly true
   3. Don't know
   4. Mostly false
   5. Definitely false

36. My health is excellent.
   1. Definitely true
   2. Mostly true
   3. Don't know
   4. Mostly false
   5. Definitely false

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# Appendix G

## Global Physical Activity Questionnaire

### 2. GPAQ version 2

#### Physical Activity

First, I am going to ask you about the time you spend doing different types of physical activity in a typical week. Please answer these questions even if you do not consider yourself to be a physically active person.

Think back about the time you were doing work. Think of work as the time on the days that you have to do such as paid or unpaid work, studying, training, household chores, farming, hunting, fishing, or hunting for food, doing employment (except for home help if you lived in a rural area). To answer the following questions, vigorous-intensity activities are activities that require hard physical work and cause large increases in breathing or heart rate, moderate-intensity activities are activities that require moderate physical effort and cause small increases in breathing or heart rate.

<table>
<thead>
<tr>
<th>Questions</th>
<th>Responses</th>
<th>Code</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Activity at work</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Do you spend at least vigorous-intensity activity that causes large increases in breathing or heart rate? For at least 10 minutes continuously?</td>
<td>Yes 1</td>
<td>P1</td>
</tr>
<tr>
<td>No 2</td>
<td>A go in P 2</td>
<td></td>
</tr>
<tr>
<td>2. How many days do you do vigorous-intensity activities as part of your work?</td>
<td>Number of days 1-7</td>
<td>P2</td>
</tr>
<tr>
<td>3. How much time do you spend doing vigorous-intensity activities at work on a typical day?</td>
<td>Hours: minutes</td>
<td>P3 1-7</td>
</tr>
<tr>
<td>4. Do you spend at least moderate-intensity activity that causes small increases in breathing or heart rate? For at least 10 minutes continuously?</td>
<td>Yes 1</td>
<td>P4</td>
</tr>
<tr>
<td>No 2</td>
<td>A go in P 2</td>
<td></td>
</tr>
<tr>
<td>5. How many days do you do moderate-intensity activities as part of your work?</td>
<td>Number of days</td>
<td>P5</td>
</tr>
<tr>
<td>6. How much time do you spend doing moderate-intensity activities at work on a typical day?</td>
<td>Hours: minutes</td>
<td>P6 1-7</td>
</tr>
</tbody>
</table>

#### Travel to and from places

The next questions exclude the physical activities at work that you have already mentioned. Next I would like to ask about the usual way you travel to and from places. For example, work, shopping, or market in place of worship (except other activities 6 minutes).

<table>
<thead>
<tr>
<th>Questions</th>
<th>Responses</th>
<th>Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>7. On your way to work or a typical path/track/local bus at least 10 minutes continuously to go at a place from place?</td>
<td>Yes 1</td>
<td>P7</td>
</tr>
<tr>
<td>No 2</td>
<td>A go in P 2</td>
<td></td>
</tr>
<tr>
<td>8. On a typical week, how many days do you walk or bicycle for at least 10 minutes continuously to go to a place from place?</td>
<td>Number of days</td>
<td>P8</td>
</tr>
<tr>
<td>9. How much time do you spend walking or biking for travel on a typical day?</td>
<td>Hours: minutes</td>
<td>P9 1-7</td>
</tr>
</tbody>
</table>

#### Recreational activities

The next questions exclude the work and transport activities that you have already mentioned. Next I would like to ask about physical activities that you engage in during your leisure time, such as exercise.

<table>
<thead>
<tr>
<th>Questions</th>
<th>Responses</th>
<th>Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>10. Do you engage in any vigorous-intensity sports, fitness or recreational activities that cause large increases in breathing or heart rate? For at least 10 minutes continuously?</td>
<td>Yes 1</td>
<td>P10</td>
</tr>
<tr>
<td>No 2</td>
<td>A go in P 2</td>
<td></td>
</tr>
<tr>
<td>11. On a typical week, how many days do you do vigorous-intensity sports, fitness or recreational activities?</td>
<td>Number of days</td>
<td>P11</td>
</tr>
<tr>
<td>12. How much time do you spend doing vigorous-intensity sports, fitness or recreational activities on a typical day?</td>
<td>Hours: minutes</td>
<td>P12 1-7</td>
</tr>
</tbody>
</table>

Continued on next page

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199
### Physical Activity (recreational activities) contd.

<table>
<thead>
<tr>
<th>Questions</th>
<th>Response</th>
<th>Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>13  Do you do any moderate-intensity sports, illness or recreational (natural) activities that cause a small increase in breathing or heart rate such as brisk walking/cycling, swimming, rollerblading at least 10 minutes continuously?</td>
<td>Yes 1</td>
<td>P13</td>
</tr>
<tr>
<td></td>
<td>No 2  If No, go to P16</td>
<td></td>
</tr>
<tr>
<td>14  In a typical week, on how many days do you do moderate-intensity sports, illness or recreational (natural) activities?</td>
<td>Number of days</td>
<td>P14</td>
</tr>
<tr>
<td>15  How much time do you spend doing moderate-intensity sports, illness or recreational (natural) activities on a typical day?</td>
<td>Hours: minutes</td>
<td>P15</td>
</tr>
<tr>
<td></td>
<td>hrs mins</td>
<td>(a-b)</td>
</tr>
</tbody>
</table>

### Sedentary behaviour

The following question is about sitting or reclining at work, at home, getting to and from places, or with friends including time spent sitting at a desk, sitting with friends, travelling in car, bus, train, reading, playing cards or watching television, but do not include time spent sleeping.

