Movement Control And Cortical Activation
In Functional Ankle Instability

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Background: Functional ankle instability (FI) is a common development following first-time lateral ankle sprain, resulting in functional limitations. Local tissue damage has not been a satisfactory explanation. Evidence exists of changes in motor control within the central nervous system in individuals with FI. Further investigation of the nature of these changes is warranted.

Methods: Twenty subjects with FI and twenty healthy control subjects allowed comparisons between ankles within groups and between groups. Two primary methods of investigation were used. A kinematic analysis using electromagnetic motion capture was used during a step down task to assess repeatability and variation in patterns of ankle dorsiflexion/plantarflexion and inversion/eversion motion and speed and phase timing characteristics. A normalized coefficient of multiple correlations was used for motion cycle comparisons, and means and variance were compared for discrete time variables. Motor control was measured with an accuracy index from an ankle tracking task. A sub-group of 8 right-involved FI subjects and 10 control subjects underwent functional magnetic resonance imaging to detect cortical activation in sensorimotor areas while performing the tracking task.

Results: With the step down task no between-group differences in the repeatability of ankle motions were found, although both groups showed greater variability in inversion/eversion than dorsiflexion/plantarflexion. Increased ankle instantaneous angular speed when contacting the step was found in the FI subjects, with trends to reversing instantaneous linear velocity and more rapid weight acceptance also noted. No differences in tracking accuracy were identified; however, differential patterns of lateralization of cortical activation were found within groups between ankles during the task, with greater contralateral hemisphere activity in the primary motor area and more symmetrical activity in the primary sensory cortex (S1) and supplementary motor areas in FI subjects tracking with the involved ankle than was observed in control subjects tracking with the right ankle. Between-group comparisons found areas of greater activation in left S1, premotor cortex, and anterior cingulate gyrus compared to control subjects.

Conclusions: The results of this study support that processing differences exist at the cortical level between FI and healthy control subjects. Motor performance differences are also present.

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CHAPTER I - INTRODUCTION

Background and Significance of Functional Instability

Epidemiology of ankle sprain

Lateral ankle sprains are among the most common injuries reported. It is estimated that one sprain occurs per day per 10,000 people, with more than 23,000 people per day seeking medical care for these injuries (Kannus and Renström, 1991). Garrick (1977) stated that the lateral ligaments of the ankle are the single most frequently injured structure in the bodies of athletes. In his study of high school athletes, 13.9% of all injuries reported were ankle injuries, and 85% of these injuries were lateral ankle sprains. Sports in which ankle sprains are common include soccer (Agel et al., 2007; Brynhildsen et al., 1990; Ekstrand and Gillquist, 1983; Ekstrand and Tropp, 1990), basketball (Garrick, 1982; Henry et al., 1982), volleyball (Schafle et al., 1990), and women's gymnastics (Marshall et al., 2007). 1974 study of the injuries recorded at the United States Military Academy, West Point, found ankle sprains were the most common injuries noted, with one third of the cadets sustaining one or more inversion sprains during their four years at the Academy (350 per year) (Jackson et al., 1974). A more recent West Point study (Gerber et al., 1998) noted 76 lateral ankle sprains occurring over a two-month period of inquiry.

Mechanism of Injury and Grading of Severity

Garrick (1977), in his study of high school athletes reported injuries sustained during poorly executed maneuvers or alighting on an uneven surface. Schafle (1993) noted that alighting on another player's foot after blocking a shot was the most common cause of ankle sprain in volleyball. Landing maneuvers in general were cited as the provoking circumstance for a sprain in multiple sports (Robbins and Waked, 1998). Often injury rates are higher during competition than during training (Agel et al., 2007; Ekstrand and Tropp, 1990; Marshall et al., 2007), at the end of each game half (Kofotolis et al., 2007), and in the early portions of the sporting season (Agel et al., 2007; Kofotolis et al., 2007). These findings suggest that conditioning, fatigue, landing surface, and technique contribute to this high incidence rate.

Less is known about the circumstances and frequency of ankle sprain occurring in situations other than organized sports. Hølmer et al. (1994) investigated the epidemiology of sprains seen at a county hospital in Denmark. Forty-five percent of the injuries occurred during sports, 20% during play, and 16% at work. In patients greater than 50 years of age, in-house accidents were more common than sports injuries, which predominated in the younger age group (i.e. < 25 years of age). In general, the mechanism of injury was most commonly stumbling or sliding on ground level surface, less frequently falling or jumping from a height, or by falling from stairs. Braun (1999) studied the latent effects of ankle sprains in a general clinic population, including outpatients. She also noted that sports-related causes were reported in a younger age group (mean age 33.1 years) compared to injuries from motor vehicle accidents or falls in a slightly older group (mean age 36.4 years and 39.5 years respectively).

Lateral sprains are generally understood to occur in an ankle position of inversion and plantarflexion (DiGiovanni et al., 2004). Therefore, the most common ligament injured is the anterior talofibular (ATFL) (Bosien et al., 1955; Karlsson and Lansinger, 1993). Wright et al. (1964) performed a simulation experiment using a forward dynamics model investigating the first half of a side-shuffle movement. The floor was modeled as four quadrants that could be independently varied in height over ± 10 cm simulating differing landing postures of the foot in dorsiflexion/plantarflexion and supination/pronation. They concluded that the degree of plantarflexion at touchdown was most linked with simulated inversion ankle sprain. A position of plantarflexion, then, should be considered for a study of recurrent sprains.

The acute lateral ankle sprain is described and graded according to the ligaments involved and degree of limitation. Despite variations in the description of grading schemes for ankle sprain, all authors agree that the order of rupture to be the ATFL, calcaneofibular (CF), and the posterior talofibular (PTFL) ligaments, with increasing severity and disability as more ligaments are injured (DeMaio et al., 1992; Gerber et al., 1998; Hergenroeder, 1990; Trevino et al., 1994; Winkel et al., 1997). Acute injuries are characterized by slight to significant swelling and ecchymosis, loss of mobility, and pain with weight bearing.

Individual risk factors for first-time sprains have primarily been reported for sports populations. A recent systematic review (de Noronha et al., 2006) reported the strongest evidence supporting limited ankle dorsiflexion as a risk factor, with less strong indications that diminished position

sense for inversion and increased postural sway as factors. Willems conducted a prospective study of physical education students using a variety of measures, and found factors for men included decreased balance and slower reaction times of the ankle muscles (Willems et al., 2005b), and for women the factors included decreased ankle position sense and postural control (Willems et al., 2005c).

Recurrent Ankle Sprains – Incidence and Consequences

A high recurrence rate of ankle sprains is a factor reported by numerous authors. Tropp (1985) reported a 2.3 times greater risk of ankle injury in male soccer players with previous injuries. Other studies report that 19.4 – 79% of recorded sprains within a sporting season or follow-up period were recurrent injuries (Bahr and Bahr, 1997; Braun, 1999; Brynhildsen et al., 1990; Bullock-Saxton, 1995; Ekstrand and Gillquist, 1983). A risk increase of 3.8 – 4.9 times has been calculated for an ankle sprain in the presence of a prior history of sprain by other authors (Bahr and Bahr, 1997; McKay et al., 2001).

The long-term consequences of ankle sprain and re-injury are significant. Harrington (1979) reported findings and treatment outcomes for thirty-six patients with lateral ankle ligament instability of greater than ten years duration. Twenty-eight (78%) patients showed evidence of degenerative arthritis in the joint. Abnormal arthroscopic findings have also been reported by others (Hintermann et al., 2002; Komenda and Ferkel, 1999; Takao et al., 2005).

Schaap et al (1989) queried 1012 patients (81% response rate) regarding residual symptoms and handicaps nine months after treatment for ankle sprain. Thirty percent of respondents reported pain, an unstable feeling, or swelling, with 13% indicating an occupational handicap and 27% a sports handicap. The nature and frequency of residual complaints reported across all the grades of injury were comparable. The authors concluded that the functional prognoses for a simple inversion injury and an injury with complete ligamentous rupture were the same. A follow-up investigation by the same surgical group (Verhagen et al., 1995) with the same patient cohort was performed 6.5 years later. A high prevalence of continued complaints (39%), even in the milder sprains, led the authors to conclude “there is no such thing as ‘a simple sprain’” (page 95).

Functional Ankle Instability

Definition and Symptoms

A frequent complaint of those with chronic symptoms following lateral ankle sprain is of repeated sprains or of the ankle “giving way”. Freeman (1965) described this syndrome as functional instability (FI). Many authors have described this syndrome’s existence and its prevalence, but no universal definition has been accepted. Forty percent of ankle sprain sufferers reported these complaints in Freeman’s study. Others have reported rates of recurrent sprains and instability of 10 - 40% (Bosien et al., 1955; Brand et al., 1977; Gerber et al., 1998; Verhagen et al., 1995).

The symptom of “giving way” is the most common description of functional instability (Bernier and Perrin, 1998; Freeman, 1965; Gauffin et al., 1988; Karlsson and Lansinger, 1993; Konradsen and Ravn, 1991; Lentell et al., 1995; Matsusaka et al., 2001; Rozzi et al., 1999; Tropp, 1985). No formal descriptions of this term have been found. It is perhaps best described as a feeling that the expected stability in weight bearing on the ankle is not experienced, and specific corrective measures must be taken to avoid a fall, much like recovery from a stumble. The second most common is the complaint of FI is recurrent ankle sprain (Bernier and Perrin, 1998; Gauffin et al., 1988; Konradsen and Ravn, 1991; Matsusaka et al., 2001; Rozzi et al., 1999; Tropp, 1985). The frequency of repeated sprains used as inclusion criteria across studies varies from not specified (Bosien et al., 1955) to greater than 7 per year (Konradsen and Magnusson, 2000). Some authors include pain (Lentell et al., 1995) or report of weakness (Lentell et al., 1995; Rozzi et al., 1999) in inclusion criteria for their studies. Konradsen (2002) includes only those reporting giving way and recurrent sprains occurring in situations where a stable ankle would not experience difficulty, so as to eliminate those sustaining repeated trauma due to high risk sporting activity.

The degree of functional limitation can be mild to severe, perhaps depending on the lifestyle and expectations of the sufferer. Basic activities such as walking can be affected (Braun, 1999; Freeman et al., 1965) as well as high level sporting activities of cutting and jumping (Brand et al., 1977; Tropp, 1986).

A more recent confusion in terms has been presented by Hertel (2002) and used in several subsequent articles (Hertel et al., 2006; Hertel and Olmsted-Kramer, 2007; Hubbard et al., 2007a; Hubbard et al., 2007b). He used the term chronic ankle instability (CAI) to distinguish repetitive bouts of instability from acute occurrences, and further states that there are dichotomous causes of CAI – mechanical and functional instability. He describes mechanical instability as joint inflammation, structural changes, and pathologic laxity. Functional instability is reported to be an impairment in proprioception, neuromuscular or postural control, or strength. Hertel does indicate that combinations of mechanical and functional instabilities may combine in varying degree to create CAI. As prior authors did not dichotomize these two types of instabilities, use of this term further complicates interpretation of the literature.

At the time this study was initiated, no reports of standardized patient-report instruments with adequate measurement properties were available. Subsequently, two such instruments were identified - the Ankle Joint Functional Assessment Tool (AJFAT) (Ross et al., 2008; Rozzi et al., 1999) and the Foot and Ankle Disability Index (FADI) (Hale and Hertel, 2005).

Clearly the definition of functional ankle instability is imprecise; however, the preponderance of studies related to this condition supports its significance. As has been reported, conflicting findings with investigations of this complaint may stem from varying inclusion criteria based on differing definitions. The most conservative definition to be drawn from the literature, based on Konradsen, is a subjective complaint of the ankle “giving way” or experiencing recurrent sprains under conditions unlikely to provoke a first ankle sprain (i.e., affect a presumably stable ankle). This was the definition used for subject selection for this study. In reviewing the literature, however, the terms used by the various study authors are given, with identification of those clearly meeting the definition of FI used in the current study. Use of “CAI” will indicate the definition of Hertel (2002).

Mechanical Instability

Stability has been described as “joint resistance to relative movement of the bones when load is applied” (Leardini et al., 2000). Mechanical instability of the talocrural joint is defined as objective indications of ligamentous disruption. These indications may include positive clinical tests for excessive movement (such as the anterior drawer test) and radiographic findings such

as positive stress films for the talar tilt and the anterior drawer sign. Variations in recommended technical procedures are noted, including whether anesthesia is recommended (Becker et al., 1993; Cox and Hewes, 1979; Freeman, 1965; Harper, 1992; Johannsen, 1978; Karlsson and Lansinger, 1993; Lentell et al., 1995; Staples, 1975).

A difficulty with the diagnosis of mechanical instability is the lack of a universal standard with which to interpret radiographic findings. A wide range of “normal” talar tilt has been reported, making the significance of small findings and interpretation of isolated measures unclear (Cox and Hewes, 1979; Harper, 1992; Karlsson and Lansinger, 1993). Findings of only 1 – 3 degrees difference between stable and unstable ankles have been reported. Therefore the diagnostic significance of the absolute measures, in the absence of comparison values, was not established.

The value of the clinical application of laxity tests, whereby a judgment of increased versus normal movement is made, has also been questioned. Hertel et al.(1999) reported greater differences in laxity between involved and uninvolved ankles were found with the anterior drawer (AD) test than with the talar tilt test. Seventy-eight percent of those with positive stress radiographs were detected with the clinical AD test; however, 25% of uninjured subjects were also found to have differences in testing with the AD test.

Subtalar instability is a less frequently described mechanical instability, which is poorly detected with radiographic methods used for talocrural studies. Its relationship to FI complaints is unclear, with some authors finding a correlation (Kato, 1995), while others did not (Louwerens et al., 1995b). Recently, reports of altered positioning of the fibula have been investigated as a contributor to continuing complaints following ankle sprain. Both posterior (Berkowitz and Kim, 2004; Eren et al., 2003; Scranton et al., 2000) and anterior (Kavanagh, 1999; Mavi et al., 2002) positional faults have been reported.

Correlation of mechanical instability with functional instability has been limited. While Lentell and colleagues (1995) reported a statistically significant pair wise difference in talar tilt between involved and uninvolved ankles, only three of 34 subjects (9%) demonstrated a difference of five degrees or more (considered by many to be an appropriate threshold for an abnormal finding). Hintermann (1998) concluded that a radiographic diagnosis of lateral ankle instability was unreliable. Freeman (1965) found that mechanical instability accounted for functional

instability in 14% of his subjects, while 40% noted functional instability with no clinically or radiographically detected mechanical instability, and 58% of subjects with demonstrable clinical or radiographic instability were without symptoms. Conflicting reports exist between those authors finding a correlation (Tropp, 1986) and those not finding a relationship (Ryan, 1994).

Based on the inconclusive evidence of the role mechanical instability may play in functional instability, and the inconsistencies in diagnosing mechanical instability, it is evident that this factor is of limited use in explaining the problem of functional instability.

Physical Performance Measures

Some investigations of standardized functional performance measures have not found differences between involved and uninvolved ankles (Munn et al., 2002) or between those with chronic complaints and healthy subjects (Demeritt et al., 2002). Those finding some differentiation found only weak correlations and lower than desirable diagnostic accuracy (Ross et al., 2008).

At the time of this study was initiated, no performance measures for the chronic instability population were found with adequate measurement properties. However, a performance protocol was reported for use with general ankle injuries (Kaikkonen et al., 1997; Kaikkonen et al., 1994) with acceptable test-retest reliability and discriminate validity. The components of this protocol include subjective assessment by the patient of overall symptoms and with walking and running specifically, objective measures of timed stair descent, number of repetitions of rising onto toes and heels, single leg stance time, dorsiflexion range of motion, and clinical assessment of laxity using the anterior drawer test. Portions of this protocol were selected for incorporation in the current study.

Research Findings

Local Joint and Soft Tissue Factors

Multiple factors focusing on the affected joint and surrounding soft tissues have been studied as potential contributors to functional instability. These include weakness of muscles acting at the ankle, proprioceptive loss, and delayed reflex response to perturbation.

Peroneal muscle weakness has been implicated as a factor in functional instability. These muscles would be expected to function in controlling inversion movement and may be weak secondary to damage from the original injury or inadequate rehabilitation post injury. However, both indications of weakness in the unstable ankle (Bosien et al., 1955; Hartsell and Spaulding, 1999; Hubbard et al., 2007a; Munn et al., 2003; Ryan, 1994; Santos and Liu, 2008; Tropp, 1986; Wilkerson et al., 1997) and no difference between involved and uninvolved ankles (Bernier et al., 1997; Kaminski et al., 1999; Lentell et al., 1995; Lentell et al., 1990; McKnight and Armstrong, 1997) have been reported. Investigations of inversion, dorsiflexion and plantarflexion strength have likewise yielded conflicting results (Bernier et al., 1997; Hartsell and Spaulding, 1999; Hubbard et al., 2007a; McKnight and Armstrong, 1997; Wilkerson et al., 1997). Lack of consistent findings, coupled with an absence of reference to the clinical and functional significance of any detected weakness, makes this factor an unconvincing primary explanation for FI complaints.

Suspected damage to the mechanoreceptors of the ankle has been proposed as a mechanism to explain recurrent sprains. However, studies of the effect of an anesthetic on the joint capsule and ligaments of healthy ankles found either limited or no effect on position sense (Feuerbach et al., 1994; Hertel et al., 1996; Konradsen et al., 1993; Myers et al., 2003). Peripheral nerve injury has also been reported immediately after inversion sprain resulting in weakness (Hyslop 1941, Nitz 1985), and slower nerve conduction velocities (Kleinrensink et al., 1994; Nitz et al., 1985). These findings support local sensory changes, most likely peripheral nerve injury, as a possible contributor to delayed recovery post ankle sprain. However, the functional implications of these findings are harder to document.

Studies of deficits in position sense in FI subjects have been presented, using a variety of methods including recognition of a passively placed position (Fu and Hui-Chan, 2005; Gross, 1987; Santos and Liu, 2008), active replication by the subject of the required position (Boyle and Negus, 1998; Glencross and Thorton, 1981; Gross, 1987; Konradsen and Magnusson, 2000) and simple recognition of the occurrence of motion (Forkin et al., 1996; Garn and Newton, 1988; Hubbard et al., 2007a; Lentell et al., 1995; Refshauge et al., 2000; Refshauge et al., 2003). More often plantarflexion and dorsiflexion than inversion and eversion (Refshauge et al., 2003) have been used. Both evidence for a deficit (Boyle and Negus, 1998; Forkin et al., 1996; Fu and Hui-Chan, 2005; Garn and Newton, 1988; Glencross and Thorton, 1981; Konradsen and Magnusson, 2000; Lentell et al., 1995; Refshauge et al., 2003) and the absence of a deficit (Hubbard et al., 2007a; Refshauge et al., 2000; Santos and Liu, 2008) were found. Here again, the issues raised about the functional significance of these study results, as well as the conflicting conclusions, make use of this information difficult in the understanding of FI.

Peroneal response time in reaction to sudden inversion motion has been used to assess both motor and mechanoreceptor function of the ankle with functional instability. Several authors found no statistically different response time (measured by EMG) for the peroneal musculature of subjects with previously sprained ankles compared to the uninjured ankle (Brunt et al., 1992; Ebig et al., 1997; Santos and Liu, 2008) or to the ankles of uninjured subjects (Brunt et al., 1992; Fernandes et al., 2000; Nawoczinski et al., 1985; Santos and Liu, 2008). Conversely, four studies found a statistically significant delay in peroneal response time for subjects with functionally unstable ankles (Konradsen and Ravn, 1990; Konradsen and Ravn, 1991; Löfvenberg et al., 1995) or chronically unstable ankles (Löfvenberg et al., 1995; Vaes et al., 2001), all compared to control subjects with stable ankles. Studies of peroneal reaction times after acute injury (Konradsen et al., 1998) suggest recovery of function at 3 weeks. Calculations based on the response of healthy subjects of the time to effective eversion produced reflexively compared to a realistic time course of unexpected inversion during activity, suggest that even a normal reflex response is insufficient to offer joint protection (Konradsen et al., 1997). Therefore positive findings with these investigations are also unsatisfactory in explaining functional instability.

Central Nervous System Factors

Given that impaired local function is insufficient to explain the problems of functional ankle instability, examination of the central nervous system (CNS) function, as it relates to motor behavior, is warranted. There are a variety of ways this had been investigated, including muscle recruitment strategies, static and dynamic postural control, and gait characteristics.

Variability in patterns of proximal muscle recruitment in the presence of FI has been reported (Bullock-Saxton et al., 1994). As well, changes in the central activation ratio in proximal muscles, reflecting motoneuron pool excitability, were found in CAI subjects, although the magnitude of the difference from control subjects was small (Sedory et al., 2007).

Postural Control

The amount of postural sway occurring under static conditions in single leg stance has been investigated in functional instability. Increased sway in single leg stance was shown to be predictive of future ankle injury in male soccer players (Tropp et al., 1984), and to be present in male soccer players with functional, but not mechanical, ankle instability compared to subjects without instability (Tropp, 1986). Other authors similarly reported decreased postural control in single leg stance (Hertel and Olmsted-Kramer, 2007; Leanderson et al., 1993; Perrin et al., 1997). However, still others have found no difference (Ross and Guskiewicz, 2004) in measures of postural sway in FI subjects. Resolution of deficits in postural control have been reported within 14 days (Evans et al., 2004) and also to remain at one year post injury (Leanderson et al., 1996). The presence of a static postural control deficit in FI is supported, but it would appear insufficient to describe the dynamic complaints of functional instability, and so other activities have also been studied.