<table>
<thead>
<tr>
<th>Questions</th>
<th>Response</th>
<th>Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>16  How much time do you usually spend sitting or reclining on a typical day?</td>
<td>Hours: minutes</td>
<td>P16</td>
</tr>
<tr>
<td></td>
<td>hrs mins</td>
<td>(a-b)</td>
</tr>
</tbody>
</table>
Appendix H

Tampa Scale for Kinesiophobia

Miller, Kori, and Todd (1991)

<table>
<thead>
<tr>
<th>Item</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. I’m afraid that I might injure myself if I exercise</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>2. If I were to try to overcome it, my pain would increase</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>3. My body is telling me I have something dangerously wrong</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>4. My pain would probably be relieved if I were to exercise</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>5. People aren’t taking my medical condition seriously enough</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>6. My accident has put my body at risk for the rest of my life</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>7. Pain always means I have injured my body</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>8. Just because something aggravates my pain does not mean it is dangerous</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>9. I am afraid that I might injure myself accidentally</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>10. Simply being careful that I do not make any unnecessary movements is the safest thing I can do to prevent my pain from worsening</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>11. I wouldn’t have this much pain if there weren’t something potentially dangerous going on in my body</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>12. Although my condition is painful, I would be better off if I were physically active</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>13. Pain lets me know when to stop exercising so that I don’t injure myself</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>14. It’s really not safe for a person with a condition like mine to be physically active</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>15. I can’t do all the things normal people do because it’s too easy for me to get injured</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>16. Even though something is causing me a lot of pain, I don’t think it’s actually dangerous</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>17. No one should have to exercise when he/she is in pain</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>
Appendix I

Psychological Response to Sport Injury

Psychological Response to Sport Injury Inventory (PRSI 19-item version)

This inventory contains a number of statements about the experience of injury. Read each statement and indicate by circling the relevant point on the scale, the extent to which the statement reflects how you presently feel. If you strongly agree, circle 5; if you strongly disagree, circle 1 – and points between as to extent of your feelings. Please make sure that you answer all questions and that you only circle one number per question. Do not place a circle between any two numbers. There are no right or wrong answers, so please answer honestly. The information will be treated in strictest confidence.

<table>
<thead>
<tr>
<th></th>
<th>Strongly Disagree</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>Strongly Agree</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>I am unable to enjoy myself.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>2.</td>
<td>I experience feelings of jealousy</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>3.</td>
<td>I have difficulty accepting that I am injured.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>4.</td>
<td>Team-mates seem to have lost interest in me.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>5.</td>
<td>I am feeling mentally stronger.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>6.</td>
<td>I feel isolated.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>7.</td>
<td>I am devastated by the injury.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>8.</td>
<td>I am unable to relax.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>9.</td>
<td>I am unusually anxious.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>10.</td>
<td>I cannot work out why my injury happened.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>11.</td>
<td>My world has fallen apart.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>12.</td>
<td>Socially I feel like an outcast.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>13.</td>
<td>I have been cheated.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>14.</td>
<td>I am beginning to feel like myself again.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>15.</td>
<td>I feel uneasy.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>16.</td>
<td>I have much more confidence in myself.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>17.</td>
<td>I experience a feeling of emptiness.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>18.</td>
<td>I don’t feel like mixing with other performers.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>19.</td>
<td>I feel as if I have been cheated by being injured.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>
Appendix J

Data Collection Form

<table>
<thead>
<tr>
<th>Demographics</th>
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</thead>
<tbody>
<tr>
<td>Participant #</td>
</tr>
<tr>
<td>Group</td>
</tr>
<tr>
<td>Involved Limb:</td>
</tr>
<tr>
<td>Dominant Limb</td>
</tr>
<tr>
<td>Age</td>
</tr>
<tr>
<td>Height</td>
</tr>
<tr>
<td>Sex</td>
</tr>
<tr>
<td>Weight</td>
</tr>
<tr>
<td>Physical Activity Level</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Order of Testing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Limb Order</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Testing Order</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
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<td></td>
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<tr>
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<tr>
<td></td>
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</table>

Assigned Version Date: 05/05/2013

APPROVED BY UNIVERSITY OF TOLEDO IRB
### Weight-Bearing Lunge Test Form

<table>
<thead>
<tr>
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<th>Right</th>
<th>Left</th>
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<tbody>
<tr>
<td>Trial 1</td>
<td>cm</td>
<td>cm</td>
</tr>
<tr>
<td>Trial 1</td>
<td>cm</td>
<td>cm</td>
</tr>
<tr>
<td>Trial 1</td>
<td>cm</td>
<td>cm</td>
</tr>
<tr>
<td>Note</td>
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### Open-chain Inclinometer Measurement of DF-ROM

<table>
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<th>Left</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trial 1</td>
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<td></td>
</tr>
<tr>
<td>Trial 1</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Note</td>
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</table>
## Ankle Laxity Test Form

**Participant #**

<table>
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<th>Ant.(Max)</th>
<th>Post.(Min)</th>
<th>Total</th>
<th>Inv.(Min)</th>
<th>Ev.(Max)</th>
<th>Total</th>
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</thead>
<tbody>
<tr>
<td>1</td>
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<td></td>
<td></td>
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<td>Avg.</td>
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</table>

<table>
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<th>Ant.(Max)</th>
<th>Post.(Min)</th>
<th>Total</th>
<th>Inv.(Max)</th>
<th>Ev.(Min)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
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<td>Avg.</td>
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**Assigned Version Date: 06/05/2013**
### Static Balance Test Form

- ________cm
- ________cm

### Number of Failed Trials

<table>
<thead>
<tr>
<th>Success</th>
<th>Failed</th>
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<td>Non-testing leg touch down</td>
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<tr>
<td></td>
<td>Testing limb off a force platform</td>
</tr>
<tr>
<td></td>
<td>Opened Eyes</td>
</tr>
<tr>
<td>Front/back</td>
<td>Side</td>
</tr>
<tr>
<td>Trial 1</td>
<td></td>
</tr>
<tr>
<td>Trial 2</td>
<td></td>
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<td>Trial 3</td>
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<td>Trial 5</td>
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<td>Trial 18</td>
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<tr>
<td>Trial 19</td>
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</tr>
<tr>
<td>Trial 20</td>
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</tr>
</tbody>
</table>
Star Excursion Balance Test Form

Participant 

Leg Length: Right= cm  Left= cm

<table>
<thead>
<tr>
<th>Right</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Trial</td>
<td>Anterior</td>
<td>PM</td>
<td>PL</td>
</tr>
<tr>
<td>1</td>
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<td></td>
<td></td>
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<tr>
<td>2</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Avg.</td>
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</tbody>
</table>

Normalized

# of failed trials

<table>
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</thead>
<tbody>
<tr>
<td>Trial</td>
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<td>PM</td>
<td>PL</td>
</tr>
<tr>
<td>1</td>
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<td></td>
</tr>
<tr>
<td>2</td>
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<td></td>
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<tr>
<td>3</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Avg.</td>
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Normalized

# of failed trials

Assigned Version Date: 06/05/2013
<p>| | | |</p>
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<td>Date:</td>
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<tr>
<td>Session:</td>
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<td></td>
<td>frontal</td>
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<td>PF_MVIC:</td>
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<td><strong>CSP Testing</strong></td>
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<td>% machine output</td>
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<td>Active</td>
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<td>120%</td>
</tr>
<tr>
<td>PF_MVIC</td>
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<td>target</td>
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<tr>
<td>Notes:</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Appendix K

Transcranial Magnetic Stimulation Screening Questionnaire

Musculoskeletal Health and Movement Sciences Laboratory
Transcranial Magnetic Stimulation (TMS) Screening Questionnaire

1. Height: __________ Weight: __________ BMI: __________ (calculated by investigators)

2. Do you currently have any pain or medical conditions that limit your function? 
   Yes   No
   a. If yes, please describe

5. Do you smoke?      Yes   No

6. Do you have any of the following conditions:
   a. Fibromyalgia Yes   No
   b. Diabetes    Yes   No
c. Peripheral neuropathy (numbness, tingling, loss of sensation in hands or feet) Yes No
d. Heart disease Yes No
e. Migraine headaches Yes No

7. Do you have any metal implants anywhere in your head, neck, or shoulders (excluding dental work)? Yes No

8. Do you or any immediate family members have a history of seizures or epilepsy? Yes No

9. Has your physician ever diagnosed you with a neurologic disorder such as Parkinson’s disease, Multiple Sclerosis, or stroke? Yes No

10. Do you have any of the following in your body:
   a. Foreign objects in your eyes Yes No
   b. Cochlear (ear) implants Yes No
c. Implanted brain stimulator Yes No
d. Aneurysm clip Yes No
e. Implanted medication pump Yes No
f. Cardiac pacemaker Yes No
g. Intra-cardiac lines Yes No

11. Is there a chance you could be pregnant? Yes No

12. Have you ever suffered a serious head injury (including concussion)? Yes No

   If yes, please answer the following questions:
   a. When did your head injury occur?

   ______________________________________________________________

   b. Did you lose consciousness?

   ______________________________________________________________

   c. Do you suffer from any memory loss as a result of your head injury? Yes No

13. Do you currently, or have you ever, had a condition that increases the pressure within your brain? Yes No

14. Do you have a history of illicit drug use, alcohol abuse, or are you currently withdrawing from any substance? Yes No
15. What medications are you currently taking? Please list all prescription and over the counter medications.

__________________________________________________________________
__________________________________________________________________

Please indicate if you have a history of any of the following conditions, experiences or pathologies.