Differences between FI subjects and control subjects have been observed in the degree of hip versus ankle movement (Pintsaar et al., 1996; Tropp and Odenrick, 1988) and timing of muscle firing (Brunt et al., 1992) used to maintain equilibrium under dynamic conditions in stance. Some authors reported diminished ability to stabilize on a mobile surface (Brown and Mynark, 2007; Perrin et al., 1997; Ryan, 1994), while others found no difference (Bernier et al., 1997). More evidence supports the existence of a deficit in dynamic control than refutes such a deficit.

Gait and Transitional Movements

Both specific differences in gait patterns between healthy controls and instability subjects (Monaghan et al., 2006; Nyska et al., 2003; Spaulding et al., 2003) and indications of a generalized increase in variability in gait parameters (Spaulding et al., 2003) have been observed.

Using cadavers, Konradsen and Voight (2002) manipulated the inversion and plantarflexion angles during simulated swing and heel strike phases of gait. They proposed that with the combination of previously demonstrated active ankle position replication errors (Konradsen and Magnusson, 2000), and the effect of small variations in the degree of inversion positioning during swing, individuals with FI had a 1000 times greater risk of an untimely collision with the ground than healthy individuals. The in-vivo and in-vitro findings collectively support that errors (variation) in positioning the foot during swing and weight acceptance may contribute to the complaints of functional instability.

Differences in behavior during transitional tasks including double to single limb support and single foot landing from a jump also support an alteration in motor control in FI subjects. Timing differences in proximal muscles (Van Deun et al., 2007), preparation for and position on landing (Caulfield and Garrett, 2002), and stability and force distribution on landing (Caulfield and Garrett, 2004; Ross and Guskiewicz, 2004) have been demonstrated as occurring with the observed timing reflecting preprogrammed responses.

Multiple studies then suggest that an alteration in central processing may occur in individuals with functional ankle instability, although it is unclear if this is a maladaptive response to ankle sprain or a predisposing factor. In addition, the nature of such alteration, and whether it is reflected in a feedforward or feedback method of control is not clear.

Most studies have investigated postural control in a fully weighted position; however, this is the position of greatest stability in inversion /eversion for the ankle based on bony configuration (Stormont et al., 1985). Perhaps this factor contributes to the conflicting study outcomes observed. As a lateral ankle sprain occurs in a position of plantarflexion and inversion, it

appears most likely that the giving way or sprain would occur before full weight bearing in a foot flat position is achieved.

Kinematics during Gait and Stair Climbing

The gait characteristics of FI subjects have been mentioned previously. Level surface gait kinematics of stance phase in healthy subjects were described similarly by Moseley et al. (1996) and Hunt et al. (2001), with differing absolute values of joint excursions. In addition, Moseley and colleagues (1996) reported between-subject variability of these motions ranging from 33-48% coefficients of variation (CV) for all ankle motions. Sadeghi et al (2001) reported CVs of 84% in the sagittal plane at the ankle. Using a different measure (coefficient of multiple correlations) to compare step cycle waveforms, Kabada and colleagues (1989) reported greater variation in the frontal and transverse planes than in the sagittal plane, as did Leardini (1999). Swing phase kinematics on level surface were not well described.

Reports of stair climbing kinematics in FI subjects were not found in the literature. Contact on the forefoot, rather than heel contact, was reported in healthy subject stair climbing (Protopapadaki et al., 2007; Reiner et al., 2002). Yu, et al. (1997) reported greater kinematic than kinetic variability in stair climbing, and greater variability in the frontal than sagittal plane data. Step descent requires weight acceptance in a plantar flexed position (Reiner et al., 2002), and therefore may be a vulnerable position for those with functional instability. The potentially increased challenge of the landing posture may make subtle differences in late swing phase and forefoot contact position and speed more readily identifiable in fewer repetitions than gait observations on level surface. Consistent alterations or increased variability in foot placement in late swing or forefoot contact may contribute to excessive inversion on weight acceptance resulting in instances of instability. Therefore, the ankle kinematics of stepping down stairs is of interest in the study of functional instability.

Proposed Research Methods

Kinematic Investigation

Electromagnetic analysis is one method of kinematic assessment suitable to analysis of a step down task. It uses a stationary transmitter with a global coordinate reference system creating an electromagnetic field and sensors placed on the moving body parts. A local coordinate system is then described from which anatomically meaningful joint information can be obtained. A joint coordinate system has been described for the ankle by the International Society of Biomechanics (Wu et al., 2002) and a different anatomic system by Nawoczenski et al. (1998). Due to the difficulty of locating and the close proximity of surface landmarks on the talus and calcaneus, a model of the rearfoot composite motion, combining talocrural and talocalcaneal joints, was used.

Movement Accuracy and Cortical Activation Investigation

While much has been studied, with inconsistent results, about the proprioceptive and reflex capabilities of the functionally unstable ankle, no investigations have been identified of the quality of motor control of these ankles when a precise movement pattern is required. Further, no has any investigation within the CNS has been accomplished to indicate sensorimotor processing differences between normal and FI subjects. A task requiring movement accuracy is likely to detect differences in motor control between involved and uninvolved ankles, and between subjects with and without functional ankle instability.

Tracking Accuracy

Tracking a sine wave and calculating an accuracy index is an established tool that has been used in studies of finger control in normal subjects (Carey et al., 1994) and subjects with stroke (Carey et al., 1998; Carey et al., 2002; Halaney and Carey, 1989), both independently and with brain imaging (Carey et al., 2004; Carey et al., 2002). Only one study has been identified using this technique on the ankle (Carey et al., 2004) in a subject with stroke. However, it is a reasonable tool to use in this exploratory study as it has been previously successfully under similar conditions with different populations.

fMRI and BOLD Signal

Finding that multiple studies exist which suggest changes in motor control occurring in the central nervous (CNS) system, it is reasonable to investigate where these changes may be observed within the CNS. One available method to assess cortical activation changes is functional magnetic resonance imaging (fMRI). Functional MRI uses the blood oxygenation level dependent (BOLD) contrast to make comparisons of cortical activation recorded during periods of task and rest. This BOLD contrast is based on the differences in the magnetic properties between oxygenated and deoxygenated blood. One explanation for the difference between rest and task activity is that oxygenated blood flow increases to levels above those required during the task phases, resulting in an increase in signal, and subsides during rest conditions. MRI uses the magnetic quantum property of spin of the hydrogen atom to create a signal detected for imaging. In the presence of a strong magnetic field, a T2* relaxation parameter is monitored following a pulse sequence to momentarily align the atoms. This parameter reflects local magnetic field variations. Due to the subject position (recumbent), and need to avoid distortion of the magnetic field, non-weight bearing small movements are required with this technology.

Individual variations in task and rest condition signal are large, resulting in questions of the reliability within subjects of this measure. Varying data processing and methods of statistical comparison can result in conflicting conclusions. Use of the Beta signal intensity method has been reported to be more reliable than other methods (Kimberley et al., 2008). Inferences about the relationship between task and signal are made based on the timing model for rest and task conditions, as well as a calculation of the delayed hemodynamic response. Typical responses are of 0.5% to 5% change in regional intensity, which develop over a three to eight second delay following task initiation (Detre and Floyd, 2001). Sensitivity to T2* changes increase as the magnet strength increases. Blood flow changes are larger for sensorimotor tasks than for cognitive tasks.

Functional imaging analyses of ankle motor tasks have been performed with healthy and neurologically impaired subjects. No study of a population considered “orthopedic” was found. Studies of localization of function (Alkadhi et al., 2002; Ciccarelli et al., 2005; Debaere et al., 2001; Dobkin et al., 2004; Havel et al., 2006; Kapreli et al., 2006; Sahyoun et al., 2004) for the

foot and ankle were found. Comparisons of active movement to preparation to move (Sahyoun et al., 2004), isolated ankle versus coupled movement with the wrist (Debaere et al., 2001), reproducibility across multiple sessions (Havel et al., 2006) and activity in ipsilateral and contralateral hemispheres (Kapreli et al., 2006) were conducted. These studies support the viability of this modality for the current investigation.

Localization of Brain Activation

Regions of interest can be defined on the anatomic MRI images to describe localization of the functional activation. Due to the exploratory nature of this study, four motor and one sensory areas were chosen a priori for investigation. These were chosen based on previous work on motor activation (Alkadhi et al., 2002; Dassonville et al., 1998; Dassonville et al., 2001; Debaere et al., 2001) in conjunction with a desire to focus the scope of the analysis. The functional regions so defined were primary motor cortex (M1), primary somatosensory cortex (S1), premotor cortex (PMC), supplementary motor area (SMA), and pre-supplementary motor area (PSMA). These were anatomically defined after Dassonville, et al. (2001) and Geyer (2000) as follows:

- M1 – posterior one-half of the precentral gyrus
- S1 – the postcentral gyrus
- PMC – bound anteriorly from a line half-way between the frontal pole and the central sulcus, posteriorly by the anterior border of M1, and inferiorly by the plane of the limit of the central sulcus or the beginning of the insular cortex. This more superior border than the border used by Dassonville et al. (i.e. intersection of Sylvian fissure and precentral sulcus) was chosen to limit the volume size with the expectation that relevant ankle activity would occur more superiorly, and to be consistent with the extent of M1 described.
- SMA – medial wall cortex from the superior pole to the cingulate sulcus, limited posteriorly by a line half-way between the central and precentral sulci, and anteriorly by a vertical line drawn through the anterior commissure.
- PSMA – the extension of the medial wall SMA from the anterior commissure forward through sections C and D in Talairach space (Talairach and Tournoux, 1988) from the superior pole to the cingulate sulcus.

Naming conventions

Multiple descriptions of motions for actions of the foot and ankle complex were used in the relevant literature. For purposes of this study, three planes of motions for the talocrural and subtalar joints combined (rearfoot) will be described as dorsiflexion/plantarflexion, inversion/eversion, and adduction/abduction. However, the terminology of the authors, clarified as needed, will be used when reviewing the literature. An additional point of clarity is needed. While in more recent texts the term “fibularis” is applied the lateral musculature that everts the foot and ankle, all literature reviewed used the term “peroneal” and this will be maintained in this text. As well, “peroneal nerve” will be used rather than “fibular nerve”.

Research Subjects

Otherwise healthy FI subjects were selected with complaint of unilateral instability and/or recurrent sprains under benign conditions, after the definition of Konradsen (2002). These subjects had a functionally limiting first-time sprain prior to the onset of the FI complaints. These FI subjects were without recent injury or current pain to avoid confounding with the influence of pain in this study of motor control. Healthy control subjects were recruited who reported no complaints of ankle instability. Right-footed individuals were chosen to eliminate confounding in brain activation due to functional laterality. All subjects were free from other activity limitations or health conditions that would make them unable to participate in the study. In particular, the subjects were screened for normal foot plantar surface sensation because impaired sensation, such as may be present in undiagnosed diabetes, could significantly alter the step down task performance and potentially impact safety. Explicit criteria are listed in the Methods section of this document.

Research Question and Hypotheses

The problem of functional ankle instability is common and has significant functional impact. While indications of a variety of differences between individuals with and without the complaint have been identified, a comprehensive explanation is lacking. Strong indications exist that alterations in CNS function are a component; whether these are due to an incomplete recovery from an acute injury or signs of a predisposing condition is not clear. No research to

date has employed the technology of functional brain imaging to investigate differences in cortical activation in this condition, nor has an accuracy task been employed to characterize movement control. In addition, while variability in motor performance has been noted in FI, no study has investigated variability in activities that are routine but still may challenge the unstable compared to stable ankle, such as descending steps. Electromagnetic motion analysis and fMRI are technologies with potential to address these gaps in the research to date.

The purpose, then, of this exploratory study was to investigate motor control in subjects with functional instability by use of electromagnetic ankle motion analysis during a step down task, an accuracy task, and fMRI imaging of brain activation during a motor accuracy task

The hypotheses to be investigated in this study were therefore the following:

1. There will be significant differences in the movement parameters of a step cycle when repeatedly descending a stair, between involved and uninvolved FI ankles and between FI subjects and healthy controls.
 - a. There will be greater trial to trial variability in the excursion of inversion/eversion and dorsiflexion/plantarflexion as measured by the coefficient of multiple correlations.
 - b. There will be a difference in the time for swing and weight acceptance phases.
 - c. There will be a difference in linear velocity in preparation for foot placement phase of swing and in the angular speed on step contact.
2. The accuracy of ankle movement, measured by an accuracy index while tracking a sine wave, will be less during inversion and eversion for involved versus uninvolved ankles and for FI versus healthy control subjects.
3. There will be a difference in cortical activation measured during the tracking task between involved and uninvolved ankles of FI subjects and control subjects measured.

CHAPTER II - LITERATURE REVIEW

Overview of Ankle Sprain

Estimates of the daily incidence of ankle sprain range from 1 per 10,000 people (Trevino et al., 1994) – 23,000/day (Kannus and Renström, 1991). Records from a one-year period in an Oslo hospital indicate 16% of those treated for a sports injury were seen for an ankle sprain (Maehlum and Daljord, 1984). A similar United Kingdom study in four adjacent health districts calculated an incidence rate of 52.7 sprains per 10,000 residents over a one year period (Bridgman et al., 2003). When applied to the entire population of England and Wales, this equated to 302,000 sprains in the same period. The lateral ankle ligaments are the most frequently injured tissue in athletes (Garrick, 1977), with injuries commonly sustained with participation in men's and women's basketball, women's cross-country, and men's football (Garrick, 1982). Men's (Ekstrand and Gillquist, 1983; Ekstrand and Tropp, 1990) and women's soccer (Agel et al., 2007; Brynhildsen et al., 1990), and volleyball (Schafle et al., 1990), women's gymnastics (Marshall et al., 2007) and men's professional basketball (Henry et al., 1982) are also notable for the rate of ankle sprain. Hosea et al. (2000), in a study of ankle injuries in basketball, found a 25% greater risk for women than men of sustaining a Grade I ankle sprain. All other reported injury rates were comparable to men. They also found a doubled risk of ankle injury for both genders at the intercollegiate level of competition compared to the interscholastic level.

Mechanisms of Injury

Ekstrand and Tropp (1990) reported a higher ankle injury rate at games than practices across all four divisions of men soccer teams studied. Studies of women's athletic injury rates also indicated higher injuries during competition in gymnastics (Marshall et al., 2007) and volleyball (Agel et al., 2007), with more injuries in Division I than III level competition for gymnastics, but no such difference in volleyball. Kofotolis and colleagues also found no difference between practice and competition injury rates with amateur soccer players (Kofotolis et al., 2007). They did report a higher sprain incidence toward the end of each half of a game and during the first two months of the season. Agel (2007) reported higher injury rates during preseason than

occurred during the regular season. Competition level, conditioning, and fatigue all appear to contribute to ankle sprain.

Variations on grading schemes were reported (DeMaio et al., 1992; Gerber et al., 1998; Hergenroeder, 1990; Trevino et al., 1994; Winkel et al., 1997). Some authors (Gerber et al., 1998; Hergenroeder, 1990; Trevino et al., 1994; Winkel et al., 1997) described a progression from partial to total rupture; others indicated only a discrete progression of ligament involvement (DeMaio et al., 1992). Another author (Hergenroeder, 1990) staged symptoms only, without defining the ligaments involved. All agreed on the order of injury – ATFL, then CF, then PTFL (Figure 1).

Figure 1. Ankle drawing depicting the lateral ligaments. PTFL – posterior talofibular ligament, CFL – calcaneofibular ligament, ATFL – anterior talofibular ligament.

Risk Factors for First-time Sprains

Risk factors for first-time sprains intrinsic to the individual have primarily been reported for sports populations. Beynnon et al. (2002) performed a qualitative literature review of prospective studies of ankle sprain risk factors, stating there were too few well-designed studies to perform a systematic review. They found little agreement in the literature, with the exception of determining that sex, anatomical foot type, and generalized joint laxity were not risk factors. Conflicting results were found for anthropometric and other anatomic factors, foot dominance, strength, reaction time, and postural sway in the literature reviewed. A more recent systematic

literature review of observational studies (de Noronha et al., 2006) reported a five-fold increase in ankle sprain risk for subjects with decreased dorsiflexion (mean 9° less than average flexibility), and noted more limited evidence for decreased passive inversion position sense and increased postural sway as predictive factors. One risk factor not supported by the review was strength. Willems, et al. (Willems et al., 2005b; Willems et al., 2005c) studied intrinsic risk factors for men and women among college-age physical education students. Factors included many that Beynnon et al. (2002) used, with the addition of the European Test of Physical Fitness and ankle joint proprioception. For men, slower running speed, less cardiorespiratory endurance, decreased balance, less ankle dorsiflexion mobility and strength, and slower reaction times of gastrocnemius and tibialis anterior while standing on a tilting platform were identified as related to risk of sprain (Willems et al., 2005b). Women were evaluated with the same methods, finding significant risk only with diminished passive inversion position sense, greater first metatarsophalangeal joint extension range of motion, and decreased postural control on a computerized balance platform (Willems et al., 2005c). Willems et al. (2005a) also reported combined data for men and women in studying gait characteristics. They reported an increased risk of sprain for subjects with a more lateral center of pressure (COP) at initial contact, and that total contact and re-supination after foot flat were delayed in the subsequent sprain group.

Incidence of Recurrent Ankle Sprains

Numerous authors report a high rate of recurrence following an initial inversion sprain. Tropp (1985a) reported a 2.3 times greater risk of ankle injury in male soccer players with previous injuries. Thacker et al. (1999) also found in a literature review that a previous sprain was the most common risk factor for an ankle sprain. In their study of female soccer players in a senior division, Brynhildsen et al. (1990), noted 39.5% of the players had sustained an ankle injury and 35% of these reported persisting symptoms (23.3% of all players). Ekstrand and Gillquist (1983) noted a recurrence rate for previously sprained ankles of 47% during a one year prospective study of men's soccer. Bahr and Bahr (1997) found that 79% of acute ankle injuries for one season of the Norwegian Volleyball Federation were recurrent sprains, and calculated a 3.8 times increase in risk of sprain for a previously injured ankle. Likewise, a study of recreational basketball players reported an odds ratio of 4.94 for sustaining an ankle sprain for those with a prior history of sprain (McKay et al., 2001). Of Braun's 467 study participants (1999), 19.4% reported a re-injury of the ankle 6-18 months after the first medical consultation

for a sprain. Forty-seven percent of patients with ankle sprain were reported to suffer a recurrent sprain on the same ankle, and 22% to sprain the contralateral ankle in a study by Bullock-Saxton (1995).

Long-term Consequences of Recurrent Sprains

The long-term consequences of ankle sprain and re-injury appear to be significant. Harrington (1979) reported findings and treatment outcomes for thirty-six patients with lateral ankle ligament instability of greater than ten years. All subjects were symptomatic, either describing anterior or medial joint pain with walking or increased instability following a reinjury. Twenty-eight (78%) patients showed evidence of degenerative arthritis in the medial half of the tibial talar joint on non-weight bearing roentgenograms, with more significant evidence on weight bearing films. Arthroscopy of twelve ankles was performed, and demonstrated significant chondromalacia or frank eburnation of subchondral bone in all ankles.

Another study reported findings in 54 subjects with complaints of chronic ankle instability (Komenda and Ferkel, 1999). Ninety-three percent of the ankles studied showed intra-articular abnormalities such as loose bodies, synovitis, osteochondral lesions, osteophytes, and chondromalacia. Hintermann et al. (2002) reported cartilage damage, most commonly on the talus, detected by arthroscopy in 55% of subjects with chronic instability. These subjects were being evaluated for ligament reconstruction due to pain and limitation with desired activities. Sixty-two percent reported limitations with walking, 88% were limited with sports, and 59% had daily symptoms. Takao et al. (2005) performed arthroscopy on 72 patients with persisting complaints of pain, giving way, functional instability or swelling more than 2 months following an ankle sprain. Those with subtalar instability were excluded. Twenty-nine percent had osteochondral lesions on the talus, with fewer numbers having anterior impingement. While the authors could not be certain that these findings were the cause of the residual pain, they felt that an arthroscopic examination added specific benefit to diagnosis in cases of residual ankle complaints.

Schaap et al. (1989) queried 1012 patients (81% response rate) regarding residual symptoms and handicaps 9 months after treatment for ankle sprain. Thirty percent of respondents reported pain, an unstable feeling, or swelling, with 13% indicating an occupational handicap and 27% a

sports handicap. Severity of the original injury was graded I - no demonstrable instability on clinical examination, II – only mild or incomplete instability, or III – joint completely unstable. Treatment of grade I injuries consisted of compression with bandages, grade II treatment consisted of partial immobilization with tape, and grade III treatment consisted of primary surgical repair of the lateral ligaments. The nature and frequency of residual complaints reported on their 9 month follow-up questionnaire were comparable across all three grades of injury. With the application of their treatment protocol, functional prognoses were comparable across categories of severity. A follow-up study by the same group (Verhagen et al., 1995) of the same patient cohort was performed 6.5 years later, the overall rate of residual complaints was 39%, with a nearly doubled rate of complaint in the subject group with grade II injuries. Fear of instability was present in 40.5% of all respondents, compared with 30.3% at 9 months (increase in grade II group from 28% to 48%). Twenty-one percent reported occupational handicap, and 9% sports handicap (of those sports participants, 73.4% of the total sample).