<table>
<thead>
<tr>
<th>Exclusion Criteria</th>
<th>Yes</th>
<th>No</th>
<th>If “yes”, please provide brief explanation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Concussion or head injury in previous 6 months</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stroke</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart Condition</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A Heart Condition</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiac Pacemaker or implanted cardiac defibrillator</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Epilepsy or Seizures</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Migraines or severe headaches</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cancer in brain or leg muscles</td>
<td></td>
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<tr>
<td>Diagnosed psychiatric disorder</td>
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<tr>
<td>Intracranial metallic Clips</td>
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<tr>
<td>Current pregnant or breastfeeding</td>
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<tr>
<td>Currently taking Pain relieving medication or neuroinhibiting or stimulating medication</td>
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Appendix M

Post-processing Visual 3D Pipeline

Building Skeletal Model
File_New

; Create_Hybrid_Model
! /CALIBRATION_FILE=

Apply_Model_Template
! /MODEL_TEMPLATE=
! /CALIBRATION_FILE=
;

Apply_Model_Template
! /MODEL_TEMPLATE=
! /CALIBRATION_FILE=
;

Set_Subject_Height
! /CALIBRATION_FILE=
! /HEIGHT=
;

Set_Subject_Weight
! /CALIBRATION_FILE=
! /WEIGHT=
;

Build_Model
! /CALIBRATION_FILE=
! /REBUILD_ALL_MODELS=FALSE
;

Set_Pipeline_Parameter_To_Folder_Path
/PARAMETER_NAME=FOLDER
!
/PARAMETER_VALUE=VISUAL3D_DEFAULT_DATA_FOLDER
;

File_Open
! /FILE_NAME=:FOLDER&*.c3d
;

Assign_Model_File
! /CALIBRATION_FILE=
! /MOTION_FILE_NAMES=
;

File_Save_As
! /FILE_NAME=
;
Gait Kinematics

Compute Model Based Data

RESULT_NAME=Trunk Kinematics
/FUNCTION=JOINT ANGLE
/SEGMENT=RPA
/REFERENCE_SEGMENT=RTA
/NORMALIZATION=FALSE
/NORMALIZATION_METHOD=FALSE
/NORMALIZATION_METRIC=FALSE
/NEGATENX=FALSE
/NEGATENY=FALSE
/NEGATENZ=FALSE
/AXIS1=X
/AXIS2=Y
/AXIS3=Z

Compute Model Based Data

RESULT_NAME=Hip Joint Angle
/FUNCTION=JOINT ANGLE
/SEGMENT=RPV
/REFERENCE_SEGMENT=RPV
/NORMALIZATION=FALSE
/NORMALIZATION_METHOD=FALSE
/NORMALIZATION_METRIC=FALSE
/NEGATENX=FALSE
/NEGATENY=FALSE
/NEGATENZ=FALSE
/AXIS1=X
/AXIS2=Y
/AXIS3=Z

Compute Model Based Data

RESULT_NAME=Knee Joint Angle
/FUNCTION=JOINT ANGLE
/SEGMENT=RPV
/REFERENCE_SEGMENT=RPV
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/NORMALIZATION_METHOD=FALSE
/NORMALIZATION_METRIC=FALSE
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/NEGATENZ=FALSE
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/AXIS2=Y
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Compute Model Based Data

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Compute Model Based Data

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File_New
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File_Open
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Exporting COP Data

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## Summary of Literature

### Studies exploring the effects of chronic ankle instability (CAI) on movement patterns and muscle activation strategies during a jump landing task

<table>
<thead>
<tr>
<th>Study</th>
<th>Pathology</th>
<th>No.</th>
<th>Jumping Height</th>
<th>Outcome Measures</th>
<th>Time frame Assessed</th>
<th>Results (Mean ± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Castfield and Garrett 2002</td>
<td>Unilateral FAI</td>
<td>14(10)</td>
<td>40cm</td>
<td>Kinematics (sagittal plane): Ankle and knee angular displacement and tuning</td>
<td>100 ms pre-IC&lt;br&gt;200 ms post-IC</td>
<td>Ankle DF: FAI &gt; Control (10 ms pre-IC to 20 ms post-IC)&lt;br&gt;Knee Flexion: FAI &gt; Control (20 ms pre-IC to 60 ms post-IC)&lt;br&gt;Timing: NS&lt;br&gt;Peak GRFs in all planes: NS&lt;br&gt;Time-averaged V-GRF (24-36 ms &amp; 85-150 ms): FAI &gt; Control&lt;br&gt;Time-averaged ML-GRF (50-40 ms): FAI &gt; Control&lt;br&gt;Time of lateral and anterior peak GRF: FAI &lt; Control&lt;br&gt;IEMG of PL: FAI &lt; Control (pre-IC)&lt;br&gt;IEMG of SO and TA: NS</td>
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<td>Castfield and Garrett 2004</td>
<td>Unilateral FAI</td>
<td>12 (10)</td>
<td>40cm</td>
<td>IEMG: PL, TA, SO</td>
<td>200 ms pre-IC&lt;br&gt;150 ms post-IC</td>
<td>Ankle Inversion: FAI &gt; Control (100 ms to 95 ms pre-IC)&lt;br&gt;Ankle DF: FAI &lt; Control (90 ms to 200 ms post-IC)&lt;br&gt;Knee kinematics in all planes: NS&lt;br&gt;Hip ER: FAI &lt; Control (200 ms to 55 ms pre-IC)&lt;br&gt;IEMG of PL: FAI &lt; Control (200 ms - 0 ms pre-IC)&lt;br&gt;IEMG of SO and TA: NS&lt;br&gt;IEMG of medial GRF: FAI &gt; Control (35 ms to 60 ms post-IC)&lt;br&gt;IEMG of vertical GRF: FAI &gt; Control (35 ms to 105 ms post-IC)&lt;br&gt;IEMG of posterior GRF: FAI &gt; Control (75 ms to 90 ms post-IC)&lt;br&gt;Sagittal power generation: FAI &gt; Control (60 ms to 145 ms post-IC)</td>
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<td>Delashmit et al. 2006</td>
<td>Unilateral FAI</td>
<td>24 (24)</td>
<td>35cm</td>
<td>Kinematics (sagittal plane): Ankle, knee, and hip angular displacement</td>
<td>200 ms pre-IC&lt;br&gt;200 ms post-IC</td>
<td>Ankle DF at IC and maximum: MAI &lt; Coper&lt;br&gt;Ankle Eversion at maximum: MAI &gt; FAI or Coper&lt;br&gt;Sagittal ankle displacement: MAI &lt; FAI or Coper&lt;br&gt;Other ankle or knee kinematic or kinetic variables: NS</td>
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Appendix N
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<tr>
<th>Study</th>
<th>Pathology</th>
<th>No. CAI (Control)</th>
<th>Jumping Height</th>
<th>Outcome Measures</th>
<th>Time frame Assessed</th>
<th>Results (Mean ± SD)</th>
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<tr>
<td>Gage et al. 2009</td>
<td>CAI</td>
<td>15 (15)</td>
<td>35 cm</td>
<td>Energy dissipation at the ankle, knee, and hip</td>
<td>IC to a point at which mechanical power curve became positive</td>
<td>All energy dissipation results: NS</td>
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<td>Double-leg Drop Landing with Perturbation (testing leg contacting the supinating device)</td>
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<td>Gutierrez et al. 2011</td>
<td>CAI</td>
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<td>EMG areas and ensemble EMG patterns: PL and TA</td>
<td>200 ms pre-IC</td>
<td>Perturbation (Supination) Condition</td>
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<td>Coper</td>
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<td>Ankle Kinematics</td>
<td>500 ms post-IC</td>
<td>Preparatory EMG: PL: CAI &gt; Coper or Control</td>
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<td>Control=15</td>
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<td>Reactive EMG: PL: CAI &gt; Coper or Control</td>
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<td>Preparatory EMG: TA: NS (Coper trend toward larger CAI)</td>
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<td>Reactive EMG: TA: NS</td>
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<td>Peak DF, Abd, and IV angles: CAI &lt; Coper or Control</td>
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<td>Single-leg Vertical Jump-landing</td>
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<td>Ross and Guskiewicz 2004</td>
<td>FAI</td>
<td>14 (14)</td>
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<td>≤ 20 ms post-IC</td>
<td>TTS A/P: FAI &gt; Control</td>
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<td>TTS M/L: FAI &gt; Control</td>
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<td>Ross et al. 2005</td>
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<td>TTS (total)</td>
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<td>TTS A/P</td>
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<td>Ross et al. 2006</td>
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<td>Ross et al. 2009</td>
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<td>EMG amplitude: TA, Peroneals, LG, and SOL</td>
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<td>Wikstrom et al. 2005</td>
<td>FAI</td>
<td>29 (29)</td>
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<td>Self-reported difficulty</td>
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<td>Difficulty. Step down &gt; Jump protocol</td>
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<td>Wikstrom et al. 2007</td>
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<td>54 (54)</td>
<td>50% V_max</td>
<td>Stability index: A/P, M/L, vertical, and composition</td>
<td>≤ 10 ms post-IC</td>
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<td>Normalized stability index to kinetic energy dissipated</td>
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<td>VSI and NVSI: FAI &gt; Control</td>
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<td>Composite SI and normalized composite SI: FAI &gt; Control</td>
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<td>Outcome Measures</td>
<td>Time frame Assessed</td>
<td>Results (Mean± SD)</td>
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<tr>
<td>Kipp and Palmieri-Smith 2012</td>
<td>CAI</td>
<td>11 (11)</td>
<td>15cm</td>
<td>Sagittal and frontal plane ankle angle and moment (at-IC, peak angles)</td>
<td>100ms pre-IC, 200ms post-IC</td>
<td>PCA: CAI &gt; Control (PC 3; Sagittal during pre-IC) CAI &gt; Control (PC 1; Frontal throughout the entire 300ms time period)</td>
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<td>Other Landing Tasks</td>
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<td>Fu et al. 2007</td>
<td>Bilateral</td>
<td>19 (20)</td>
<td>Self-initiated and unexpected drop of 30cm</td>
<td>Pre-landing EMG (latency and co-contraction) of TA, MG, TFL, PL</td>
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<td>Slower self-initiated drop EMG latency of TA and TFL in CAI than Control vGRF (Self-initiated): CAI &gt; Control Other variables for self-initiated drop: NS Any variables for unexpected drop: NS</td>
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<td>Suda et al. 2009</td>
<td>FAI</td>
<td>21 (19)</td>
<td>Volleyball blocking: CAI=41.0 ± 6.1 cm. Control= 42.1 ± 7.6 cm</td>
<td>RMS and Onset of muscle activity of TA, PL, LG Co-contraction Index</td>
<td>200ms pre-IC, 200ms post-IC</td>
<td>RMS of PL (pre-IC): FAI &lt; Control RMS of TA (post-IC): FAI &gt; Control Slower muscle activation of LG in FAI than Control Co-contraction index: NS</td>
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<td>Lateral Hoping</td>
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<td>Lateral hop distance: 30cm</td>
<td>IEMG of RF, PL, TA, SOL Kinematics (joint angular displacements and angular velocities: ankle, knee, and hip in the sagittal, frontal and transverse planes) Kinetics (peak GRF and Timing of peak GRF: medial, lateral, posterior, and vertical)</td>
<td>200ms pre-IC, 200ms post-IC</td>
<td>Less everted position of the ankle during the time period from 45ms pre-IC to 95ms post-IC in the CAI group than the control group. Peak GRF posterior: CAI &lt; Control IEMG of RF, TA, and SOL (Pre- and post-IC): CAI &gt; Control Other kinematic, kinetic, EMG variables: NS</td>
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</tbody>
</table>