Another follow-up study conducted with subjects seven years after treatment for a lateral ankle sprain (defined as inversion mechanism with local tenderness and swelling) found 32% of respondents experienced pain, swelling, and recurrent sprains. Seventy-two percent of these subjects reported functional limitations, primarily in sport participation (Konradsen et al., 2002). These subjects had all undergone a functional rehabilitation program. A different follow-up study (mean interval 4.2 years) used subjects identified with stress radiography for talar tilt as an objective measure of ligamentous rupture (Hansen et al., 1979). The subjects received no formal physical therapy intervention. Twenty-one percent of subjects reported residual complaints, but only 6% of these had difficulty with daily activities, and 23% discontinued their preferred sport. The authors noted that no correlation between the severity of injury as measured by radiography and residual complaints was found.

Functional Instability

Description

Functional instability is described as recurrent sprains of a feeling of instability often described as “giving way” (Freeman et al., 1965). Forty percent of ankle sprain sufferers reported these complaints in Freeman’s study, while Bosien et al. (1955) reported a rate of 33% . As

previously stated, Verhagen et al. (1995) reported 38.8% of subjects with prior ankle sprain claiming fear of instability. Gerber (1998), in a prospective study of all cadets at the United States Military Academy suffering an ankle sprain during a two-month period, observed that 40% of these subjects had residual symptoms at 6 months. A study at the United States Naval Academy found 10% of the freshman class complained of functional instability (Brand et al., 1977).

Symptoms of giving way and recurrent sprains are the most common descriptors of FI (Bernier and Perrin, 1998; Freeman, 1965; Gauffin et al., 1988; Hubbard et al., 2007a; Kaminski et al., 1999; Karlsson and Lansinger, 1993; Konradsen and Ravn, 1991; Lentell et al., 1995; Matsusaka et al., 2001; McKnight and Armstrong, 1997; Munn et al., 2003; Rozzi et al., 1999; Santos and Liu, 2008; Tropp, 1985). Some authors include pain (Hubbard et al., 2007a; Lentell et al., 1995) or report of weakness (Lentell et al., 1995; Munn et al., 2003; Rozzi et al., 1999) in inclusion criteria for their studies. Konradsen (2002) included only those reporting symptoms occurring in situations where a stable ankle would not experience difficulty. When asked if perhaps he were studying a different population than other researchers in this area who did not make this specification, he responded (personal communication e-mail 8/18/02) that he perhaps was the only writer to specify this, but felt others were in agreement, and that sufferers themselves would make the same distinction.

Varying degrees of functional limitations were reported. Braun (1999) found limitations in jumping, pivoting, and walking. Brand et al. (1977) reported complaints as well as difficulty running on uneven surfaces, and with cutting maneuvers and jumping. Tropp (1986) found interference with sporting activity. Subjects in Freeman et al.'s study (1965) noted the greatest symptoms on uneven ground.

Self-report Instruments

Subsequent to the initiation of this study, two reports of standardized patient-report instruments to identify and measure ankle instability became available. Ross et al. (2008) used the Ankle Joint Functional Assessment Tool (AJFAT) (Rozzi et al., 1999) in a study assessing the cutoff point for a self-report and performance measure useful in distinguishing FI subjects from controls. This tool asks participants to choose one of four responses ranging from “much less

than the other ankle” to “much more than the other ankle” for 12 questions related to activities commonly associated with chronic ankle instability. Total possible score was 48, with a higher score indicating greater limitation. Fifteen FI subjects, identified by a history of first-time sprain, at least one additional sprain and two episodes of giving way were compared to 15 healthy control subjects. A cutoff point was determined for the AJFAT was determined from the receiver operating characteristic curves. The authors reported no false positives or false negatives at this score, suggesting this was an excellent tool for use with the FI population. However, there appeared to be a problem with selection bias in this study as the concepts behind the AFJAT were the criteria used to select the FI subjects to be tested.

Hale and Hertel (2005) reported on the measurement properties of the Foot and Ankle Disability Index (FADI) which was then used later in several studies as inclusion criteria by the same group investigating chronic ankle instability (CAI) defined below. This instrument has an activities of daily living section and a sports section. Participants selected an answer as to how difficult they perceived an activity on a 0-4 point scale, with 4 being “no difficulty or pain” and 0 being “unable to do”. They reported moderate to good reliability over a 6-week period, responsiveness to change with rehabilitation programs, and ability to distinguish between healthy and chronically unstable ankles. A systematic review of patient self-report measures for chronic ankle instability (Eechaute et al., 2007) found the FADI to be one of two most appropriate instruments to characterize disability in this patient group. This same review found the least documentation for the clinimetric properties of the AJFAT. In a survey of self-report outcome measures for the foot and ankle, Martin and Irrgang (2007) indicated finding published evidence related to construct validity, reliability, and responsiveness for the FADI, but not content validity.

Measures of Physical Performance

Some investigations of standardized functional performance measures have not found differences between involved and uninvolved ankles (Munn et al., 2002) or between those with chronic complaints and healthy subjects (Demeritt et al., 2002). Demeritt et al. used a cocontraction test with elastic resistance during a shuffle step, a shuttle run, and an agility hop test. These authors concluded that the subjective complaints of FI subjects do not limit functional performance. This appears an overly broad conclusion given the limited extent of their study. Munn and colleagues (2002) used a single leg triple hop test and a shuttle run,

neither of which differentiated involved from uninvolved limb of subjects with unilateral functional instability. These authors offered several theories as to why their results were negative; among them were that the tests were not sufficiently challenging for the ankle, that compensation takes place at more proximal joints, allowing completion of the closed chain, multijoint task, or that the subjects reporting functional instability have a false perception of their actual abilities. Seventy-five percent of Munn et al.'s subjects reported either modifying their sport activity or using an external ankle support to continue to participate.

Docherty et al. (2005) used four unilateral hop tests to assess for physical performance limitations in 42 FI subjects and 18 healthy controls. In an attempt to measure the degree of disability in the FI subjects, six questions were asked concerning sprain history and circumstances of instability. Possible scores ranged from 0-6, with a higher score indicating greater disability. Weak but positive correlations were determined between the figure-of-8 hop ($r = 0.31$) and the side-hop ($r = 0.35$) and the self-report scores. Between-group means were not specifically compared. Ross et al. (2008), in a previously described study, calculated time to stabilization values from force plate data for a single leg jump landing for 15 healthy subjects and 15 FI subjects. They used a receiver operating characteristics curve to determine a cutoff score useful for distinguishing healthy from FI subjects. They chose a time of 1.58s, but acknowledged this was a somewhat unsatisfactory balance between false negative findings (5 of 15 FI subjects) and false positive findings (4 of 15 control subjects). Specificity values were not provided, sensitivity was 0.67. The clinical usefulness of this scoring remains unclear.

Ankle/Local Tissue Explanations for Functional Instability

Mechanical Instability

Talocrural Joint

Stability has been described as “joint resistance to relative movement of the bones when load is applied” (Leardini et al., 2000). Mechanical instability of the talocrural joint is often tested with radiography. To test the anterior drawer using radiography, a force is applied to the ankle to cause anterior translation of the talus relative to the tibia/fibula, and the distance between the posterior margin of the talus and the tibia observed on the radiograph is compared to the

measure without the translatory force (Johannsen, 1978). The radiographic examination for talar tilt is performed in maximum supination with the leg stabilized. Johannsen (1978) recommended measuring the distance from the articular surface of the talus at the lateral talar trochlea to the tibia (measured in millimeters). Others (Cox and Hewes, 1979; Harper, 1992; Karlsson and Lansinger, 1993; Lentell et al., 1995) suggested measuring the angle between joint surfaces, with no displacement (normal alignment) as 0 degrees.

One difficulty with diagnosis of mechanical instability is the lack of universal standard based on radiographic findings. A wide range of “normal” talar tilt has been reported, making the significance of small findings and interpretation of isolated measures unclear. Harper (1992) summarized findings from other researchers indicating up to 20 degrees of talar tilt in asymptomatic adults. Cox and Hewes (1979) measured the talar tilt of 202 U.S. Naval Academy midshipmen with no history of ankle injuries. In contrast to Harper, they reported only 9.7% had any measurable tilt and only 1.7% had a tilt greater than 5 degrees.

Harper (1992) evaluated involved and uninvolved ankles in 13 subjects with complaints of chronic instability. The average talar tilt in the unaffected joint was 3 degrees (range 0-12) compared to 6 degrees (range 0-13) for the affected joint. The difference was not statistically significant. Lentell et al. (1995) reported an average talar tilt of 5.0 degrees for the functionally unstable ankles and 4.0 degrees for the uninvolved ankles. While statistically significant for pair wise comparisons, the diagnostic significance of the absolute measure was not established.

Normal measures for the anterior drawer sign have also not been established. Harper (1992) chose greater than 6 mm as the threshold for an abnormal finding. Karlsson and Lansinger (1993) described mechanical instability as 10 mm or more anterior talar translation (anterior drawer sign) or a talar tilt of 9 degrees or more. Alternatively, they described a difference in anterior talar translation of 3 mm or more or a difference in talar tilt of 3 degrees or more compared to the uninvolved ankle. Kaikkonen et al. (1994) used 5 mm translation as the criterion for laxity in clinical testing. Johannsen (1978) compared x-ray findings with surgical confirmation of ligamentous disruption, and found only five percent of cases of verified ligamentous disruption were radiographically negative with both the anterior drawer sign and the talar tilt examination. Twenty-five percent of the cases had negative findings on one or the other of the two radiographic assessments. Criterion for a positive examination for talar tilt was

a 3 mm or greater difference in measurement compared to the unaffected side, and a 2 mm or more difference for the anterior drawer sign. He concluded that the two examinations were complementary.

Some researchers (Freeman, 1965; Staples, 1975) reported the use of anesthesia to assist in minimizing the effects of pain and muscle spasm while obtaining stress films to avoid false negative results. Others make no mention of anesthesia with these films (Johannsen, 1978; Lentell et al., 1995). Still others (Bosien et al., 1955) describe clinical tests with occasional radiographic confirmation of finding, or no radiographic confirmation (Peters et al., 1991) while diagnosing mechanical instability. Johannsen (1978) recommended use of local anesthesia to minimize the false negative rate of these examinations after reviewing the results of his study. Becker et al. (1993) compared results of stress radiographs with the anterior drawer test taken with and without anesthetic injection in 65 male soldiers with acute inversion ankle injury. They found statistically significant differences in the amount of displacement, and estimated a 20% under-evaluation rate without the use of anesthesia.

Subtalar Joint

Subtalar instability is a less frequently described mechanical instability, which is poorly detected with radiographic methods used for talocrural studies. In describing subtalar instability, Karlsson et al. (1997) described patient complaints of “giving-way” during activity, stiffness and swelling, and possibly pain complaints in the sinus tarsi. Clinically detected increased internal rotation of the calcaneus was also reported to be commonly present. Kato (1995) reported pain in the posterior part of the foot during walking or exercising associated with a feeling of instability. He reported a less obvious anterior drawer sign than that observed with talocrural instability. Clanton (1989) described involvement of the calcaneofibular, lateral talocalcaneal, cervical and/ or interosseous ligaments of the talocalcaneal joint. Karlsson et al. (1997) stated the injury occurs primarily in conjunction with lateral ankle injury/instability. Kato (1995) specified that the elongation or rupture of the interosseous talocalcaneal ligament occurs only after injury to the ATFL and calcaneofibular ligaments, corresponding to a grade II or III sprain. Staples (1975) consistently found injury to the talocalcaneal ligaments with accompanying abnormal mobility when calcaneofibular and ATFL disruption were noted at surgery.

Clanton (1989) and Kato (1995) supported use of a stress film centered on the talonavicular joint to demonstrate anterior movement of the calcaneus on the talus. Karlsson et al. (1997) reported a finding of > 2 mm separation of talocalcaneal surfaces in anterior-posterior views compared to the asymptomatic side on tibiotalar stress radiographs. These authors also advocated the Broden view (30-45 degrees off vertical) as more specific to the talocalcaneal joint. This film visualizes the posterior facet of the subtalar joint. A loss of parallelism of the joint surfaces, with lateral joint opening (average 5 mm) is indicative of disruption of the calcaneofibular ligament. Louwerens et al. (1995b) discovered a wide range of movement which did not correlate with complaints of functional instability. Kato (1995), however, found a more significant correlation between complaints of instability and displacement of the subtalar joint > 4 mm in patients he had diagnosed with subtalar instability, compared with patients diagnosed with ankle (talocrural) instability. Displacement measures for the asymptomatic group, however, were not reported. Harper (1992) observed an average of 8 mm of lateral subtalar opening (range 5-9 mm) in 13 out of 14 symptomatic ankles. The asymptomatic ankles averaged 7 mm of opening (range 5-11 mm). Side-to-side comparisons between individuals were not reported.

Distal Tibial-fibular Joint

Recently, reports of altered positioning of the fibula have been investigated as a contributor to continuing complaints following ankle sprain. Both posterior (Berkowitz and Kim, 2004; Eren et al., 2003; Scranton et al., 2000) and anterior (Kavanagh, 1999; Mavi et al., 2002) positional faults have been reported using a variety of clinical and radiographic methods. Hubbard et al. (2006) found significantly more anterior positioning in the involved ankles for CAI subjects compared to the uninvolved ankles and to the ankles of healthy controls using fluoroscopic imaging. Mavi et al. (2002) also found a (slightly) anterior fibular placement in subjects with recurrent ankle sprains with magnetic resonance imaging (MRI). Kavanagh (1999) reported a clinical determination of anterior positioning based on manual mobility testing. Berkowitz and Kim (Berkowitz and Kim, 2004), however, reported a nearly doubled measure of posterior placement using computed tomography(CT)/MRI in a series of patients who underwent a surgical stabilization procedure. A posterior position of the fibula was also found by Eren et al. (2003) using CT in patients with ankle sprain, as did Scranton et al. (2000) with a retrospective analysis of past surgical stabilization patients.

Based on the inconclusive evidence of the nature of the role mechanical instability may play in functional instability, and the inconsistencies in diagnosing mechanical instability, it is evident that this factor is of limited usage in explaining the problem of functional instability.

Muscle Weakness at the Ankle

Strength of musculature at the ankle has been assessed by many authors, with a variety of methods. Differing measurement tools, testing positions, types of contractions, and assessed muscle groups were seen. The majority of studies employed isokinetic testing, more often of concentric than isometric or eccentric contractions, and usually at one slower and one faster speed – e.g. 30 and 120 °/s. Less frequently inversion, dorsiflexion, and plantarflexion were investigated. Subject knee positioning varied from full extension (McKnight and Armstrong, 1997) to seated with 90° of flexion (Hartsell and Spaulding, 1999; Tropp, 1986). This lack of uniformity in methodology may be associated with the variability of results between studies.

Bosien et al (1955) used manual muscle testing to find mild peroneal (fibularis) muscle weakness in 22% of college students at follow-up 29 - 45 months after lateral ankle sprain. When considering those with continuing symptoms, this represented 66%; when considering those without symptoms, this represented 5% of the subjects.

Five authors found no peroneal/evertor concentric or isometric weakness, measured by peak torque, in the involved ankles compared to the uninvolved ankles of FI subjects (Lentell et al., 1995; Lentell et al., 1990; Munn et al., 2003; Ryan, 1994), or between chronic sprain subjects and controls (Kaminski et al., 1999; McKnight and Armstrong, 1997; Munn et al., 2003). Bernier found no difference for inversion or eversion eccentric contractions between involved and uninvolved ankles or between FI subjects and healthy controls (1997). McKnight and Armstrong (1997) also found no difference from control subjects for dorsiflexion, plantarflexion, or inversion peak torque.

Other researchers reported varying combinations of strength deficits. Wilkerson (1997) detected relative weakness in eversion between ankles of FI subjects as did Tropp (1986) and Hartsell and Spaulding (1999). Wilkerson et al. also reported greater between-ankle differences for FI subjects in inversion than eversion; these deficits were less than those identified for

subjects with acute ankle injuries. Santos and Liu (2008) reported eversion differences between ankles in FI subjects, and greater between-ankle differences in the FI group compared to the control group. Hubbard reported a regression analysis whereby the ratio of plantarflexion to dorsiflexion peak torque was a significant predictive factor for group, with controls having a higher ratio than subjects with chronic ankle instability (2007a). Munn (2003) reported eccentric weakness in inversion only of the involved ankle of FI subjects compared to the uninvolved ankle and to either ankle of a control group. Hartsell and Spaulding (1999) reported both concentric and eccentric weakness for inversion and eversion of the involved ankle in chronically unstable subjects. Ryan (1994) reported only concentric inversion weakness, with no difference in concentric eversion strength, in the involved compared to uninvolved ankle of his subjects.

While further investigation of concentric inversion and eccentric strength of all ankle muscle groups may be warranted, the current state of the evidence does not provide strong support for the significance of ankle strength as a primary explanation for the complaints of functional instability. It is also noteworthy that these studies reported weakness, when present, relative to the uninvolved ankle or to a control group. Designation of clinically meaningful deficits, and reference to established population strength norms, were not discussed.

Local Nerve and Mechanoreceptor Damage

Effects of Ankle Joint and Ligament Anesthesia

Michelson and Hutchins (1995) examined both medial and lateral ankle ligaments of five cadavers using fresh frozen specimens, looking for mechanoreceptors that had previously been identified in feline ligaments. They found mechanoreceptors in all specimens examined, with type II and type III being most predominant. No differences related to proximity to bony attachment or ligament depth could be determined. Wyke (1972) described type II receptors as low threshold, rapidly adapting mechanoreceptors active at the initiation of movement. He described type III receptors as high-threshold, slowly adapting mechanoreceptors becoming active only towards the extremes of motion. Michelson and Hutchins suggested that the output of the mechanoreceptors from the ligaments influence muscle stiffness and coordination to

increase joint stability. This is accomplished by influencing gamma motor neuron output, as described in studies of the knee (Freeman and Wyke, 1967; Johansson et al., 1991).

Several studies have been conducted under the supposition that ligament damage results in diminished position sense at the ankle. Two studies have investigated the effect of anesthetizing the ligaments and assessing position sense. Konradsen et al. (1993) used both detection of repositioning performed passively and active replication of position on subjects after injection to anesthetize the joint and ligament nerves. They found significantly poorer passive position sense but preservation of active replication of inversion at the ankle. Feuerbach et al. (1994) anesthetized the lateral ligaments and measured active replication of positions of dorsiflexion and plantarflexion, inversion and eversion. They reported no differences in accuracy, measured by constant, variable, and absolute error, from pre-anesthesia measurements.

Myers et al. (2003) examined responses before and immediately after injection of the ATFL and CFL with either an anesthetic or placebo solution. A thirty-degree excursion at 440°/s velocity was used to provide a perturbation into inversion. A significant effect was found for injection, but no difference between the anesthetic or placebo solution was present. Conversely, Hertel (1996), in testing postural sway in single leg stance on a stable surface with eyes closed, found a change in the vertical COP measurements after anesthetic injection to the ATFL. During the static condition, the COP shifted laterally. During conditions of anterior-posterior and medial-lateral sway of the support surface, the COP shifted medially. No changes in postural sway of the subjects were observed. They also tested detection of a passively achieved ankle position in these normal subjects, but found no effect of anesthesia.

DeCarlo and Talbot (1986) also anesthetized the ATFL in subjects who were then asked to balance on bilateral ankle discs which were fitted with circuitry that was completed whenever the disc tilted and touched the base. Time out of balance was recorded. No significant differences pre and post anesthesia were found, except for a trial effect, indicating a learning effect for the subjects over five 30 second trials, despite anesthesia of the ligament.

Nerve Injury Following Ankle Sprains

Three case reports were published by Hyslop (1941) reporting on significant weakness immediately post ankle sprain in the peroneal nerve distribution. All subjects recovered adequate function within six months. Nitz et al. (1985) measured nerve conduction velocities on subjects with grade II (30) and grade III (36) ankle sprains two weeks post injury, and found denervation potentials in the tibial and peroneal nerves of some subjects. Seventeen percent of the grade II sprains and 86% of the grade III sprains had evidence of injury to the peroneal nerve and 10% of the grade II sprains and 83% of the grade III sprains of injury to the tibial nerve. They also observed a prolonged recovery time as detected by the ability to heel-toe walk and return to full activities in the grade III versus grade II sprains. Subsequent EMG post recovery was not performed.

Kleinrensink et al. (1994) performed motor nerve conduction velocity tests on subjects 4-8 days post ankle inversion sprain, and then again at five weeks post injury. They included those with Grade I sprains among the subjects. Group means for the injured ankle at 4-8 days post injury were significantly slower than a control group, but returned to normal by five weeks post injury for the superficial peroneal nerve. However, the deep peroneal nerve did not recover in this time frame. Neither Kleinrensink et al. nor Nitz et al. hypothesized as to how the nerve injuries were sustained. Possible mechanisms include a traction injury to the nerve or compression secondary to swelling in confined spaces. O'Neill et al. (2007) used 16 cadaver lower legs to assess the effect on the superficial peroneal nerve during simulated inversion sprain with and without an intact ATFL. They found strain magnitudes within the range of known damaging values for the nerve during simulation, with increased magnitude in the absence of the ATFL. No studies were identified that investigated nerve conduction velocity or EMG of subjects with chronic instability, or of subjects longer than 5 weeks post-injury.