NS = Non significant group difference, FAI = Functional ankle instability, MAI = Mechanical ankle instability, DF = Dorsiflexion, PF = Plantarflexion, IV= Inversion, EV= Eversion, ER = External rotation, IR = Internal rotation, Abd = Abduction, GRF = Ground reaction force, pGRF = posterior GRF, V = Vertical, M/L = Mediolateral, A/P = Anteroposterior, PL = Peroneus longus, SO = Soleus, VM = Vastus Medialis, MMH = Medial hamstring muscles, LMM = Lateral hamstring muscles, TA = Tibialis Anterior, LG = Lateral gastrocnemius, VL = Vastus lateralis, RF = Rectus femoris, PCA = Principal component analysis, IEMG = Integrated Electromyography, EMG = Electromyography, RMS = Root mean square, TTP = Time to peak, IC = Initial foot contact with ground, TTS = Time to stabilization, CAIT = Cumberland ankle instability tool, SD Shearth = Standard deviation of horizontal medio-lateral shear forces, SD Shreadh = Standard deviation of horizontal antero-posterior shear force, SD Shreadh = Standard deviation of resultant of the horizontal medio-lateral and antero-posterior shear forces, RVVTS = resultant vector time to stabilization, CV_{i} = Coefficient of variation, SD_{i} = mean standard deviation, CI = Co-contraction index
### Studies exploring the effects of Chronic ankle instability (CAI) on movement and neuromuscular patterns during walking, running, and cutting tasks

<table>
<thead>
<tr>
<th>Study</th>
<th>Pathology</th>
<th>No. CAI (Control)</th>
<th>Walking and running speed or distance</th>
<th>Outcome Measures</th>
<th>Time frame Assessed</th>
<th>Results (Mean ± SD)</th>
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<td>Walking</td>
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</tbody>
</table>
| Louwerens et al. 1995 | Bilateral or unilateral CAI | Bilateral=18 Unilateral=7 Control=10 | A self-selected speed (range 3.7-4.3 km/hr) or half (1.8 - 2.2 km/hr), 20 steps | Peak of the EMG linear envelop: PL and TA | The stance phase (the first 60% of the stride following IC) | TA: CAI > Control (1/2 and 3/4 quarter of the stance phase)  
PL: NS  
Bilateral differences in Unilateral CAI: NS  
Significant delay to the time of peak force under the central foot, lateral foot, and toes in CAI compared to Control  
Relative forces under the heel and toes: CAI < Control  
Relative forces under the midfoot and lateral foot: CAI > Control  
Ankle angle at IC and toe-off: CAI < Control  
PF during foot contact: CAI > Control  
Kinetic gait parameters: significant group by surface condition interaction |
| Nyska et al. 2003 | Bilateral or unilateral CAI | Bilateral=5 Unilateral=7 Control=10 | A self-selected speed, 7m walkway, walking with barefoot | Relative peak and time of force: the heel, midfoot, lateral, central, and medial foot, and the toes | - |                                                                                  |
| Spaulding et al. 2003 | CAI | 10 (10) | 30m walkway  
Surface conditions: (1) a level walkway, (2) an 18 cm step up resembling a typical sidewalk curb, and (3) a 58 incline ramp representing a curb cut-out at street corners. | Ankle kinematics  
Step length  
Gait-temporal characteristics  
GRF | IC to toe-off | Ankle angle at IC and toe-off: CAI < Control  
PF during foot contact: CAI > Control  
Kinetic gait parameters: significant group by surface condition interaction |
| Santilli et al. 2005 | Unilateral CAI | 14 (0) | - | Duration of muscle activation: PL | Stance phase of walking | Duration of PL muscle activation: non-involved > involved side |
| Kakihana et al. 2005 | Bilateral CAI | 25 (25) | A self-selected cadence (95.8±4.0 steps/min for CAI and 102.1±7.4 steps/min for control), 7m walkway | Frontal-plane angle and moment of the subtalar and knee joints  
Moment arm distance: subtalar joint  
GRF: vertical, ML  
COP excursion | Stance phase of walking | Vertical GRF: CAI < Control  
Other variables: NS |
| Delahunt et al. 2006 | FAI | 24 (22) | Walking on a treadmill at a speed of 4 km/h | Angular displacements: hip, knee, and ankle joints  
Vertical foot-floor clearance  
IEMG: RF, PL, TA, SOL | 200ms pre-HS  
200ms post-HS | Kinematics IV (from 50ms pre-HS to 50ms post –HS): FAI > Control  
Hip and knee kinematics: NS  
Vertical foot-floor clearance during the terminal swing: FAI < Control  
IEMG of PL: FAI > Control (post-HS)  
IEMG of RF: FAI > Control (pre-HS)  
IEMG of SOL or TA: NS |
<table>
<thead>
<tr>
<th>Study</th>
<th>Pathology</th>
<th>No. CAI (Control)</th>
<th>Walking and running speed or distance</th>
<th>Outcome Measures</th>
<th>Time frame Assessed</th>
<th>Results (Mean± SD)</th>
</tr>
</thead>
</table>
| Wikstrom et al. 2010 | Unilateral CAI | 20 (20)          | A self-selected speed 12m walkway Planned/unplanned gait termination Walking with barefoot | Propulsive and braking force magnitude EMG Gmed, SOL, TA Dynamic postural stability index | 6 phases of gait (4 during the stance phase of the lead limb and 2 for the swing leg) | • Propulsive force: CAI > Control  
• Braking force: CAI > Control  
• Dynamic postural stability index: CAI < Control  
• EMG (Planned) TA, SOL, Gmed: CAI < Control (lead limb)  
• TA: Involved < Uninvolved in CAI (phase 4 of gait)  
• SO: Involved > Uninvolved in CAI  
• EMG (Unplanned) CAI increased TA activity very late in stance  
Control: increased TA activity steady throughout stance  
Preparatory TA activity of the involved limb during swing phase was 150% of the uninvolved side |
| Hass et al. 2010 | Unilateral CAI | 20 (20)          | A self-selected speed 12m walkway Walking with barefoot | Normalized COP Excursions (AP and ML):  
1. Peak excursion  
2. Peak resultant  
3. Average velocities | S1, S2, and S3 phases of gait initiation | • ML resultant Excursion (S1 and S2) when the involved limb of CAI served as the initial stance limb:  
i. CAI < Control  
ii. CAI: Involved < non-involved  
• ML COP velocity (S3): CAI < Control |
| Brown 2011       | MAI       | MAI =11           | Walking at a speed of 1.2 to 1.4 m/s on a raised walkway with barefoot | Ankle and foot kinematics Minimum metatarsal height | The terminal swing phase (250ms pre IC) | • Minimum PF: MAI < FAI or coper  
• Maximum PF: MAI < FAI  
• Foot ER: MAI or FAI > Coper  
• Foot IR: MAI < Coper  
• Eversion: MAI < Coper  
• Tibial IR: FAI > MAI or Coper  
• Minimum metatarsal height: NS |
| Hopkins et al. 2012 | FAI       | 11 (11)           | Walking speed for the data collection period was normalized to leg length. | COP trajectory: ML EMG: TA and PL | Five consecutive stance phases | • COP trajectory: more laterally deviated in FAI than Control (at HS and from 25% to 90% of the stance phase)  
• TA activation: FAI > Control (from 15% to 30% and 45% to 70% of stance)  
• PL activation: FAI > Control (at HS and toe off) |
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<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Walking with perturbation</td>
<td>Unilateral FAI</td>
<td>21 (21)</td>
<td>Walking at a cadence of 110 beats/minutes, 8.5m walkway, 30° of inversion perturbation</td>
<td>H:M ratio; PL EMG amplitudes; PL</td>
<td>Average EMG values: the 100-ms period following the onset of muscle after sudden inversion.</td>
<td>• H:M ratios&lt;br&gt; - FAI: Involved &gt; non-involved&lt;br&gt; - Control: NS between the ankles&lt;br&gt; • PL activation after inversion perturbation&lt;br&gt; - FAI: Involved &lt; Non-involved&lt;br&gt; - Control: NS between the ankles&lt;br&gt; • No relationship between the peroneal H:M ratio and peroneal EMG&lt;br&gt; • Delayed peroneal latency and EMD in FAI compared to Control&lt;br&gt; • Peroneal latency&lt;br&gt; - FAI: slower in involved non-involved&lt;br&gt; - Control: NS between the ankles&lt;br&gt; • Peroneal EMD&lt;br&gt; - FAI: slower in involved non-involved&lt;br&gt; - Control: NS between the ankles</td>
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<td>Hopkins et al. 2009</td>
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<td>Peroneal latency Peroneal EMG</td>
<td>-</td>
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<tr>
<td>Running/jogging</td>
<td>FAI MAI Coper</td>
<td>FAI=21 MAI=21 Coper=21</td>
<td>Running at 2.5–3.5 m/s on walkway</td>
<td>Kinematics (sagittal and frontal planes): 1. Ankle and knee angles at IC and at maximum 2. The total angular displacement Kinetics: 1. Peak normalized GRF 2. TTP-GRF in the anterior, posterior, medial, lateral, and vertical directions</td>
<td>IC to Toe-off</td>
<td>• All variables: NS</td>
</tr>
<tr>
<td>Drewes et al. 2009</td>
<td>CAI</td>
<td>7 (7)</td>
<td>Jogging at 9.00 km/h on a treadmill for 15s trials</td>
<td>Sagittal-plane ankle kinematics</td>
<td>IC to terminal swing</td>
<td>DF: CAI &lt; Control (9-25% of the gait cycle), but NS during terminal swing phase</td>
</tr>
<tr>
<td>Study</td>
<td>Pathology</td>
<td>No. CAI (Control)</td>
<td>Walking and running speed or distance</td>
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<tr>
<td>Lin et al. 2011</td>
<td>CAI</td>
<td>15 (15)</td>
<td>CAI: 3.45 ± 0.40 m/s</td>
<td>Ankle kinematics</td>
<td>200 ms prior to FS</td>
<td>- Ankle IV: CAI &gt; Control (pre-FS)</td>
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<td></td>
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<td>Control: 3.46 ± 0.45 m/s</td>
<td>Ankle joint stiffness</td>
<td>to the moment at</td>
<td>- Peak ankle IV or EV: NS</td>
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<td>CI (TA/PL, TA/GL)</td>
<td>which the</td>
<td>- Joint stiffness: CAI &lt; Control</td>
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<td>RMS of TA, PL, and GL</td>
<td>foot lifted off</td>
<td>- EMG variables: NS</td>
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<td>the force plate.</td>
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**Cutting and lateral shuttle**