Bullock-Saxton (1995) found decreased vibration sense and two point discrimination compared to the normal ankle after severe (grade II+ - III) ankle sprain in 20 men 2 –18 months post injury. She did not suggest whether this was due to local receptor damage or nerve damage.

Considered together, these findings support the possibility of nerve injury as a mechanism contributing to delayed recovery form acute sprain. Ligament receptor damage has less support

as an immediate cause. However, the interplay between altered peripheral sensation and central motor planning and execution resulting in instability is unknown.

Proprioceptive/Kinesthetic Deficits

To appropriately interpret the literature describing “proprioception” related to ankle function requires some clarity of terms. Wilkerson and Nitz (1994) defined proprioception as the cumulative neural input to the central nervous system (CNS) from mechanoreceptors located in multiple tissues. This input, after processing and modification at many CNS levels, eventually results in excitation or inhibition of motoneurons. They distinguished this sense from kinesthesia and postural balance. They cited Garn and Newton’s definition (1988) of kinesthesia as the conscious awareness of position and movement which can result from proprioception. Postural balance was defined as the ability to maintain the center of gravity (COG) over the base of support of the feet, which is influenced not only by proprioception, but also visual and vestibular function. These distinctions are not consistently made in the literature when reporting the findings on deficits related to ankle sprains. Below is a summary of literature relevant to the issues of position and motion sense of the ankle which uses the terms proprioception and kinesthesia as applied by the authors. Postural balance will be discussed in a subsequent section.

Konradsen et al. (1998) used passive repositioning to monitor kinesthesia in inversion at 1, 3, 6, and 12 weeks after acute ankle sprain, and found deficits in perception at all time points for all 44 subjects compared to healthy controls, regardless of the presence or absence of joint laxity. It remains unclear when passive position sense may return to normal levels.

Lentell et al. (1995) and Garn and Newton (1988) used detection of passive motion to study proprioception in subjects with functional instability (recreational athletes) and subjects with a history of multiple ankle sprains (subjects from the US Navel Academy), respectively. Both used a platform moving at 0.3 °/s to passively introduce movement to the foot and ankle in dorsiflexion and plantarflexion. Lentell et al. (1995), in 42 subjects, recorded the displacement required before a subject perceived motion, finding a significant difference in mean values of motion perception between the involved and uninvolved joints. Garn and Newton (1988) used a 5° movement into plantarflexion and asked the subjects to report whether or not motion had

occurred. They also monitored a “false alarm” rate, as positive responses when no movement had occurred. A total of 30 trials were performed. No statistical significance was found for a positively biased response between the injured and uninjured limb of the 24 subjects, although the authors reported a tendency toward more “yes” responses on both limbs. The ability to correctly detect motion was significantly poorer with the injured ankle. Forkin et al. (1996) described the studied variable as kinesthesia, and compared ankles of 11 gymnasts with a history of unilateral recurrent sprains. Five degrees of plantarflexion was the movement for 15 trials, and no movement occurred for 15 of the trials. The subjects were better able to detect movement with the uninjured ankles.

Refsauge et al. (2000) studied the excursion necessary to achieve a 70% detection rate of passive motion in dorsiflexion and plantarflexion at velocities of 0.1 °/s, 0.5 °/s, and 2.5 °/s, in healthy control and recurrent ankle sprain groups (N = 43). No between-group difference in detection rates was found. The same researchers, in a subsequent study (Refsauge et al., 2003), performed a similar experiment to detect inversion and eversion movement, again in a healthy control and a recurrent ankle sprain group (N = 39). In this study, the recurrent sprain group demonstrated a deficit in motion detection at all three velocities of inversion and eversion. Hubbard and Kaminski (2002) reported differing results when testing subjects with functional, but not mechanical, instability. These researchers reported the time to motion detection of inversion and eversion at a velocity of 0.5°/ms, and found no difference between stable and unstable ankles (N = 16).

The recognition by the subject of a passively replicated position was used by Gross (1987) in his experiment with university staff and students reporting unilateral recurrent lateral ankle sprain. Each subject indicated when a previously identified position of inversion or eversion was passively replicated by the examiner at a velocity of 5 °/s. The accuracy was compared to the accuracy of active replication by the subject of a previously positioned angle. The only positive finding here was that controls with no history of ankle injury were more accurate with passive than active replication. No difference between injured or uninjured ankles was detected. Fu and Hui-Chan (2005) also used passive replication of plantarflexion, an excursion of 5° delivered at a rate of 1°/s, in their study of basketball players with chronic recurrent bilateral ankle sprains. They reported a significantly increased detection error rate for the subjects with recurrent sprains compared to healthy subjects. Santos and Liu (2008) used an

excursion of 30° inversion for subjects with functional instability and healthy controls, and found no significant difference between groups using a passive replication method.

Glencross and Thornton (1981) studied 24 young adults age 18-25 who had sought treatment at a Sports Medicine Clinic for an ankle injury at least 8 months prior. They were grouped according to severity of injury. The task was to actively replicate a previously passively achieved position of plantarflexion. Findings indicated a greater error rate for the more severely injured ankles and a linear trend of increasing error at the greater excursions of plantar flexion. Konradsen and Magnusson (2000) also used an active replication design in studying 23 unilateral functionally and mechanically unstable ankles, comparing accuracy both to the uninvolved side and to control subjects with no history of ankle injury. Detailed subject information was not presented for the subjects, but it was reported that they all were sufficiently disabled to be scheduled for surgical stabilization procedures, and specifically were excluded if they participated in sports at a competitive level. Inversion and eversion movements were used. Statistically different error rates were found, with greater error rate for the injured ankles compared to the unaffected limb and to the uninjured group. Boyle and Negus (1998) measured both passive detection and active replication of inversion in plantarflexion in ankles with a history of recurrent sprains (N = 25) and healthy ankles (N = 67). The between-group comparisons indicated diminished accuracy of the subjects with recurrent sprains for both active replication in the early portions of the range of motion, and for passive detection throughout the range.

Jerosch and Bischof (1996) used active replication of inversion at 4°/s at 5°, 15°, and 20° in 14 healthy and 16 instability subjects to assess proprioception. It is unclear whether the subjects were functionally or mechanically unstable, or some combination of the two. They reported a mean error difference between groups of 0.9°, which was significant. While precisely controlled, allowing greater accuracy, the task bears little resemblance to functional activity.

More evidence in support of a kinesthetic (to use the term of Wilkerson and Nitz (1994)) deficit was found than evidence against such a deficit. However, it is unclear when, post acute injury, the distinction between those who recover and those with persisting complaints becomes evident. As well, how this contributes to the functional limitations of functional instability has not been established by these studies.

Peroneal Response Time

The complaints of repeated injuries and feelings of “giving way” in individuals with functional instability have prompted researchers to examine the reflex response of the peroneals to an unexpected inversion perturbation. As inversion is the primary motion most associated with ankle sprains, these studies have investigated the response of the ankle evertor (peroneal) musculature.

Most studies of peroneal response time used a trapdoor mechanism to displace the ankle into inversion and recorded the onset of EMG activity in the peroneal muscles while the subject was standing (Ebig et al., 1997; Konradsen and Ravn, 1990; Konradsen and Ravn, 1991; Löfvenberg et al., 1995) or inversion and plantarflexion (Löfvenberg et al., 1995; Nawoczenski et al., 1985). These authors used 30-35° of displacement. Konradsen and Ravn (1990) used fifteen functionally unstable ankles and fifteen controls in their study. They observed the same pattern of response between the groups – a contraction of the peroneals to resist the inversion and a pattern of flexion of the hip, knee and ankle which decreased the vertical pressure on the ankle and caused eversion. They noted a prolonged reaction time for the functionally unstable ankles (84 msec versus 69 msec). They reported similar results in a second study (Konradsen and Ravn, 1991). Löfvenberg et al. (1995) used a similar format, also including the tibialis anterior and detected a similar difference in response time. Controls responded faster than FI subjects, but both groups had faster onset of muscle activity, 49 msec and 65 msec, respectively, than in the Konradsen studies. Nawoczenski et al. (1985) observed a trend towards longer response time, but did not find a statistical difference. Their subjects had had a unilateral ankle sprain within the prior 3-10 months, and may therefore have had different characteristics than chronically unstable ankles. Ebig et al. (1997) monitored both tibialis anterior and peroneals, and found no statistical difference between functionally unstable ankles and stable controls for peroneal or tibialis anterior responses, with results comparable to the times reported by Nawoczenski et al. (1985). All studies used 13-15 subjects per group.

Fernandes et al. (2000) examined the effects of three different angles of perturbation (5°, 10°, and 15°). The displacement was delivered to the 34 male soccer and rugby players while standing. The speed of the tilt was determined by gravity. They reported no difference in response time between healthy subjects and those with a history of at least one ankle sprain

(including 29% categorized as functionally unstable). They did find that the dominant limb reacted faster than the non-dominant limb, and a small increase in reaction time was observed as the angle of perturbation increased. These findings can be contrasted with those of Johnson and Johnson (1993), who found no differences between ankles of control subjects dropping into 35° of inversion suddenly.

Other methods of investigation of peroneal response times included a tilting solid platform which provided an eversion motion on one limb and an inversion motion on the opposite ankle (Brunt et al., 1992). In this study, the velocity of movement was 70°/msec over an arc of 10.5° (N = 34). No differences between limbs or between subjects with recent sprains and control subjects were found. Vaes (2001) unilaterally inverted the foot of 17 subjects while standing and secured in a device that began in 40° plantar flexion and 15° supination (adduction and inversion), with supination occurring unexpectedly to 50°. These authors reported longer reaction times in subjects with unstable ankles.

Santos and Liu (2008) used an isokinetic device to suddenly move the subject's ankle from neutral into inversion at 120°/s while the subject was supported in a semi-recumbent position. The response instructions were to voluntarily stop the motion by actively everting the ankle. No differences between involved and uninvolved ankles or between the FI subjects and healthy controls were reported. While novel, this approach appears to have minimal applicability to the real world complaints of the population with FI.

A study (Konradsen et al., 1998) investigating recovery from acute inversion injury followed forty-four patients with grade I or II injuries for 12 weeks. Mechanical instability was recorded in 47.5% of patients at 1 week and 9% at 4 weeks, using talar tilt and anterior drawer sign with stress radiography. No differences were seen in peroneal reaction times to sudden inversion between injured and uninjured ankles at 3 weeks or longer post injury. Eversion strength, measured as maximal isometric and eccentric contractions, was 88% of the contralateral ankle at 3 weeks, and 96% at 12 weeks. At 12 weeks, the error rate of active replication of inversion of the injured ankle was 33% higher than the uninjured side, with no difference between mechanically stable or unstable ankles. These findings suggest a divergence of kinesthetic sense and reflex response to stretch in the recovery period after acute injury. How this can be

reconciled with peripheral nerve conduction changes and injury to mechanoreceptors in the ligaments is unclear.

Konradsen et al. (1997) tested ten subjects with mechanically stable ankles on a trapdoor platform, measuring EMG of the peroneals while standing, and using 2-D video recording of sagittal plane motion of the hips and knees during walking. During standing, they observed peroneal activity at a median time of 54 msec after onset of inversion, quadriceps and hamstring activity at 68-73 ms, active subtalar eversion motion occurring at 176 ms, with active changes in hip and knee position at 202 ms. While walking when a sudden inversion perturbation was delivered, peroneal activity began at 48 ms. Calculating time for sufficient tension to be developed to provide stabilization against unexpected inversion and comparing that to the likely speed of unexpected inversion during activity, the authors estimated that the peroneal muscles were not capable of responding to unanticipated displacement quickly enough to provide protection.

To characterize normal motor behavior, another research group also looked at the responses in healthy subjects for peroneal reaction times. Lynch et al. (1996) monitored tibialis anterior, peroneus longus and brevis, using two speeds (50°/s and 200°/s) of perturbation and two angles (neutral and 20° of plantarflexion) of displacement of a hydraulic platform. They reported shorter latencies at faster speeds, longer latencies in the planter flexed position, and shorter latencies on the non-dominant limb for the peroneus longus.

The evidence for the presence of a prolonged protective peroneal response in functionally unstable ankles is contradictory. The work of Konradsen et al. (1997) questioning the potential effectiveness of this response, even if normal, also creates doubt of the usefulness of any related impairment in understanding the resulting complaints in FI.

Taken together, the research findings which consider a local tissue and simple reflex cause for FI fail to convincingly describe this condition. Inconsistencies exist between study results regarding strength, persisting mechanical instability, mechanoreceptor function, and reflex responses.

Central Nervous System Findings

Observations have been made of proximal muscle coordination changes and postural and stability changes in individuals with FI. These findings suggest changes in the central nervous system beyond the spinal cord reflex level. A variety of methods have been used to further investigate the motor behavior related to such findings.

Several studies examined muscular recruitment proximal to the ankle to investigate more central control influences in instability. Bullock-Saxton et al. (1994) monitored the patterns of activation of musculature during a non-weight bearing hip extension task, comparing eleven normal controls to twenty men at least four months post severe unilateral ankle sprain. They noted a consistent pattern in control subjects of near simultaneous activation of the ipsilateral gluteus maximus, hamstrings, erector spinae and contralateral erector spinae. Variability between sides in timing of onset of contraction was noted in the ankle sprain patients. The gluteus maximus was the muscle most consistently delayed in firing. The authors proposed that the changes may be due to alteration of the “central motor plan”.

Sedory et al. (2007) computed a central activation ratio (CAR) for the hamstrings and quadriceps of both limbs for 21 controls and 20 CAI subjects. The CAR is the ratio of the force of a maximum voluntary isometric contraction (MVIC) to the force elicited with an MVIC and superimposed electrical stimulation, and is thought to represent change in the motoneuron pool excitability in the spinal cord. The authors reported an increased CAR for the quadriceps, indicating facilitation, for the involved versus uninvolved extremity, and a decreased CAR, indicating inhibition, bilaterally in the hamstrings of CAI subjects. They did note, however, that the differences were only of a magnitude of 2-3%, making the clinical significance unclear.

In a study using subjects with unilateral excessive inversion mobility and a history of at least one inversion sprain, Beckman and Buchanan (1995) monitored EMG responses of bilateral gluteus medius and peroneal musculature during an inversion perturbation of one limb while standing. Subjects included 10 healthy controls and 10 hypermobile individuals. They observed a decreased latency for the ipsilateral glutei in the hypermobile group compared to controls, but no difference in peroneal latency. The observed times were faster than expected

for a supraspinally mediated reflex. The authors suggested a feedforward mechanism of enhanced gamma motoneuron activity for the hip musculature.

Postural Stability

Multiple methods have been used to study the effect of ankle sprain on postural control and stability. In this section, research related to static postures with force plate measurements will be presented; those discussing more dynamic activities will be presented in subsequent sections. Evans et al. (2004) conducted a prospective study of college athletes and reported the status of subjects 1-28 days post acute unilateral ankle sprain. Center of pressure (COP) excursion velocity was calculated during single leg stance with eyes open for 15-second trials on each leg. Compared to data collected prior to injury, both ankles of the injured subjects showed deficits the day following injury. The uninjured ankle returned to baseline values by day 7, while the injured ankle did not recover until day 14.

Leanderson et al. (1996) also performed a prospective study of postural stability in single leg stance and the effect of ankle sprains using ballet dancers. Of 53 dancers initially studied, those six who sustained a sprain demonstrated a larger mean sway and sway area on the injured side the day after injury than in pre-injury measures, and this change persisted for several weeks. With rehabilitation four of the injured dancers returned to baseline levels by twelve weeks, but one dancer persisted with increased sway at one year post-injury. The impact on dance performance was not discussed.

Other authors investigated the effects of recurrent sprains using force plates recording a variety of parameters during single leg stance. Ross and Guskiewicz (2004) reported medial-lateral (M-L) and anterior-posterior (A-P) sway separately in 16 control and 16 FI subjects while standing in 20° hip and 45° knee flexion on one limb with eyes open. No significant differences were reported. Santos and Liu (2008) calculated the COP area from M-L and A-P excursions of both limbs of control subjects and subjects with unilateral FI. Balance control, indicated by the amount of sway, was significantly different between ankles of the FI subjects, but not for controls, with no between-group differences detected.

Perrin et al. (1997) recorded postural sway in bilateral stance for basketball players with one or more ankle sprains and control subjects with no history of sprain. Those with sprains had a greater area of postural sway than controls under both eyes open and eyes closed conditions, and the area of sway positively correlated with number of ankle sprains sustained.

Stabiliometry similarly measures postural sway, and has been used to assess postural control in single leg stance in subjects with functional ankle instability. Subjects stand on a force plate, and the x-y trajectory is recorded, corresponding to medial-lateral and anterior-posterior sway respectively. A confidence ellipse is calculated, which includes consideration of a correlation between x and y values (Sahlstrand et al., 1978; Tropp et al., 1984). Tropp et al. (1984) found no difference between soccer players with or without a history of ankle injury in stabilometry values of single leg stance, but did report that an abnormal value (a value exceeding the reference group mean by two standard deviations) for players without previous injury was predictive of a future ankle injury during the playing season.

In a subsequent study, Tropp et al. (1985b) found a significantly poorer ability to maintain equilibrium in single leg stance measured with stabilometry in male soccer players with functional instability than those without. No effect was noted for players with mechanical ankle instability without FI complaints. In a third study, Tropp (1986) reported no differences between affected and unaffected ankles, but did find significant differences between both ankle of FI subjects and controls. In a study of basketball players Leanderson et al. (1993) used stabilometry to investigate postural sway during single leg stance in players with and without a history of ankle sprain. The injured players had a larger mean sway using a larger area than control subjects, and this difference also was not related to the presence of mechanical stability.

Jerosch and Bishof (1996) in a previously cited study, used single leg stance under eyes open and eyes closed conditions to assess “proprioception”. They, however, used a compliant surface and counted the number of times over a one minute trial the subjects touched down (failure) with the contralateral limb to regain balance. Significantly more episodes of failure occurred for the unstable ankles.

A different measure of postural stability was used by Hertel and Olmsted-Kramer (2007) when comparing 10 healthy subjects and 10 subjects with complaints of unilateral chronic instability

during single leg balance. Time to boundary (TTB) measures use the COP trajectory and instantaneous velocity data to project the time needed to reach a base of support boundary, and therefore be at risk of a loss of balance. These TTBs were calculated for medial-lateral, anterior-posterior boundaries, and the minima (shortest times) were compared between groups. Lower minima suggested relatively greater postural instability. Subjects with chronic ankle instability had lower mean, absolute, and standard deviation values for all measures except medial-lateral absolute minimum.

While reports of the effects of acute sprain on postural stability and time to recover balance vary, research results are fairly consistent that such deficits are present in subjects with FI. However, this conclusion may be insufficient to explain the complaints with dynamic activity, as only one of the previous studies reported actual loss of balance.

Dynamic Postural Control

Study of dynamic postural control is of interest in the case of FI as individuals are customarily moving when episodes of instability occur. Study designs have included perturbations or rhythmic oscillations of the support surface in stance and a foot reaching task while in single leg stance. Gait has also been studied and is discussed in a subsequent section.

Female dancers were monitored for lateral oscillations and time to return to equilibrium after a sudden inversion perturbation (Hiller et al., 2004). These factors were measured in both a foot flat position (15° displacement) and in single foot demi-pointe (balancing on the toes in ballet point shoes, 7.5° displacement). Significantly more instances of failure of condition (unable to complete the trial) were found for dancers balancing on a functionally unstable ankle (N = 16) than a healthy ankle (N = 26) with the exception of foot flat without perturbation. As well, the baseline oscillation of the control group was larger than the FI group in the demi-pointe position, with a larger dispersion about the mean for controls. The FI ankle trials showed a longer time to equilibrium after a 15° perturbation in foot flat than controls, but no difference in the demi-pointe position.

Bernier et al. (1997) found no differences in postural sway in double leg stance under conditions of eyes open and eyes closed when comparing nine FI subjects and nine controls. They also

delivered perturbations in inversion/eversion tilt and horizontal slides in a right to left direction of the platform; no between-group differences were found under these dynamic conditions either. Brown and Mynark (2007) recruited 40 recreational athletes, 20 healthy and 20 with recurring sprains, to test tibial nerve stimulation as a perturbation. Using force plate data they measured the time post stimulus needed to return to a stable baseline, reported as time to stabilization, and COP excursion and velocity. No differences between controls and sprain subjects were found except in the time to return to stability in an anterior-posterior direction. Ryan (1994) used a wobble board which could be tilted in either a side-to-side or anterior-posterior direction, and recorded contact with a circuit when the board tilted 4° or more (time out of balance). He recorded time out of balance over 30-second trials of single leg stance on the board. Forty-five FI subjects demonstrated more time out of balance on the involved than uninvolved ankle.

Soderberg et al. (1991) monitored EMG activity from tibialis anterior, peroneus longus, and gastrocnemius while subjects actively rotated a Biomechanical Ankle Platform System (BAPS) board. The BAPS board was used with either a large or small diameter hemisphere, rounded edge to the floor, and the subjects' task was to maintain balance and maneuver the board to describe a circle by progressively touching the board edges to the floor while maintaining a consistent self-selected velocity. Both subjects with healthy ankles and those with recurrent sprains were evaluated. No between-group differences for task were noted in any of the three monitored muscle groups.

In the study by Perrin et al. (1997) of basketball players, in addition to monitoring of postural sway in double leg stance, the COP response of the subjects to a 0.5 Hz sinusoidal sway of the platform was recorded. The players with a history of ankle sprain had a higher rate of recordings at variance with expected patterns when standing with eyes closed. These responses were characterized by low frequencies of high amplitude shifts indicating a more erratic response to the shift of the supporting surface than controls.

Pintsaar et al. (1996) studied thirty-eight female soccer players in single limb stance by providing a perturbation in a medial direction. They interpreted data using the ankle and hip strategies for postural control outlined by Horak and Nashner (1986), who described these responses in bilateral stance with anterior-posterior displacement. Rotation of the rigid body

over the ankle (ankle strategy) results in no horizontal shear against the support surface. The hip strategy involves generation of horizontal forces against the support surface proportional to the acceleration of the hip angle. The 15 players with functional ankle instability demonstrated less use of ankle strategies and more use of hip strategies with these perturbations compared with controls or players with mechanical instability. These findings were improved to levels seen in controls after ankle disk training.

A study of the kinetics of frontal plane balance during gait (MacKinnon and Winter, 1993) reported that the human body is in a state of dynamic imbalance in single limb stance, and foot placement lateral to the center of mass (COM) helped ensure that the COM accelerated toward the line of the forward progression. Fine tuning of balance control was observed at the subtalar and hip joints. The variance seen in the COP measurements due to subtalar joint motion, the authors contended, may demonstrate plasticity in balance control while responding to errors in foot placement or other perturbations. They contrasted their conclusions with those of Tropp and Odenrick (1988). In this study, responses of body segments were measured with 2-D video analysis to assess different patterns of motion in maintaining balance in single leg stance (Tropp and Odenrick, 1988). However, these subjects were monitored in single limb stance and displacements of body segments were observed when ankle motions were inadequate to correct posture. Large corrective movements of the hips and trunk then occurred, described as a multisegmental chain. Fifteen physically active men with functional ankle instability showed larger variations in the center of pressure and hip and trunk positions in the frontal plane than the 15 control subjects in this task, and this motion was centered about the hip. Tropp and Odenrick suggested that subjects with functional ankle instability demonstrated an inadequate ability to correct postural sway at the ankle.

A single-leg hop test over an uneven course was used by Jerosch and Bishof (1996). Fifteen degree anterior, posterior, and lateral inclinations were provided over the course. Failure to maintain control on a single limb (by touching down with the other foot) added one second per instance to the timed score. A significant difference of one second was shown, with a longer time for the unstable ankles.

A balance test performed on level ground is another method used to investigate dynamic postural control in chronic ankle instability. The Star Excursion Balance Test (SEBT) (Hertel et

al., 2006) measures the distance that can be reached by the non-weight bearing foot along each of 8 directions equally dispersed from the center of a star upon which the support limb is placed. Hertel et al.'s study found that performance in the anteromedial, medial, and posteromedial directions were the least correlated and most useful in clinical assessment in chronic ankle instability. Subjects with history of recurrent sprains reached a shorter distance in these directions while supported on their involved than uninvolved ankle, as well as compared to control subjects.

In summary, while a few studies suggested no deficits in FI subjects, a larger number of studies using various methodologies, supported the conclusion of diminished dynamic postural control in individuals with functional instability.

Postural Control Interventions and Outcomes

As research has supported both static and dynamic diminished postural control, several researchers have investigated the effects of balance training in subjects with functional ankle instability. Tropp et al. (1985a) compared the effects of ankle disk training to an ankle orthosis for those soccer players with a history of ankle sprains or instability. The training consisted of balancing on a platform mounted on $\frac{1}{2}$ of a sphere, rounded edge to floor. The subjects balanced on one leg, arms across chest, for 10 minutes five times per week for 10 weeks, then three times per week for five minutes for the remainder of the study. The training reduced injury rates to the level of normal controls and those using the orthosis, lower than players with a history of ankle problems who didn't participate in the training.

Gauffin et al. (1988) trained 10 subjects with functional instability on a similar ankle disc for 10 minutes, five times a week for 8 weeks, training the symptomatic ankle only. At the completion of training, both ankles were assessed using stabilometry. Decreased postural sway was noted in both the trained and untrained limbs.

Matsusaka et al. (2001) studied 22 university students with functional ankle instability using the ankle disc. One group had two pieces of non-elastic adhesive tape applied to the distal third of the leg and sole of the foot on the lateral side prior to training. Both groups trained 10 minutes, five times per week, for 10 weeks. The group with the tape showed faster improvements and

greater overall improvement in postural stability than the non-taped group. The authors concluded that the increased afferent input was beneficial during the training. This suggests the interplay between local and central factors.

Rozzi et al. (1999) used a commercially available balance and assessment system (Biodex, Shirley, NY) to train under a variety of preprogrammed stability conditions. Subjects fitting the criteria of functional instability were compared to controls. Pre-training stability indices were less for the FI subjects on either ankle than the controls. Post-training, all subjects showed significant improvement to levels above the pre-training levels of control subjects.

Bernier and Perrin (1998) used another commercial balance system (Chattanooga Group, Inc, Hixson, TN) in their study of functional instability. Subjects trained on a program of increasing difficulty with balance activities such as tilt board (unidirectional), wobble board (multidirectional) with eyes open or closed in single limb stance. Improvements in medial/lateral and anterior/posterior sway, but not postural sway index, were achieved in the trained group compared to the sham training and control groups. No change in joint position sense was achieved.

A four-week program which included single leg balance tasks and dynamic activities on a stable surface was studied in subjects with CAI (Hale et al., 2007). Strength training and stretching were also included. Outcome measures were the Star Excursion Balance Test (SEBT), center of pressure velocity (COPV), and a self-report measure. No differences between CAI and control groups were reported before training on these physical measures, but greater change pre-post SEBT scores on the involved limb of CAI subjects who trained were found compared to healthy and CAI controls. No changes in COPV were found. The CAI group who participated in the program improved on the self report measures.

Eils and Rosenbaum (2001) reported improvements in recognition of a passively achieved position, postural sway in single limb stance, and reaction times of tibialis anterior, peroneus longus and brevis to a sudden 30° inversion tilt after a rehabilitation program. The six-week program was completed by 30 subjects with FI complaints. The rehabilitation program consisted of 12 standardized exercises on uneven and moving surfaces.

Osborne et al. (2001) studied 10 subjects with a history of non-rehabilitated unilateral inversion sprain who then were trained for 8 weeks with an ankle disk to improve balance. Reaction time of the anterior tibialis, posterior tibialis, peroneus longus, and flexor digitorum longus during trapdoor inversion of 20° was measured before and after training. A statistically significant increase in anterior tibialis response time was reported in both the trained and untrained limb. The functional benefit of this result was not reported.

Use of balance training after a first-occurrence sprain or as a prevention strategy has been reported by several authors. Goldie et al. (1994) trained 24 post sprain subjects for 8 weeks in single leg stance on an unstable surface. Those trained subjects demonstrated no differences in postural sway between limbs post-training compared to untrained subjects who showed a significant difference between sprained and unsprained limbs. Wester et al. (1996) used wobble board training for 12 weeks after ankle sprain, and reported a significant reduction in recurrent sprains over a mean of 230 ($\pm$ 62.9) days compared to untrained subjects. In a prospective study of primary prevention, Verhagen, et al. (2004) used balance exercises in single leg stance on a stable and unstable surface for volleyball players. During the season, all ankle sprains were recorded. A reduction in ankle sprains was seen in the trained versus untrained players, but the reduction was significant only for those players with a prior history of sprain. These results are similar to those of Tropp et al. (1985a) in soccer players in terms of reduction in sprains among those who trained on an ankle disc. In the study by Tropp et al., however, only those with a history of FI trained during the season.

The consideration of these findings indicates that some form of compensation or retraining can be achieved for ankle instability subjects with practice at a task which challenges postural control and motor output of the ankle. This suggests that a structured learning process can help overcome the limitations of functional instability. A deficient adaptation/recovery process as a contributor to the development of FI is an intriguing but untested possibility.

Studies of Gait in Functional Instability

Harrington (1979) observed intermittent inversion positioning of the rearfoot, as much as 20 degrees greater than the contralateral limb, during late swing and early heel-strike of gait, in 21 (58%) of 36 subjects with ankle ligament instability of greater than 10 years duration. He did

not comment on the stability of the limb under these conditions, or on specific complaints of instability at this point in the gait cycle.

Nyska et al. (2003) used plantar pressures to characterize the force distribution during level surface walking in subjects with chronic ankle instability. They reported a longer contact of the heel and midfoot during the stance phase, a slowing of the weight transfer from heel strike to toe off, and reduced impact during loading and unloading.

Monaghan et al. (2006) used 3-D video motion analysis to compare the gait of 25 healthy controls with 25 subjects with chronic ankle instability. They detected 6 - 7° greater inversion positioning in the involved ankle compared to control left ankles during the 100 ms pre- to 200 ms post-heel strike. As well, increased angular velocity in the frontal plane at heel strike was found for the involved ankles ($0.5 \text{ rad/s} = 29^\circ/\text{s}$) compared to healthy ankles ($0.1 \text{ rad/s} = 6^\circ/\text{s}$). An additional observation was that the unstable ankles were controlled by concentric eversion in early stance while the control ankles used eccentric inversion. This has interesting potential correlations with studies of weakness

Spaulding et al. (2003), in examining the influence of two ankle supports, reported on kinematic differences between 10 healthy and 10 chronically unstable subjects in walking on a level surface up a 5° incline, and stepping up a step. The differences during the trials without ankle support included longer stance time for the unstable subjects walking on a level surface, greater variability in the measured gait parameters, and a using a more plantarflexed position during foot contact.

Louwerens et al (1995a) described the EMG activity of the peroneus longus (PL) and tibialis anterior (TA) during the stance phase of gait in 25 subjects with chronic ankle instability and 10 control subjects. The subjects walked at a self-selected pace on a treadmill under conditions of no balance support and the support of a hand rail. There was no difference in PL activity between the instability and control subjects. In both groups, greater variability in PL activity was noted with use of the handrail. Tibialis anterior activity was increased in subjects with bilateral instability, but no side to side differences were found in unilateral instability subjects. In contrast, Santilli et al. (2005) monitored PL activation during the stance phase of gait in 14 FI subjects and reported a decrease in mean activation time in the affected versus unaffected limbs.

It appears that differences in gait patterns exist between healthy and FI subjects, but the direct effect of these variations on symptoms of instability has not been delineated.

Background for Study Design

Normal Ankle Kinematics of Gait

The initial kinematic research was performed on cadaver specimens and concerned the locations of motion axes and descriptions of motion about the multiple articulations in the region (talocrural, talocalcaneal, talonavicular, etc.). More recent work has been done in vivo, using electromagnetic tracking systems and cinematography during functional activities. The research has demonstrated that all joint axes of motion are complex, with descriptions including a hinge joint model (Areblad et al., 1990; Engsburg and Andrews, 1987; Hicks, 1953; Olerud and Rosendahl, 1987; Scott and Winter, 1991; Wright et al., 1964) and a universal joint model (Olerud and Rosendahl, 1987; Wright et al., 1964).

Actions during the stance phase of gait on a level surface have been investigated by Moseley et al. (1996) using three dimensional video analysis. They found slight dorsiflexion position at heel strike progressing to plantar flexion angle of $6.8^{\circ} (\pm 1.3^{\circ})$ just prior to foot flat, and then progressing to dorsiflexion of 7.2° after heel rise, followed by plantarflexion until toe off. The initial inversion angle at heel strike was not recorded, but progressive eversion to $7.3^{\circ} (\pm 1.0^{\circ})$ before heel rise was noted, and with a return to inversion of $3.8^{\circ} (\pm 0.4^{\circ})$ at toe off. Abduction increased following heel strike to $2.7^{\circ} (\pm 1.3^{\circ})$ at heel rise. The mean between-subject coefficients of variation (CV) for dorsiflexion/plantarflexion (DF/PF), inversion/eversion (IV/EV) and adduction/abduction (AD/AB) were 48%, 33%, and 40% respectively. Within-subject CVs were 12% for both PF/DF and IV/EV, and 13% for AD/AB.

Hunt et al. (2001) performed video analysis of the stance phase of gait, using eight cameras. It appears that 3-D analysis was performed, but the transformation sequences were not recorded. Similar patterns to those recorded by Moseley et al. (1996) were found, although the maximum angles were somewhat varied. Maximum dorsiflexion was 11.9° , maximum eversion was 5° , maximum inversion was 2.9° , maximum adduction was 7.2° and abduction was 2.5° .

Scott and Winter (1991) described combined motions of dorsiflexion, eversion, and abduction (pronation) or plantarflexion, inversion, and adduction (supination) about the talocrural and talocalcaneal joints separately. They reported supination at heelstrike for the talocrural joint, and pronation for the talocalcaneal joint, with reversals of motion during the stance phase until just before push-off, when the directions were again reversed.

Leardini et al. (1999) created multiple joint coordinate systems for the foot and ankle to measure the kinematics of tibia-calcaneus, calcaneus mid-foot, mid-foot-first metatarsal, and first metatarsal-proximal phalange joints during gait. They also used the CMC described by Kadaba et al. (1989) as a measure of repeatability of these motions within subjects over three trials. They reported mean ($\pm$ SD) values of 0.91 (0.084) and 0.76 (0.191) for tibial-calcaneal dorsiflexion/plantarflexion and inversion/eversion, respectively.

Sadeghi et al (2001) reported on sagittal plane motion of the hip and ankle during level surface gait in 20 young, healthy males. Three dimensional data were collected with a video camera system. The focus of the study was the kinetic data, but hip and ankle angular displacement was reported, and indicated greater variability at the hip (CV = 184%) than ankle (CV = 84%). This is considerably higher than the 48% CV reported by Moseley et al. (1996).

Kadaba et al. (1989) used 3-D video analysis to assess the repeatability of measures of normal adult gait. They monitored foot rotation (adduction/abduction) and ankle dorsiflexion/plantarflexion, as well as temporal parameters of gait. Sagittal plane measures showed excellent repeatability using a coefficient of multiple variations (adjusted coefficient of multiple correlations - CMC) of the recorded waveforms, but greater variation of transverse and frontal plane motions (CMC 0.858 – 0.834). Within-day measures were more consistent than between-day measures, which could also reflect changes in placement of the video markers.

Cornwall and McPoil (1999) used an electromagnetic tracking system to monitor ankle and foot motion in level surface walking. They found good reliability on repeat trials (mean standard deviation 0.278 for dorsiflexion/plantarflexion and 0.205 for inversion/eversion), and noted that the foot appeared to move about a resting-standing position, rather than about subtalar neutral as is often described in the clinical literature, and observed that this may account for difference in

motion description found in the literature. They also reported mean CMC values for the calcaneal movement across all subjects of DF/PF 0.946, IV/EV 0.846, and AD/AB 0.846.

Swing phase kinematics were not well described in the literature. Simoneau (2002), summarized swing motion as returning to neutral dorsiflexion to clear the toes and returning to a slightly inverted position in preparation for heel strike.

A summary paper by van Emmerick and van Wegen (2002) speaks to the concept of the role of variability in postural control. They report that reduced variability in dynamic coordination during gait has been associated in Parkinson's disease with difficulty in transitioning between movements. The authors hypothesize that to adapt to postural requirements and perturbations, some level of variability is required to explore the limits of stability within known postural configurations and that lack of such variability is associated with aging and neurological disease. This corresponds somewhat to the findings of Mackinnon and Winter (1993) of the use of the subtalar joint to make position corrections during gait.

From the above descriptions, it appears that the absolute values of a given parameter may vary based on the description of the neutral position from which the changes are described, the alignment of the axes chosen, and by the method of analysis, as well as measurement error. Also, notable variation in excursions was observed between subjects. This limits the ability to draw conclusions about specific angular measures, or to compare measures between studies. It is also unclear what level of variability in foot and ankle motion is desirable.

Normal Kinematics of Stair Climbing

Only sagittal plane kinematics were recorded in a study by Livingston et al. (1991) of women of varying heights climbing stairs of differing dimensions, and compared temporal parameters between subjects grouped by subject height and stair height. They noted dorsiflexion ranges of 20 - 35° and plantarflexion ranges of 20 - 30° in stair descent. It is not stated whether the ranges were observed during stance or swing phase, but is assumed to be stance phase. No intrasubject variability was reported, although 15 trials on each staircase were performed. Andriacchi, et al. (1980) recorded kinematics of stair descent in men, and found swing phase excursions of 23.2

to 25.6° in plantarflexion at the ankle. Swing phase motions for inversion/eversion were not recorded, nor was intrasubject variability reported.

Reiner et al. (2002) used 3-D video analysis to monitor stair climbing in ten healthy males. They recorded only sagittal plane motion. While specific intra-subject variability values were not reported, they commented that this variability was generally less than that observed between subjects. They noted clear distinctions between level surface walking and stair climbing, reporting increased angular movements and forefoot contact rather than heel contact on stairs. They postulated that the rationale for forefoot contact during stair descent was to allow energy absorption.

Video analysis of three trials of stair ascent and descent was used to record cycle time and sagittal plane joint angles at hip, knee, and ankle (Protopapadaki et al., 2007). Step cycle duration was faster during descent (mean 1.32 ± 0.13 s) than ascent (mean 1.45 ± 0.14). Greater amounts of ankle dorsiflexion and plantarflexion were used during descent. Eleven of the original 33 healthy subjects were retested on a second occasion. Averaged intra-subject coefficients of variation (CV) reported were 4.94% for ankle dorsiflexion and 5.77% for plantarflexion during step descent. It is interesting to note that the CV for plantarflexion with ascent was 17.53% and 3.31% for dorsiflexion. These values were markedly less than reported by Sadeghi et al. (2001) reported for walking on a level surface, but similar to those of Moseley et al. (1996).

Five trials of stair ascent and descent in three healthy male subjects were used by McFadyen and Winter (1988) in their kinetic and kinematic analysis of stair climbing. They investigated only sagittal plane kinematics. Like Reiner et al. (2002), they reported the role of the ankle plantarflexors in energy absorption. They described sub-phases of swing as “leg pull-through” and “preparation of foot placement”, and sub-phases of stance as “weight acceptance” (36% of stride), “forward continuance”, and “controlled lowering” (at 70% of stride). The graphical representations of joint excursion at the ankle mirror those reported by Andriacchi et al. (1980). After normalizing a cycle to 100% with a stance to swing ratio of 64:36, they reported Pearson’s correlation coefficients for hip, knee, and ankle joint angles, measuring similarity but not magnitude, between the averaged strides of each subject. All correlations were greater than 0.95.

Yu et al. (1997) studied the reproducibility of stair-climbing in normal subjects using 3-D video analysis. They found that while generally reproducible, kinematic data was less reproducible than kinetic data, and greater variations were observed in frontal and transverse plane motions than sagittal plane motion. Unfortunately, actual measures were not reported, only the coefficients of multiple correlations (CMC), a measure of waveform similarity. Specific ankle values were not reported; a summary statement was made that most joint angle CMCs were greater than 0.8, indicating similarity. The authors ruled out tracking error and residual errors in centers of pressure as causes for the variation because these variances were too small to account for the observed differences, and problems with skin slip should be uniform from trial to trial. They therefore concluded that variation in motor performance was the major cause of the intrasubject variations seen. It is interesting to note that this consideration was not raised by Kadaba et al. (1989) in their study of normal walking.

Therefore it is seen that there has been little investigation to date of normal ankle kinematics in stair climbing. It has been suggested that the observed variations in kinematics are more likely due to differences in motor performance, especially in the frontal and transverse planes and that some level of variation is desirable. Confirmation was provided of the normal initial foot contact in stair descent in plantarflexion. No reports of the kinematics on stairs of ankle sprain or instability subjects were found, yet this would appear to be an activity where differences are likely and potentially related to functional complaints.

Naming Conventions for Ankle/Subtalar Motions

Multiple descriptions of motions exist for actions of the foot and ankle complex. Dorsiflexion and plantar flexion are generally described as motions about an approximately transverse/mediolateral axis (Hicks, 1953; Lundberg et al., 1989a; Wright et al., 1964) in the sagittal plane. This is most commonly described as occurring predominantly at the talocrural joint. Much less agreement exists about description of motions primarily ascribed to the subtalar joint. Inversion and eversion have been described as components of motion occurring about an anterior-posterior axis in the frontal plane, and adduction/abduction as occurring about a vertical axis of rotation in the transverse plane (Wright et al., 1964). These conventions then use the terms supination and pronation for the composite motions of the three cardinal plane movements described as occurring about the subtalar axis (Close et al., 1967; Engsburg and

Andrews, 1987). However, some authors describe motion about an anterior-posterior axis as supination and pronation (Hicks, 1953; Lundberg et al., 1989b; Olerud and Rosendahl, 1987). For purposes of this study, the motions will be described as dorsiflexion and plantarflexion, inversion and eversion, and adduction and abduction.

Anatomical Coordinate Systems

Two forms of anatomical coordinate systems have been presented in the literature for use in studying ankle/foot biomechanics. The joint coordinate system is formed from one axis, of the tibial reference frame, usually describing dorsiflexion/plantarflexion, another is formed from the calcaneal/foot reference frame, usually describing inversion/eversion, and a floating axis, which is orthogonal to both the segment fixed axes, about which abduction/adduction is described. Because the segment fixed axes change relationships as the limbs move, the axes are non-orthogonal. If studies of translational movements, in addition to angular movements, are desired, this convention may present difficulties. Translations are not described as independent operations if the axes are not perpendicular (Grood and Suntay, 1983).