<table>
<thead>
<tr>
<th>Dayakidis and Boudolos 2006</th>
<th>Unilateral FAI</th>
<th>15 (17)</th>
<th>A 45° forward v-cut after running straight forward for 7m at a speed of at 5.0 ± 0.2 m/s A side shuffle</th>
<th>Peak GRF, vertical, ML</th>
<th>Absorption and propulsion phase</th>
<th>The v-cut movement</th>
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<td>F₁,₁: FAI &gt; Control</td>
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<td>Involved &gt; Uninvolved (CAI)</td>
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<td>t₁,₁: FAI &lt; Control</td>
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<td>Involved &gt; Uninvolved (CAI)</td>
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**The lateral shuffle**

<table>
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<tr>
<th>Huang et al. 2011</th>
<th>CAI</th>
<th>11 (11)</th>
<th>Lateral shuffling as fast as possible All participants performed tasks with the same type of sport shoes</th>
<th>Foot contact area: 3 regions</th>
<th>From initial HS (0%) to last FC (100%)</th>
<th>The lateral shuffle</th>
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<tr>
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<td>Peak pressure: 7 areas ML COP displacement (positive = the COP was positioned medial to the heel-to-M₃₃ axis)</td>
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<td>Foot contact area</td>
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</table>

NS = Non significant group difference. FAI = Functional ankle instability. MAI = Mechanical ankle instability. DF = Dorsiflexion. PF = Plantarflexion. IV = Inversion. EV = Eversion. ER = External rotation. IR = Internal rotation. ABD = Abduction. ADD = Adduction. GRF = Ground reaction force. V = Vertical. ML = Mediolateral. AP = Anteroposterior. PL = Peronial longus. SO = Soleus. TA = Tibialis Anterior. LG = Lateral gastrocnemius. GMed = Gluteus medius. RF = Rectus femoris. PCA = Principal component analysis. IEMG = Integrated Electromyography. EMG = Electromyography. RMS = Root mean square. TTP = Time to peak. IC = Initial foot contact with ground. FS = Foot strike. MARF = Mean absolute relative phase. DP = Deviation phase. COP = Center of pressure. CI = Co-contraction index. EMD = electromechanical delay. M₃₃ = the 1st to 4th head of metatarsal bone. t₁,₁ = relative time to peak GRF. SI = the first section of initial gait initiation (beginning with auditory cue and ending with the COP located in its most posterior and lateral position toward the initial stepping foot). S₂ = the 2nd section of initial gait initiation (representing the movement of the COP toward the initial stance foot and ending at the position under the initial stance foot on which the COP begins to move forward. S₃ = the 3rd section of initial gait initiation (from the end of S₂ to toe-off of the initial stance limb as the COP translate forward.)