The joint coordinate system has been used by several authors (Reinschmidt et al., 1997; Stacoff et al., 2000a; Stacoff et al., 2000b; Stacoff et al., 2000c) in investigations of running and walking kinematics. These authors reported results using bone pins. Other authors also used this coordinate system in observing the influence of arch height on running kinematics using skin markers (Nigg et al., 1993). Leardini et al. (1999) used the tibial tuberosity, and head of the fibula, and the malleoli for the tibial landmarks, and the posterior calcaneus, peroneal tubercle, and sustentaculum tali for the calcaneal landmarks of their joint coordinate system in gait assessment.

The International Society of Biomechanics (ISB) had proposed a definition of a joint coordinate system for the ankle (Wu et al., 2002) using the conventions above - the Z axis is the mediolateral tibial axis, the Y axis is the longitudinal axis fixed in the calcaneus, and the floating axis is the X axis, orthogonal to Y and Z. These authors note when using external landmarks it is not possible to distinguish between talocrural and subtalar joint motion. Landmarks proposed include only tibial landmarks, such as the most medial and lateral points of the tibial condyles, the tips of the medial and lateral malleolus, and the tibial tuberosity.

Midpoints of the condylar and malleolar landmarks are taken. The neutral configuration takes the plantar aspect of the foot as a reference point, without describing any positional components to stance. This creates difficulties clinically if significant variations in foot posture exist within a sample population. It is unsatisfactory to this researcher that no anatomic landmarks on the foot are used.

A second anatomical coordinate system has been used by Nawoczenski et al. (1998) for the ankle and by Wei et al. (1993) for the knee. This uses the proximal anatomic reference frame as the reference to describe the position of the distal frame, by means of conversion of a rotation matrix describing the relationship of the two frames (in direction cosines) to angular terms. This preserves the orthogonal relationship should a study of translations be desired, which may be useful for further study of the behavior of unstable ankles. Nawoczenski et al. used the tibial tuberosity, fibular head, and lateral malleolus for the tibia and posterosuperior, posteroinferior, and lateral calcaneus for her video analysis. She described the orientation of axes as Z longitudinal, positive superiorly, X mediolateral, positive laterally, and Y anteroposterior, positive anteriorly (right ankle). Order of rotation was Z-Y-X, about which abduction/adduction, inversion/eversion, and dorsiflexion/plantarflexion are described, respectively.

Foot Dominance

The determination of foot dominance has received far less attention than that of hand dominance. Compared to descriptions of hand dominance, defining foot dominance is complicated by the consideration of the role of the lower limb, which includes postural stability as well as manipulation of objects. Gabbard and Hart (1996) suggest that three actions of the foot should be considered in defining dominance – stability, mobility, and stability/mobility. Chapman et al. (1987) asked subjects to perform tasks with whichever foot would perform most skillfully. Peters (1988), in reviewing literature related to foot preference and skill, suggested that the dominance or preference is defined by the extent to which the activity requires attention, which is usually to manipulate objects.

Several studies (Chapman et al., 1987; Coren, 1993; Peters, 1988; Zverev, 2006) reported that the predominant foot preference was for the right side, as is found with handedness. Chapman et al. (1987) found a stronger correlation between handedness and footedness with right handed

subjects than with left handed subjects, and noted a substantial independence between hand self-reported preference and foot task performance. Peters (1988) also found a stronger correlation for foot and hand preference for right handed subjects than for left handed subjects. Coren (1993) found that females were far more likely to be consistently right-sided for indices of hand, foot, ear, and eye preference.

Chapman et al. (1987) developed a behavioral measurement of foot preference by selecting 13 behaviors described by other authors which they found most compelling. They then tested 220 college age subjects, and assessed the internal consistency of the scale and an item to scale correlation for each task. Based on low correlation, two of the items were dropped from the scale. Test-retest reliability was 0.94 (Pearson's correlation coefficient). Hoffman et al (1998), in a study of the effect of foot dominance on postural control, determined dominance by observing three functional activities, conducting three trials of each. The activities were kicking a ball for accuracy, stepping up on a 20-cm step, and stepping forward to regain balance after a push delivered between the scapulae. No reliability data were reported. No difference in postural sway was found between dominant and non-dominant limbs.

Kalaycioglu et al. (2008) used 14 performance measures drawn from multiple instruments to assess foot preference, finding good reliability and internal consistency with the nine best items. A factor analysis indicated factors of "skilled" and "unskilled movement" reflecting distal muscle and proximal muscle activation, respectively. Interestingly, they reported higher correlations of the "skilled" tasks with hand preference than that of the "unskilled" movements.

Foot dominance determination by self-report is commonly made by asking a subject which foot they would kick a ball with; however, other methods have been developed that consider more activities. The Waterloo Footedness Questionnaire (Elias et al., 1998) consists of 13 questions to be answered as right or left "always", "usually" or "both equally". The questions are allocated to two groups by the type of task – manipulation of an object or providing support during an activity. It has been used in a study of emotional lateralization (Elias et al., 1998) and in hand and foot preference in Korean college students (Kang and Harris, 2000). Another possibility is a subscale of Coren's lateral preference inventory for hand, foot, ear and eye (1993), for which norms for young adults have been established. This inventory is administered by questionnaire, and contains four questions related to the foot. Answer choices are left, right,

or either. The results are scaled according to the number of answers for right and left, ranging from – 4 (all left preferences) to 4 (all right preferences). Three of the four questions included in the inventory were compared to performance tests of the same activity, with an overall percentage agreement of 88%, $p < 0.001$ (chi square) (Coren et al., 1979). Test-retest reliability over one year was reported as 96% agreement between responses for the ball kicking item (Coren and Porac, 1978). This inventory was concise, easy to administer, and had adequate measurement properties, and so was chosen for use in this study. Three of the tasks (stepping on a bug, stepping up on a stool, and kicking a ball) were used in the study by Kalaycioglu et al. (2008) and loaded to the “skilled” movement factor.

Functional Magnetic Resonance Imaging of Ankle Motor Tasks

Importantly, no studies utilizing fMRI in foot and ankle dysfunctions typically considered orthopedic were identified. Recently more studies related to ankle movement in healthy and neurologically impaired subjects have been published. Debaere et al. (2001) compared regional activation during isolated activities of the wrist and ankle, synchronous flexion-extension and asynchronous flexion-extension of the wrist and ankle. They noted additional activation during activities of both joints in the supplementary motor area (SMA), cingulate motor cortex (CMC), premotor cortex (PMC), primary sensorimotor cortex (M1/S1), and cerebellum. No specific target or accuracy requirements were a part of the tasks. Sahyoun (2004), in preparatory work for use of brain analysis in pathologic gait, reported on the patterns of brain activation with anticipation, preparation and execution of foot movements. Twelve healthy subjects, right hand and foot dominant, performed ankle dorsiflexion and plantarflexion of 10-20° excursion at 1.25 Hz. Knee position was not reported. The four conditions were preparation for movement, execution of the movement, anticipation of passive movement, and allowing/experiencing passive movement delivered by the examiner. Comparing mean levels of activation during the active versus passive movement conditions, the authors reported greater activation, in contralateral and ipsilateral M1/S1, SMA, and PMC (rostral dorsal), cingulate and secondary sensory (SII) cortices with active movement. In particular, a relatively bilateral M1/S1 cortex activation was reported during active movement. No significant activation during preparation to move compared to rest was noted; more widespread, but relatively low intensity activation along the medial wall in cingulate and supplementary motor areas was noted during preparation compared to anticipation conditions.

Dobkin et al. (2004) also used an ankle dorsiflexion/ plantarflexion movement to explore the potential for use of fMRI in studies of gait, for their purposes in inform rehabilitation efforts. These authors studied 12 healthy subjects performing only dorsiflexion movements of 10° at 0.3 - 0.4 Hz. They used a block design of alternating task and rest conditions lasting 30 s for a total of 4 movement periods. Cortical activation during the task conditions was observed in M1/S1, SMA, and cingulate motor cortices contralaterally, and bilateral secondary somatosensory cortex (SII). They also reported similar distribution in motor areas with passive movement, of less intensity and volume than with active movement. Four hemiparetic stroke subjects were also studied; those results are not summarized here.

In a study of the reproducibility of fMRI results in movements of four body regions (hand, foot, mouth, and tongue), Havel et al. (2006) had 15 subjects, on three occasions spaced 2-16 days apart, perform ankle dorsiflexion at 0.67 Hz. They used a block design of 20 s task and rest periods, for a total of six movement conditions per run. Reporting the foot results over the three sessions, the authors noted changes between the first and third sessions only for the precentral gyrus, and found the highest reliability in the paracentral lobule. They also compared the use of two different thresholds, 0.05 and 0.001, both corrected for multiple comparisons. With a more liberal threshold, differences over session were also noted for SMA. Alkadhi et al. (2002) examined the somatotopy of the ipsilateral primary motor (M1) cortex during hand, finger, wrist, elbow, foot, and tongue movements using 12 healthy subjects. Self-paced movements were performed at approximately 0.5 Hz in 45° plantarflexion and 10° dorsiflexion. Duration of the task period was not specified. Both contralateral and ipsilateral cortical activation were reported for in M1 and SMA, cingulate, and PMC. However, only 17%, or 4/21 subjects, showed ipsilateral M1 activation during the ankle movement. In general, the authors noted ipsilateral activation in the presence of higher activation in the other motor areas.

Ciccarelli, compared the activation found between active and passive ankle movements in healthy subjects (2005) , and then correlated these responses with disease severity in subjects with multiple sclerosis (MS) (2006). For both experiments the subjects' knees were flexed and thighs supported while the ankles moved at 0.6 Hz for a comfortable excursion from dorsiflexion through plantarflexion to return to the starting position. Eleven blocks of 20 s each of passive and active movements were interleaved with 20 s rest periods. All subjects were right foot dominant. When assessing the results in control subjects in the first study, the authors

found activation in the contralateral primary motor and sensory cortices in the paracentral lobule, and the contralateral SMA. Also, the right foot movement produced activation in the ipsilateral SMA. The passive movement activated primarily the contralateral M1 motor and sensory (S1) cortices. When comparing active to passive movements, greater activation was seen in the ipsilateral M1 in the paracentral lobule and contralateral SMA and S1, and, for the right ankle, greater ipsilateral SMA activity. In the second study, subjects with MS showed greater activation levels than controls in motor control and secondary sensory areas. Some negative correlations were found between activation levels in the inferior frontal gyrus and cerebellum and disease status.

Ashe and Ugurbil (1994), in a review article, summarized findings about activity in the motor cortex using PET and fMRI techniques. Among the observations made was that more complex task activities provoked a greater increase in bilateral SMA and ipsilateral M1/S1 blood flow than simple tasks. They reported that the lateral PMC was more active during tasks in response to visual stimuli. In M1, more widespread activation was noted with movement with one digit than with all digits. The authors concluded that there is not a simple relationship between activation and output, and that differences in activity in cortical areas may be more quantitative than qualitative (type of activity).

In another review article, Mattay and Weinberger (1999) reported that conflicting results have been made regarding changes in cortical activation with learning. They also reported an increase in ipsilateral M1/S1 activity with more complex tasks. Karni et al. (1995), using fMRI, detected an increase in M1 activity once a motor sequence was learned. Hazeltine et al. (1997) and Grafton et al. (1995; Hazeltine et al., 1997)) used PET to study sequence learning in normal adults, and reported that increased activation varied by region in response to the nature of the task (implicit versus explicit learning). Jenkins et al. (1994) noted some regions of increased activation during learning of a motor sequence task with eyes closed, but reduced activity in the visual cortex during the same task, suggesting that selective attention may involve depression of activity in regions not engaged in the activity.

Dassonville, et al. (1998) studied the effects of the predictability of movement on fMRI measured cortical activation. They observed that an unpredictably guided motor behavior was

related to a generalized increase in motor area activation, with the exception of the primary motor cortex. They also observed that repetition of a behavior lead to a decrease in activation.

Summary

Collectively, the literature reviewed supported the impact of FI on the lives of those with the condition, as well as a high prevalence in the population. While much work has been done investigating possible local joint, muscle and nerve contributions, these studies have failed to provide a consistent picture of the causes of FI. More evidence exists, however, for distinguishing differences between healthy subjects and FI subjects in activities controlled by the CNS. Where within the CNS evidence for such control changes may be found has not been reported. However, fMRI has been used extensively to investigate motor control primarily in the upper extremity in healthy subjects and in subjects with neurologic conditions (Carey et al., 2004; Carey et al., 2006; Dassonville et al., 2001; Lungu et al., 2007; Sahyoun et al., 2004). Use of this imaging modality for the current study holds promise to demonstrate processing changes related to the impaired function in FI. An accuracy task has been used successfully in studying motor control in other populations, and holds promise to demonstrate differences in motor skill between FI and healthy subjects.. Questions have been raised about the nature of sufficient, yet not excessive, variation in foot placement during gait and stair climbing. It has been reported that a position of plantarflexion, such as is found in weight acceptance during stair descent, is the most likely position in which to sustain an ankle sprain. This suggests that use of this position, while still occurring in a familiar task, may expose variation in ankle control that would aide in understanding instability. The technologies of electromagnetic motion capture and analysis and fMRI brain imaging were believed to be important to this investigation.

The unique application of valid research methods to this common orthopedic problem may provide important information about differences between FI and control subjects that will lead to improved understanding, prevention and treatment of this condition.

CHAPTER III - METHODS

Subjects

Forty volunteers were recruited by word of mouth and advertisement, twenty with complaint of unilateral functional ankle instability (FI) and twenty control subjects. Inclusion and exclusion criteria are listed below.

Inclusion criteria for all subjects:

- Age 18-50 years
- Able to perform a full squat pain free
- Pain free ascent and descent of steps and performance of ankle inversion/eversion
- Right foot dominance
- Normal sensation
- Pain free palpation at the ATFL, PTFL, CFL, deltoid ligament, and anterior talocrural joint capsule

Exclusion criteria for all subjects:

- Recent ankle injury with acute pain or swelling
- Surgery to either ankle
- Systemic disease affecting bone, joint, muscle, ligament, or nerve
- Diagnosed vestibular or balance impairment, or complaint of dizziness
- Medication usage with potential to alter cognitive or motor function
- Health problem limiting ability to negotiate stairs repeatedly
- Claustrophobia, pregnancy, or medical devices/metal implants incompatible with MRI
- Allergy or sensitivity to adhesive tape, or broken skin under electromagnetic sensor locations

Inclusion criteria for FI subjects:

- History of the first-occurrence inversion ankle sprain requiring at least a 24-48 hour period of protected weight bearing (i.e. limp or use of an assistive device)

- Unilateral repeated episodes of giving way and/or inversion ankle sprains under circumstances unlikely to provoke a first-occurrence sprain
- Last episode of sprain occurring at least 3 months prior to testing

Exclusion criterion control subjects:

- Recurring complaints of ankle sprains (single, uncomplicated sprain at least six months prior acceptable)

Phone and e-mail screening were performed prior to enrollment for inclusion/exclusion criteria of foot dominance, health history, and FI qualifications. Foot dominance was determined from the foot subscale of the Lateral Preference Inventory (Coren, 1993) (Appendix A). This self-report instrument has been validated by comparison with activity performance of the ball-kicking, bug-squishing, and stepping up on a stool items (Coren and Porac, 1978; Coren et al., 1979) and test-retest reliability established over a one year period for the ball-kicking item (Coren and Porac, 1978). Item responses are scored -1 for a “left” response, +1 for a “right” response, and 0 for an “either” response. To be deemed right-footed and included in the study, subjects needed a total score of +1 or greater and at least two responses “right”.

Once enrolled, subjects were screened by history and clinical examination for the remaining inclusion/exclusion criteria. Plantar sensation was evaluated by the Diabetic Foot Screen for Loss of Protective Sensation (Appendix B). Stimuli at all four points on each foot needed to be detected to be considered normal sensation. An anterior drawer test (Magee, 2008) was applied manually, with a subjective assessment by the examiner. A test was deemed positive with mobility greater than 5 mm, based on the physical performance measure reported by Kaikkonen et al. (1994). A visual assessment of the squat excursion was performed. The subjects hips needed to progress lower than the knees, and the heels were to be kept in contact with the floor. Notation was made of subjects whose excursion below this point was limited by report of calf musculature tightness, but this was not a rationale for exclusion.

Demographic and anthropometric data were obtained. Hand preference was determined by the Edinburgh Handedness Inventory (Oldfield, 1971) (Appendix C). To be deemed right or left handed, eight responses in the respective column were required. All others were considered

mixed preference. Sports and leisure participation was categorized by a scale modified from Konradsen (2002) (Appendix D). The subjects were asked to indicate the highest level of sport/leisure participation they felt reflected their customary activity. No studies to assess the measurement properties of this scale are available.

Table 1. Subject Descriptive Statistics.

		Functional Instability		Control	
		Frequency or Mean ($\pm$ SD)		Frequency or Mean ($\pm$ SD)	
		All	Right-involved fMRI	All	fMRI
N		20	8	20	10
Age (years)		29.9 (8.4)	28.3 (9.1)	26.9 (9.0)	28.0 (9.3)
Sex	female	15	7	14	9
	male	5	1	6	1
Height (cm)		167.1 (8.4)	166.9 (6.1)	167.6 (5.6)	165.9 (19.8)
Weight (kg)		72.8 (15.0)	78.8 (17.4)	68.9 (13.3)	65.8 (11.0)
Hand preference	right	15	7	19	10
	left	1	0	1	0
	mixed preference	4	1	0	0
Anterior drawer +					
	right			4	2
	left			2	1
		*
		involved ankle	17	7	
		uninvolved ankle	5	2	
Involved ankle					
	right	14	8		
	left	6	0		

* - significant at $\alpha = 0.05$.

Subject descriptive statistics are provided in Table 1. The FI and control groups were not significantly different for these factors with the exception of positive anterior drawer test findings; the FI group had a higher incidence of positive anterior drawer findings on the involved ankles than the right ankles of the control group ($p < 0.001$). Complete statistical results are in Appendix E. Figure 2 displays the distribution of categorical ratings on the Sports and Leisure Activity Scale. There is a greater concentration of FI subjects in the fourth category, non-contact sports/leisure such as track and field, tennis, and basketball, but overall a similar dispersion of activity between groups.

Figure 2. Distribution of 40 subjects according to the self-report Sports and Leisure Activity Scale. A – All 40 subjects. B – 20 subjects that underwent fMRI. Categories: 1 – international level contact sports, 2 – college competition contact sports, 3 – non-contact sports, e.g. tennis, 4 – non-contact sports/leisure, e.g. soccer, badminton, 5 – sports/leisure, e.g. running > 5 times per week, 6 – leisure, e.g. jogging > 2 times per week, 7 – leisure, e.g. occasional jogging, 8 – leisure, e.g. walking on uneven surfaces, 9 – leisure, e.g. walking on even surfaces, 10 – sedentary. Number one is the highest performance level, number ten is sedentary.

Sprain history was queried during the intake screening. Eleven control subjects had never experienced an ankle sprain, six had had one occurrence without residual problems, and data was not available for three subjects. Ten FI subjects reported 1-5 episodes of giving way per

year, four reported 5-10, and six reported greater than 10 per year. Twelve FI subjects reported 1-5 sprains per year and one reported 5-10. The FI subjects also completed an incidence form that defined a sprain as resulting in swelling or limited weight bearing tolerance. On this form, seven FI subjects indicated no recurrent sprains per year; during the phone screening, three of these indicated 1-5 sprains per year, one indicated sprains several times per week, and data was missing from two subjects.

A subset of ten FI and ten control subjects were selected to undergo the fMRI portion of the study. They were assigned on a blocked, pseudo-randomized basis in groupings of two to four based on the timing of subject recruitment. The FI subjects receiving fMRI were further divided into a group of eight with right ankle involvement and a group of two with left ankle involvement based on subsequent decisions to use fMRI group analyses. Descriptive statistics for the right-involved group are presented in Table 1 and Figure 2 (Appendix E). These fMRI groups were not statistically different from each other regarding the descriptive features listed above, with the exception of greater positive anterior drawer tests on the involved ankle of the FI subjects compared to control right ankles ($p = 0.015$). For the control subjects, five had not experienced an ankle sprain, three had experienced one sprain without residual complaint, and data were missing from one subject. In the right-involved FI group, four reported giving-way episodes 1-5 times per year, two reported 5-10 episodes per year, and two reported greater than 10 per year. Regarding recurrent sprains, six reported 1-5 per year, and two indicated none per year on the incidence form where swelling and limited weight bearing were specified. One of these had reported 1-2 sprains per year during phone screening. The two left-involved subjects' descriptive information is presented in Table 2. One left-involved subject reported 5-10 episodes of giving-way and the other greater than 10 per year; one reported no recurrent sprains and the other 1-5 per year.

Table 2. Descriptive Information for the Two Left-involved FI Subjects Undergoing fMRI

	Subject S109	Subject S133
Age (years)	20	36
Sex	female	female
Height (inches)	65.5	65
Weight (lbs)	143	126
Hand preference	left	mixed
Sport/activity scale	4	8

This study was approved by the University of Minnesota Institutional Review Board and all enrolled subjects completed an informed consent document (Appendix F), and a Health Insurance Portability and Accountability Form (Appendix G) prior to beginning the study. The order of performance of the study components at the first visit was physical performance measures, tracking task, and kinematic assessment. Those allocated to the fMRI portion of the study were scheduled at a later date for that part of the investigation. The following methods descriptions have been reordered for ease of presentation. Order of performance by ankle was randomized at the start of the study for each subject with the same ankle order used for each subsequent task.

Physical Performance Measures

A subset of four items from the Performance Test Protocol of Kaikkonen et al. (1994) developed to evaluate ankle injuries and recovery post primary ligament repair, was used as a comparison measure of functional ankle movement. It consisted of the following:

- time to descend 2 flights of stairs (sixteen 28.89 cm deep and 17.78 cm high (11 3/8 inch by 7 inch) steps with a landing mid-way per flight) as fast as possible safely
- number of times (up to forty) the subject could rise onto the heel of the foot (heel rises)
- number of times (up to forty) the subject could rise onto the ball (toes) of the foot (toe rises)
- single leg stance time (up to 60 seconds)

To adequately complete the stair task, contact of the heel was required on each step. Time was recorded with a stop watch to the nearest 0.01 s. For both the heel and toe rise tasks, the knee on the tested limb was straight, and the other knee flexed to avoid foot-floor contact. In contrast to Kaikkonen, who asked subjects to keep the hands behind the back but allowed a touch of the wall to regain balance before continuing, the subjects in the present study were allowed continuous finger tip contact on a table for balance assist. This was primarily a convenience modification, but potentially could have affected this study's measures by diminishing the time effect of a loss of balance. These motions were performed at a pace of 60/minute with the assistance of a metronome. A one centimeter clearance, judged by the researcher visually at floor level, was required for both heel and toe rises. The test was concluded when a subject failed to reach the required clearance, was unable to keep pace with the metronome, or reached

40 repetitions. Single limb stance time was performed with arms at the side and the untested knee flexed while standing on a 10.16 cm by 30.48 cm (4" by 12") balance beam.

Each physical performance measure has been reported to have excellent test-retest reliability with healthy control subjects, and to demonstrate statistically significant differences between a group of control subjects and subjects having undergone surgical repair with good to excellent outcomes, and a subject group with fair to poor surgical outcomes (Kaikkonen et al., 1997). No group total scores for this study were calculated as only subtests of the Test Protocol were used.

Instrumentation and Procedure – Kinematics Assessment

The kinematic data were obtained with the Flock of Birds electromagnetic system (Ascension Technology Corporation, Burlington, VT) which uses pulsed DC magnetic technology. Four sensors are available which allowed simultaneous measurement at 100 samples/s with six degrees of freedom relative to a transmitter. Systems electronics units recorded the position of the sensors accurately within 76.2 cm (30 inches) in any direction, as reported by the manufacturer (Ascension Technologies, Milton, VT). A prior investigation found angular errors to be less than one degree when dynamic analysis was performed using a pendulum model (McQuade et al., 2002). Potential distortion from metal in the floor of the laboratory space used for this study was assessed, and shown to be insignificant at four inches above the laboratory floor (Appendix H), which is the lowest level of the wooden step platform used during data collection.

MotionMonitor software (Innovative Sports Technology, Inc., Chicago, IL) was used for data conversion. Signals were low pass filtered at 20 Hz by a Butterworth fourth order zero phase filter prior to analysis. Bony landmarks were digitized on the leg and foot (Appendix I), and used to create a 3-D coordinate system that was anatomically meaningful. These points were chosen to reflect the tibial landmarks advocated by the ISB, but using calcaneal landmarks to better reflect actual foot position, and selecting for anatomic points most easily located. Three non-collinear points are required to create a reference plane, and the cross products of these axes are used to create the third axis and correct for orthogonality of the second. For this analysis, the convention of maintaining orthogonal axes was chosen, with a rotation matrix defining the relationship of the calcaneal to the tibial reference frames (Appendix J). In the

shank, the Z axis ran longitudinally between the midpoints of the medial and lateral tibial plateaus and the malleoli, directed positive superiorly. This means that adduction of the right foot on the leg was described as a positive rotation about the Z axis according to the right hand rule (values are multiplied by -1 for the left foot to achieve the same convention). Inversion was a positive rotation about the Y axis, and dorsiflexion was a positive rotation about the X axis (multiplied by -1 in the left foot). Angular measurements were achieved by matrix algebra (Appendix J). The foot and lower leg were modeled as rigid bodies, and talocrural and talocalcaneal motion were observed as a single segment rearfoot motion.

Digitization errors under experimental conditions have been shown to be less than 0.76% in distances 5.08 to 254 mm apart (Milne and Lee, 1999). Reliability measures for this researcher were made over several months, and at most variable the RMS error was 4.2° for adduction/abduction, 1.6° for inversion/eversion, and 3.7° for plantar and dorsiflexion. This was tested by digitizing and then recording static position, and was complicated by the difficulty of exactly repositioning the subject over time. A separate analysis of local digitized points was performed using an autofeedback mode which demonstrated accuracy within a few mm for any one coordinate.

The patient was digitized at nine points on the distal thigh, leg and foot (Appendix I). Sensors were affixed with tape to the distal medial tibia and medial calcaneus in areas of minimal skin slip (Figure 3). Lead wires were taped to the limb to minimize movement, and attached to a belt to prevent interference with the stepping task. Two voltage switches were taped to the recorded foot on the plantar surface, one at the metatarsal pads (forefoot) and one at the heel (rearfoot). The wooden step platform was aligned within the 76.2 cm (30-inch) radius hemisphere range of the transmitter. Step heights were 45.72 cm (18 inches), 27.94 cm (11 inches), and the platform was 10.16 (4 inches) above the floor. Tread depth was 27.94 cm (11 inches). Step/platform width was 60.94 cm (24 inches). A visual target at eye level for the subject while on the second step was established directly in front of the steps.

The subject practiced two or three times stepping down (until familiar) before data collection was initiated. The subject was asked to stand feet forward and a comfortable width apart, for three to four seconds at the beginning of recording. The instructions then were to descend the steps on cue at a normal pace (step over step) leading with the recording limb while keeping the

eyes fixed on the visual target. Figure 3 shows the experimental set-up. Ten trials were recorded for each limb. The order of ankle recording was randomized.

Figure 3. Experimental set-up for the data collection for kinematic analysis of the step down task. Sensors were secured to the distal tibia and medial calcaneus, and voltage switches were attached under the metatarsal heads and plantar surface of the heel. The transmitter was off camera to the left at the level of the second step. A visual target at the subject's eye level while on the second step was provided, located behind the camera.

Instrumentation and Procedure - Tracking Task

The task consisted of tracking a 0.4 Hz sine wave with a computer cursor, connected to a potentiometer that recorded ankle inversion/eversion motion. To accomplish this, an orthosis containing an electrogoniometer was applied to the ankle. The orthosis consisted of 1) a cuff fitted to the calf at mid shank or above, depending on the length of the tibia, 2) a foot piece that encompassed the posterior calcaneus and extended to at least the midfoot on the plantar surface (to minimize mid and forefoot motion), and 3) wooden strips inserted into a receptacle on each piece. The potentiometer (Waters Manufacturing and Co., Wayland, MA, USA) was attached between the wooden arms and aligned just above the posterior superior aspect of the calcaneus such that the moveable arm was attached to the foot component parallel to the vertical midline

of the posterior calcaneus and the stationary arm parallel to vertical midline of the calf. A commercial heel cup was used within the calcaneal portion of the orthosis to minimize movement between the foot and the device. The foot component was secured with Velcro straps in a criss-cross placement around the foot. This placement was further reinforced with a flexible wrap at the distal shank to minimize movement of the wooden piece and potentiometer in relation to the limb (figure 4). The subject then moved through maximal excursion of inversion and eversion several times, and the straps were adjusted until the orthosis was secure. The orthosis did not strictly limit sagittal plane movement of the ankle, and the subject self-selected the sagittal plane talocrural position of comfort and best task performance.

The voltage signal from the potentiometer was connected to a computer (Micron Computers, Boise, ID, USA) through an analog-to-digital converter (Interactive Structures, Inc., BalaCynwyd, PA, USA) that sampled the signal at a frequency of 60Hz. The electrogoniometer was calibrated each session to ensure accurate recording. The subject was positioned in a chair, with manual support of the thigh and the knee flexed to a comfortable position for active ankle range of motion (AROM) measurement and six practice trials. Three trials of AROM in inversion and eversion were recorded for the ankle, and the average of the three trials was used to determine the excursion of the sine wave for the tracking task. The average maximum inversion was considered as 0% of the AROM, and the average maximum eversion was considered as 100% AROM. The upper (eversion) peaks of the target sine wave were then set at 85% of the maximum AROM, and the lower (inversion) peaks at 15%.

The subject was positioned seated, to avoid fatigue, as stated above, for six practice trials to familiarize them with the task. A brief rest period was allowed as requested between trials. Data were then collected from three 10-second test trials performed in the standing position, with the non-tracking limb elevated on a three inch step to allow adequate floor clearance for the tracking ankle (figure 4). Balance assist was allowed by hand contact on a supporting surface. Real time feedback was available on the computer screen during both the practice and test trials. The computer monitor was adjusted for each position to allow full and comfortable view of the screen. Average accuracy data (see data analysis) were recorded for each test trial.

Figure 4. Ankle tracking orthosis and electrogoniometer as used in the standing tracking task.

Tracking Task Concurrent with fMRI

The application of the orthosis, signal connections, and equipment were as previously described for the standing tracking task (with the exception of the computer used, Dell Computer Co., Round Rock, TX, USA). For this tracking series, the subject was positioned supine on the scanner bed. A foam block with a trough cut out for the stationary arm of the electrogoniometer was positioned under the leg proximal to the ankle, with the knee flexed between 15° and 35° based on the length of the subject's tibia. This ensured that the orthosis and electrogoniometer rested free of contact with the scanner bed and the ankle was allowed unrestricted movement. The ankles therefore rested between 10° and 40° of plantarflexion. A second orthosis and electrogoniometer were attached to the non-tracking ankle to monitor for any extraneous activity, including mirror movements (Cramer et al., 1997). Figure 5 shows the patient positioning before entering the bore of the magnet.

The upper and lower peaks of the target were established as stated above. For this sequence, the duration of each tracking trial was 60 seconds. Practice was performed in the supine position for up to thirty seconds until the subject was comfortable and indicated understanding of the task. The subject was visually monitored for extraneous movement of the lower extremities

both during the practice and during the scanning session. The average accuracy data were recorded for each trial.

Figure 5. Subject positioned for the fMRI scanner with the orthosis and electrogoniometer connections visible.

Figure 6. Experimental arrangement for ankle tracking task during fMRI data acquisition. The subject was able to view the rear projection computer screen, displaying the sine wave target and the response, through a mirror on the head coil. The orthosis applied the electrogoniometer to the ankle, and was connected to the recording computer.

A mirror attached to the head coil was adjusted to allow viewing of the entire rear projection computer screen placed just outside the magnet (figure 6). Three 60-second periods of rest were alternated with three 60-second periods of tracking. Cues of “Rest” or Track” were provided at the bottom of the screen to direct the patient. The 0.4 Hz sine wave target and the subject performance were visible on the screen during the “Track” condition. As stated previously, the order of the ankle tracking for each subject randomized initially and was the same for each subject as that done in the initial standing tracking tests.

Instrumentation and Procedure - fMRI

Anatomical and functional images were acquired with a 3 Tesla whole-body magnet (Magnetron Trio, Siemens, Munich Germany). A standard head coil was used with stabilization of the subject provided by pads at each side of the head. A high resolution (1 mm³) T₁-weighted 3D anatomic image dataset (3D FLASH, T_R = 20ms, FA=30 deg, total acquisition time = 10:44 min) was acquired over the entire brain to serve as a template for localization of cortical activity with overlay of the functional image. Functional images were obtained during 145 3-second scans (total scan time 7:15 min for each ankle) while the subject performed the tracking task. A box car design was used alternating 60-second rest and track conditions, with a three- to four-second delay between conditions to switch the computer display. The T₂*-weighted 4.5 mm slice thickness functional images of the blood oxygen-level dependent (BOLD) signal were obtained in the transverse plane using an gradient echo EPI sequence (T_E = 30ms, T_R = 3000 ms, FA = 80 deg, FOV = 192 x 192 with a matrix size of 64 x 64, resolution of 3 x 3 x 4.5). The total imaged volume extended from the superior cortical pole to a depth of 162 mm (inferior cerebellum) in 36 interleaved slices.

Data Analysis

The researcher screened all subjects and collected all data and therefore was not blinded to subject group for this portion of the study. For data analysis, no blinding was done for physical performance or kinematic analysis. During the initial process of analysis for the fMRI data, the researcher was blinded to subject group. This occurred from file creation in Brain Voyager, preprocessing of the functional data, coregistration of functional to anatomic images, and

drawing of the anatomic regions of interest. Subject group assignment was then revealed to allow group analysis.

Kinematic Data

The kinematic data was exported in two ways. First, the initiation of the first step was determined by the visual inspection and marking of the graphical representation of the voltage meter data of the last frame where a voltage meter indicated full foot contact, followed by a period of zero voltage readings for both heel and toe indicating a swing phase of the entire foot. The frame just preceding the swing phase was chosen as the step initiation, and any prior foot shifts without sustained complete lack of contact were ignored. The conclusion of the step cycle was marked as the first frame of foot flat indicated by voltage readings from both the heel and metatarsal voltage meters (figure 7). This single step sequence from the data stream was then normalized in MotionMonitor to 100 frames per sequence and exported for analysis. Several subjects were inconsistent in pattern of step descent: Two control subjects each had one sequence without heel contact (no foot flat, remaining on forefoot only until the subsequent step) and four FI subjects had between 2-6 steps without heel contact (Appendix K). These step sequences were then calculated as ending with the forefoot contact. Three FI subjects were missing one sequence each on one limb due to data collection errors.

An adjusted coefficient of multiple correlations (CMC) (positive square root of the adjusted R^2) was calculated (Kadaba et al., 1989) for each subject on each limb for the motions of dorsiflexion/plantarflexion and inversion/eversion. This coefficient indicates the degree of similarity of the complete waveforms graphed from the normalized step cycles, and has been used as a measure of the repeatability of these cycles (Cornwall and McPoil, 1999; Kadaba et al., 1989). When the cycles are very similar, the adjusted R^2 approaches 1; conversely, when they are very dissimilar, the value approaches zero. A Fischer r to z transformation (Snedecor and Cochran, 1980) was applied to allow application of parametric statistics.

Figure 7. Example of the graphical indication of the start and end of the step cycle used for normalization of the cycle to 100 frames.

To allow a more discreet investigation of specific portions of the step cycle while preserving the timing component, a second method of exporting the data was used, whereby no normalization was performed. These data were then reviewed to locate the initiation (here forefoot off), based on voltage meter readings, of the swing phase and the first frame of subsequent full foot contact (combined toe and heel contact). From these findings, the number of frames (representing 0.01s) of foot completely off the supporting surface to forefoot contact (swing phase), and forefoot contact to heel contact (weight acceptance phase) were computed for each trial and the mean for all trials per individual subject were calculated. In addition, the instantaneous angular speed of the ankle at forefoot touch and the instantaneous linear velocity in forward progression of the foot (sagittal plane motion in the Y direction) at 80% of the swing cycle were derived. Means ($\pm$ SD) or median (interquartile ranges) were then calculated for each group and variable over the 10 trials collected.

In addition to the data collection errors and subject performance variations reported above, two subjects on two or three trials of one foot lacked a distinct forefoot to heel contact progression, instead stepping in a foot flat position. Ankles missing three or less forefoot or heel contact records were included in the weight acceptance phase analysis without those trials. Ankles with data missing from more than three step sequences for either absent forefoot or heel contact were not included in the analysis of the weight acceptance phase (Appendix K).

Tracking Task Data

The tracking performance scores are computer generated accuracy indices based on the root mean square (rms) error between the target line and the subject performance. Since the amplitude of the sine wave is determined by the subject's active range of motion, this value is normalized to the subject, thereby making comparisons across subjects valid. The accuracy index (AI) (Carey, 1990) is calculated as

$$AI = 100(P-E)/P$$

where E is rms error between the target and response line and P is the amplitude of the target pattern, calculated as the rms difference between the sine wave and the midline separating the two halves of the sine wave. The maximum possible score is 100%, and negative scores are possible when the response falls to the opposite side of the midline. No studies were found which validated the discriminative power of this index between healthy controls and subjects with ankle problems. It has been validated in studies of stroke subjects with finger tracking (Carey, 1990; Carey et al., 1998). Accuracy indices were generated for each trial – three 10-second trials performed by all subjects, and three 60-second trials for those subjects performing ankle tracking during an fMRI session.

fMRI

Brain Voyager (Brain Innovation B.V., Maastricht, the Netherlands) was used for data processing and analysis. Versions 1.2.6 was used for the earlier, within-group analyses and the individual analyses, and 1.8 for the later between-group analyses. Functional images were preprocessed to correct for head motion in 3-D, slice acquisition time differences, and temporal linear trends. The data from the 8 right-involved subjects and the control subjects were also spatially smoothed using a Gaussian kernel at 8mm full-width half maximum to allow for enhanced group analysis. The amount of head motion corrected was assessed for an acceptable limit of 3 mm in any direction. One control subject violated this limit when tracking with the left ankle, and these data were discarded from further analyses. The functional data were co-registered with the anatomic images, and both were converted to Talairach space dimensions (Talairach and Tournoux, 1988) to allow for standardized description of location.

Four within-group general linear model (GLM) analyses were performed comparing the BOLD signal intensity during track versus rest conditions. The four groups were the control group tracking with the 1) right ankle, 2) left ankle, and those in the right-involved FI group tracking with the 3) involved ankle, and 4) uninvolved ankle. A statistical threshold of $p < 0.05$ with Bonferroni correction for multiple comparisons ($p(\text{Bonf}) < 0.05$) was used to identify cortical activation. This threshold was chosen to be most conservative yet still be informative. Use of this level was possible due to the large volume of activation present. Beta signal intensity values were calculated for voxels meeting the significance threshold. Beta signal intensity represents the percentage increase in BOLD signal intensity during the track condition from the rest condition. The mean Beta $\pm$ SD for the group is reported.

The Beta signal intensity was calculated for the significant voxels within each of the following functional cortical areas:

- M1 – primary motor cortex
- S1 – primary sensory cortex
- PMC – premotor area
- SMA – supplementary motor area
- PSMA – pre-supplementary motor area

Figure 8 provides a representation of these regions of interest (ROIs) in a transverse view. In addition, a region of activation in the anterior cingulate gyrus was subsequently identified in the between group analysis described below, as active only when the FI subjects tracked with the (involved) right ankle. Within-group analysis data were then obtained. M1, S1, PMC, SMA, and PSMA regions were identified on the anatomic images based on the boundaries described by Dassonville, et al. (2001). These definitions left an unexamined portion of the medial wall that may have contained foot and ankle motor representation (Luft et al., 2002; Penfield and Rasmussen, 1950). This region, designated PCL, is that portion of the paracentral lobule posterior to the defined SMA and exclusive of the M1 and S1 designations.

A second, between-group GLM analysis was performed to identify regions of activation that differed between FI and control groups tracking with either the involved (right) or uninvolved (left) ankles. Here voxels were identified that showed a greater Beta signal intensity in one group over the other during the track condition. Thresholds were set at $p < 0.001$, with a post-

analysis cluster size ≥ 50 voxels. This p-value threshold allowed visualization of activation differences while maintaining a more conservative cluster size requirement, thereby minimizing the potential to overstate differences. Clusters were localized within each region by the center of mass if activation was demonstrated in the same hemisphere for both FI and control groups or for the same group when tracking with different ankles. Localization accuracy and therefore comparative value is compromised by the spatial smoothing performed in preprocessing for group analysis. No mathematical analysis was used to make judgments about variations in location of center of mass, rather only observational comments are made.

Figure 8. Transverse view of a representative slice of the anatomically defined regions of interest, shown in the right hemisphere. $Z = 60$ for M1, PCL, S1, 58 for PMC, 54 for SMA and PSMA. M1 – primary motor cortex, PCL – paracentral lobule, S1 – primary sensory cortex, PMC – premotor cortex, SMA – supplementary motor area, PSMA – pre-supplementary motor area.

For the two subjects allocated to fMRI testing that were left-involved, individual analyses were performed. Significance level was set at False Discovery Rate (FDR) = 0.01 (Genovese et al.,

2002). The FDR is a statistical method that controls the false positive rate (inaccurately rejecting the null hypothesis) to the specified level, but only among those voxels initially judged as positive (active). This is reported to address the multiple comparisons problem for the large numbers of voxels examined in fMRI research, yet be less conservative than a Bonferroni correction which may obscure potentially meaningful activation. The regions of interest were defined not on the common brain used for the group analysis, but on the specific subjects' anatomical image. The Beta signal intensity and number of significant voxels are reported

Statistical Analyses

For between group comparisons, the right ankle of the control group was compared to the involved ankle of the FI subjects. This was based on the predominance of affected right ankles and a desire to match ankles by dominance. All paired tests indicated no difference between the ankles of the control subjects for kinematic and tracking measures, which further supports this choice.

Demographic and anthropometric subject data were compared using t tests for ratio data and chi-square for nominal and ordinal data. Mann-Whitney U, Wilcoxon signed-ranks, and Fischer's Exact Test were used for physical performance measures. Statistical software NCSS 2000 and 2007 (Kaysville, UT) was used.

Kinematic Data

Mixed model ANOVAs were calculated to assess for differences between ankles and groups for the dorsiflexion/plantarflexion and inversion/eversion normalized cycle kinematic data (the Fisher r-to-z transformed coefficient of multiple correlations).

The angular and linear velocity data were not normally distributed, and each exhibited outlier data for a few subjects. An outlier was defined as a value greater than 1.5 times the interquartile range above the 75th percentile or less than 1.5 times the interquartile range below the 25th percentile. These values were deleted from the data before further computation. The remaining data were then normal. Mixed model ANOVAs were used to assess for differences between ankles and groups for duration of swing phase, weight acceptance phase time, instantaneous

angular speed of the ankle at forefoot touch, and instantaneous linear velocity of the foot at 80% of swing phase.

Tracking Data

A repeated-measures ANOVA indicated no significant differences between trials for either group on data from all subjects, and so the mean AI for each ankle was used in subsequent analyses for both the full group and the fMRI subgroup. Not all the data in the subject groups were normally distributed and, where not normal, were skewed left, so non-parametric methods were used.

fMRI Data

For the within-group analyses, comparisons were made of activation between contralateral and ipsilateral hemispheres of each anatomic region present while tracking was performed with the same ankle. These comparisons were conducted separately for each ankle of the FI and control groups using paired t tests or Wilcoxon signed-rank tests for normal and non-normal distributions, respectively. Spearman rank correlations were computed to assess for correlation between the Accuracy Index and the Beta signal intensity values within each group for each region investigated.

Summary data for the between-group analyses were reported. Beta signal intensity and significant voxel number were reported. As an exploratory inquiry, paired t tests on the Betas were performed for regions that showed activation during both ankles in the same subjects. While we are unable to be certain whether or not these are the same voxels being activated during different conditions, any potential Beta differences may be informative.

Evolution of the Project

Mention should be made of changes in the methods of the study that occurred after the proposal stage. First, a deactivation of the 4 tesla (T) scanner and the addition of the 3T resulted in slight changes to sensitivity of signal changes of the imaging, but greatly increased the efficiency of use. Second, the change in scanner resulted in a change in imaging processing and analyzing

software from Stimulate (Strupp, 1996) to Brain Voyager (Brain Innovation B.V., Maastricht, the Netherlands). The greater capabilities of Brain Voyager allowed more detailed analyses. As well, with the passage of time, preferences for fMRI analyses changed, such that signal intensity rather than significant voxel count became the more accepted method of comparison. In addition, group analyses became more common. These approaches were adopted for the analyses in the current study.

Regarding the kinematic analysis, the use of coefficients of variation was abandoned due a concern that these values would be differentially influenced by the small mean values obtained in some, but not all measures. The z-transformed coefficient of multiple correlations was chosen instead of multiple discrete variables related to motion excursion to more efficiently and completely reflect step cycle variation. It is felt these changes resulted in an improved study.

RESULTS

Physical Performance Measures

All Subjects

No significant differences were found for within-group paired comparisons between right and left ankles for control subjects and between involved and uninvolved ankles for FI subjects for single leg balance time, number of heel and toe rises, and stair descent time (Appendices L - O). For balance time, two FI subjects were unable to balance on the involved limb for 60 seconds, and one control subject on the right limb and one control subject on the left limb were unable to balance for 60 seconds; all other subjects completed the 60-s task. These balance findings were not statistically different between FI and control groups (Appendix L). However, between-group significant differences were found for both heel ($p = 0.002$) and toe rise ($p = 0.041$) tasks, with the FI subjects demonstrating the ability to perform fewer repetitions of the tasks with the involved ankle (Table 3, Appendices M and N). For timed stair descent, a trend to significance was found ($p = 0.056$) where the median FI time was 2.3 seconds slower than that of controls (Appendix O). Eight FI subjects and four control subjects demonstrated calf tightness, evidenced by limited excursion during a squat while keeping heels on the ground. There were no correlation between reduced heel rise performance and calf tightness in either ankle of each group (Appendix P).

Table 3. Heel and Toe Rise Physical Performance Data

	All		fMRI	
	FI	Control	Right-involved FI	Control
	Median(IQR)	Median(IQR)	Median(IQR)	Median(IQR)
Toe rises (#)				
right ankle		40 (0)		40 (0)
left ankle		40 (0)		40 (0)
involved ankle	40 (4)		36 (18.3)	
uninvolved ankle	40 (4)		37.5 (8.8)	
Heel Rises (#)				
right ankle		40 (9.8)		40 (12.8)
left ankle		40 (5.3)		40 (8)
involved ankle	32.5 (24.5)		28 (32.0)	
uninvolved ankle	36.5 (15.8)		35.5 (14.8)	

FI – Functional instability

* indicates statistical significance at $\alpha = 0.05$.

Right-involved fMRI Subjects

No significant within-group differences were found for comparisons between right and left ankles for control subjects and involved and uninvolved ankles for FI subjects for toe or heel rises, or single leg balance time (Appendices 12 – 15). For single leg balance time, one FI subject was unable to balance on the involved ankle for 60 seconds. Between-group significant differences were found for both the right-involved ($p = 0.002$) and left-uninvolved ($p = 0.017$) ankles for toe rises only, whereby again the FI subjects were unable to perform as many repetitions as the control subjects on either ankle (Table 3). Four FI and two control subjects demonstrated calf tightness during the squat. There were no correlations between reduced heel rise performance and calf tightness in either ankle of each group (Appendix P).

Kinematic Analysis of the Step Down Task

When comparing the similarity of the normalized step cycles during the step down task using the Fischer z-transformed adjusted coefficient of multiple correlations (z-CMC) for inversion/eversion and dorsiflexion/plantarflexion motions, no differences were found between ankles for either FI or control groups. As well, no between-group differences were found for either motion comparing involved ankle to right ankle and uninvolved to left ankle of the FI and control groups, respectively (Table 4, Appendix Q). Inspection of the means indicated a greater similarity between step cycles in the dorsiflexion/plantarflexion motion compared to the inversion/eversion motion for both ankles of the FI and control groups. A post hoc comparison indicated a significant main effect for motion ($p < 0.001$).

Table 4. Mean Fisher Z-transformed Coefficients of Multiple Correlations ($\pm$ SD) for Inversion/Eversion and Dorsiflexion/Plantarflexion.

Ankle	Functional Instability		Controls	
	Involved	Uninvolved	Right	Left
Inversion/eversion	0.55 (0.46)	0.51 (0.37)	0.61 (0.42)	0.44 (0.31)
Dorsiflexion/plantarflexion	1.01 (0.26)	0.99 (0.26)	1 (0.21)	1.01 (0.12)

]

* significant at $\alpha = 0.05$

The discrete variable results, with the time component preserved, are presented in Table 5. No differences were found for the duration of the swing phase (Appendix R). A trend towards a difference between groups ($p = 0.09$) was found for the time of weight acceptance (forefoot to heel contact, Appendix S). The FI subjects progressed to foot flat more rapidly, with the involved limb taking an average of 0.01 seconds less time in forefoot only weight bearing than the uninvolved limb, and 0.02 seconds less than the control subjects on either limb. With a current power of 0.39, 45 subjects would be needed to reach significance at 0.8 power for this effect size of group.

Table 5. Discrete Kinematic Time and Velocity Results, without Outliers.

	Functional Instability Mean ($\pm$ SD)		Controls Mean ($\pm$ SD)	
	Involved	Uninvolved	Right	Left
Ankle				
Swing phase (s)	0.58 (0.11)	0.58 (0.92)	0.55 (0.07)	0.55 (0.06)
Weight acceptance phase (s)	0.09 (0.03)	0.10 (0.04)	0.11 (0.03)	0.11 (0.03)
Instantaneous angular speed ($^{\circ}$/s) *	95.7 (25.3)	114.2 (32.2)	99.3 (15.7)	102.0 (29.9)
Instantaneous linear velocity (m/s)	-0.06 (0.09)	-0.02 (0.09)	0.01 (0.12)	0.02 (0.13)

* - significant at $\alpha = 0.05$.

Instantaneous angular speed at forefoot contact had a significant main effect for ankle ($p = 0.038$), with the involved/right ankles being slower than the uninvolved/left ankles (Figure 9). While not significant, the interaction probability level was low ($p = 0.129$). Inspection of the means indicated the ankle effect was primarily due to the faster speed of the uninvolved ankle of the FI subjects (Appendix T). A scatter plot of the individual data is presented in Appendix V. One FI subject and two control subjects had velocity results for the involved/right ankles that were outliers, all three being higher than the rest of the subjects. These values were deleted from analysis. The uncorrected data are presented in Appendix U.

Instantaneous linear velocity of the foot in forward progression (Y) at 80% of the swing phase showed a trend toward a main effect for group ($p = 0.075$, power 0.43), with the FI subjects moving backward at this time compared to the controls (Figure 10, Table 5, and Appendix U). Forty-five subjects would be needed to reach significance at 0.8 power for this effect size. A

scatter plot of the individual data is presented in Appendix W. One FI subject had a higher linear velocity in the involved foot and one control subject had a lower velocity on the right limb. Both were outliers and deleted. The uncorrected data are presented in Appendix X.

Figure 9. Instantaneous angular speed of the ankle at forefoot contact. * significant at $\alpha = 0.05$. FI – Functional instability.

Figure 10. Instantaneous linear velocity of the foot in the forward direction (y) at 80% of swing phase. $p = 0.075$, not significant at $\alpha = 0.05$. FI – Functional instability

Tracking Task

Figure 11 shows examples of tracking data for both a standing task completed by all subjects and a supine task completed by fMRI subjects while in the scanner. The accuracy data were not normally distributed. Figure 12 displays the AI data for each group and ankle for all subjects. No statistical differences were found for group or ankle tested. For the right-involved and control fMRI subjects, as well, no differences between ankles or groups were found (Figure 12, Appendix Y). Scatter plots of the individual data are presented in Appendix Z.

Figure 11. Sample tracking tests of functional instability subjects tracking with the involved ankle. 0 degrees equals maximum inversion. A – Subject tracking during a 10-second standing trial, AI = 69.18%. B – Subject tracking during a 60-second fMRI trial, 55.24%.

Figure 12. Median and interquartile ranges (IQR), of the Accuracy Index, for the ankle tracking task using inversion and eversion movements. A -10-second standing task performed by all 40 subjects, B - 60 second supine ankle tracking task performed by 8 right-involved and 10 control fMRI subjects. Whiskers represent values 1.5 times the IQR above the 75th percentile and below the 25th percentile. Data points beyond the whiskers are outliers. No significant differences between groups or ankles were found.

fMRI – Group Analyses

Within-group Analyses

Figure 13 displays the regions of activation in the track versus rest contrast (within-group analysis) in the right-involved FI group for each ankle and Figure 14 shows the Beta signal intensities for right and left ankle tracking. Scatter plots in individual data are presented in Appendix AA. In the FI group comparisons, only the M1 (primary motor cortex) and PCL (paracentral lobule) regions showed inter-hemispheric activation differences. In M1, when tracking with the involved (right) ankle, the contralateral (left) hemisphere showed a significantly greater Beta signal intensity than the ipsilateral (right) M1 ($p = 0.003$); this difference was not apparent when tracking with the uninvolved (left) ankle ($p = 0.135$). As well, in the PCL the contralateral hemisphere showed greater activation than the ipsilateral hemisphere when tracking with the involved ankle ($p = 0.042$); this difference was also not apparent when tracking with the uninvolved extremity ($p = 0.301$).

Figure 13. Functional instability right-involved subjects (N = 8) within-group fMRI analyses: contrast tracking versus rest. A – tracking with the involved (right) ankle, B – tracking with the uninvolved (left) ankle Talairach slice coordinates $x = 0$, $y = -22$, $z = 60$.

Figure 14. Mean Beta signal intensity ($\pm$ SD) in the right-involved functional instability group. A - tracking with the involved (right) ankle, B - group tracking with the uninvolved (left) ankle, comparing the two hemispheres in the indicated regions. Ipsi – hemisphere ipsilateral to the tracking ankle, contra – hemisphere contralateral to the tracking ankle. M1 – primary motor cortex, PCL – paracentral lobule, S1 – primary sensory cortex, PMC – premotor cortex, SMA – supplementary motor area, PSMA – pre-supplementary motor area. * indicates statistical significance at $\alpha = 0.05$ level.

In the control group, different patterns of lateralization emerged. When tracking with the right ankle, S1 (primary somatosensory cortex, $p = 0.004$), PCL ($p = 0.008$) and SMA (supplementary motor area, $p = 0.005$) all demonstrated greater contralateral than ipsilateral activity (Figure 15). M1 showed a trend toward a difference, again with the contralateral region having a greater Beta ($p = 0.051$). With a current power of 0.52, 56 subjects would be required to reach a power of 0.8 with this effect size. When tracking with the left ankle, M1, S1, and

PCL were not statistically different between hemispheres. SMA continued to show a difference; however, tracking with the left ankle resulted in greater *ipsilateral* activation ($p = 0.008$). Figure 16 displays the mean Beta signal intensities tracking with the right and left ankles, respectively. Scatter plots of the individual data are presented in Appendix AB.

Figure 15. Control subjects (N = 10) within-group fMRI analyses: contrast tracking versus rest. A – tracking with the right ankle, B – tracking with the left ankle. Talairach slice coordinates $x = 0$, $y = -22$, $z = 60$.

Figure 16. Mean Beta signal intensity ($\pm$ SD) in the control group tracking with the right ankle (A) and left ankle (B), comparing the two hemispheres in the indicated regions. Ipsi – hemisphere ipsilateral to the tracking ankle, contra – hemisphere contralateral to the tracking ankle. M1 – primary motor cortex, PCL – paracentral lobule, S1 – primary sensory cortex, PMC – premotor cortex, SMA – supplementary motor area, PSMA – pre-supplementary motor area. * indicates statistical significance at $\alpha = 0.05$ level.

A region of the left anterior cingulate gyrus demonstrated a significant Beta between track and rest conditions only for the right-involved FI group while tracking with the right ankle. This cluster was centered at Talairach coordinates $x = -15$, $y = 36$, $z = 15$. The mean Beta was 0.262 ± 0.288 , volume was 304 voxels. Appendices AC - AF summarize the Beta signal intensities

for all regions, the comparative statistics for FI and control groups, and significant voxels numbers, respectively, for both groups.

No significant correlations were found between the Accuracy Index and Beta signal intensity; however, a trend toward significance was noted when tracking with the left ankle in the FI subjects in the contralateral PMC ($p = 0.058$) and with the left ankle in controls in the ipsilateral M1, contralateral and ipsilateral S1 ($p = 0.058$, 0.058 , and 0.067 , respectively; Appendices AG and AH). Figures 17 and 18 show these correlations and comparative graphs for the opposite, non-significant hemisphere data.

Figure 17. Correlations of mean Beta signal intensity with left Accuracy Index (%). PMC – premotor cortex, M1 – primary motor cortex. * trend to significance (FI-PMC $p = 0.058$, controls-M1 $p = 0.058$).

Figure 18. Correlations of mean Beta signal intensity with left Accuracy Index (%). S1 – primary sensory cortex. *trend to significance (controls-right S1 $p = 0.058$, controls-left S1 $p = 0.067$).

Between-group Analyses

Clusters of activation within each region were identified that were more active during the track condition in one group over the other group. Figures 19 and 20 display the between-groups activation differences while tracking using the right and left ankles, respectively. Fewer regions demonstrated greater activation in the FI group tracking with either ankle than greater activation in the control group. There was no activation in the PSMA (pre-supplementary motor areas) that was greater in one group over the other.

For the FI group greater-intensity contrast, the left S1 and PMC areas showed activation when tracking with either ankle. Table 6 presents the descriptive information on these active clusters with comparison information for the control group. There was no statistical difference between the Betas for either region between tracking with the right and left ankles (Appendix AI). It should be noted, however, that these are not identical voxels between the two conditions and the data were collected on different runs, so the comparison is primarily descriptive. There was a slight difference in center of mass (COM) between the clusters active in the PMC, with the

activation during right ankle tracking being slightly superior to that observed during left ankle tracking.

Figure 19. All fMRI (N = 18) subjects tracking with the involved/right ankle. Positive (orange) areas indicate those voxels where there was significantly greater Beta signal intensity during tracking in the control group, and negative (blue) indicating those voxels where there was significantly greater signal intensity Betas in the functional instability group. Talairach slice coordinates $x = 0$, $y = -22$, $z = 60$.

Figure 20. All fMRI (N = 18) subjects tracking with the uninvolved/left ankle. Positive (orange) areas indicate those voxels where there was significantly greater Beta signal intensity during tracking in the control group, and negative (blue) indicating those voxels where there was significantly greater signal intensity Betas in the functional instability group. Talairach slice coordinates $x = 0$, $y = -22$, $z = 60$.

For the control subjects greater-intensity contrast, significant activation were detected in all regions except the right PMC while tracking with the left ankle, and the right PCL while tracking with the right ankle (as noted above, there also was no PSMA activation tracking with

either ankle). Table 7 contains mean Betas for all regions where significantly greater activation was found in the control subjects, with comparison information from the FI subjects. A significant difference in Betas was noted only in left PMC in the control group where tracking with the right ankle produced greater activation than tracking with the left ankle (Appendix AI). It should be noted, however, that these are not identical voxels between the two conditions and the data were collected on different runs, so the comparisons are primarily descriptive. Appendix AJ lists the number of significant voxels by group and region.

Table 6. Descriptive Statistics for fMRI Activation Clusters More Active in the Right-involved Functional Instability Subjects than in Controls during Tracking.

	Functional Instability			Control
	Location of Center of Mass (Talairach)			Mean Beta ($\pm$ SD)
	x	y	z	
Left S1				
right ankle	-33	-37	58	0.54 (0.92)
left ankle	-32	-37	60	0.60 (0.90)
Left PMC				
right ankle	-22	-5	63	0.83 (1.04)
left ankle	-21	-8	56	0.54 (0.34)

Beta – BOLD signal intensity increase relative to rest, S1 – primary sensory cortex, PMC – premotor cortex. ($p < 0.001$, minimum cluster size = 50).

Table 7. Mean Beta Signal Intensity ($\pm$ SD) by Region in Voxels More Active in the Control Group than in the Functional Instability Group during Tracking.

	Tracking with right ankle		Tracking with left ankle	
	FI	Control	FI	Control
	Mean Beta ($\pm$ SD)	Mean Beta ($\pm$ SD)	Mean Beta ($\pm$ SD)	Mean Beta ($\pm$ SD)
Right M1	0.06 (0.19)	0.29 (0.22)	0.05 (0.17)	0.35 (0.20)
Left M1	0.23 (0.23)	0.46 (0.22)	0.08 (0.12)	0.35 (0.13)
Right PCL	#	#	0.54 (0.27)	0.87 (0.34)
Left PCL	0.45 (0.25)	0.66 (0.35)	0.44 (0.22)	0.75 (0.26)
Right S1	0.03 (0.25)	0.24 (0.21)	0.03 (0.19)	0.33 (0.21)
Left S1	0.29 (0.21)	0.55 (0.30)	0.10 (0.09)	0.38 (0.15)
Right PMC	0.20 (0.18)	0.61 (0.72)	#	#
Left PMC	0.25 (0.29)	0.50 (0.20)	-0.02 (0.11)	0.27 (0.18)
Right SMA	0.71 (0.38)	0.85 (0.70)	0.78 (0.32)	1.07 (0.57)
Left SMA	0.69 (0.35)	0.84 (0.55)	0.90 (0.36)	1.18 (0.65)

FI – Functional instability
- no activation present

Both left S1 and left PMC showed activation of greater intensity for both groups while tracking with either ankle. Based on the analysis, these cannot be the identical voxels. Table 8 shows the COM coordinates for each group. In left S1, the control group COM was more inferior and anterior than that of the FI group while tracking with either ankle. In left PMC, the control group COM was more lateral and inferior with either ankle than that of the FI group. For the control group, those regions that showed bilateral activation showed only negligible differences in location as indicated by COM, although there were some volume differences as indicated in Appendix AJ. Appendix AK displays the center of mass coordinates for the activation in the control groups.

Table 8. Talairach Coordinates for the Center of Mass for Significant Voxel Clusters with Greater Beta Signal Intensity in Each Group Found in the Same Brain Regions.

		FI			Control		
		x	y	z	x	y	z
Left S1							
	tracking with right ankle	-33	-37	58	-37	-27	46
	tracking with left ankle	-32	-37	60	-33	-25	43
Left PMC							
	tracking with right ankle	-22	-5	63	-33	-9	48
	tracking with left ankle	-21	-8	56	-42	-3	32

An active voxel cluster was also identified from the between-group analysis in the left anterior cingulate gyrus, present only with tracking with the right ankle and of greater intensity in the FI subjects. The center of mass was located at $x = -12$, $y = 36$, $z = 11$, the mean Beta signal intensity was 0.206 ± 0.505 , and there were 3375 significant voxels.

fMRI Individual Analyses of Left-involved Subjects

Table 9 presents the physical performance and accuracy index data for the two left-involved subjects who underwent fMRI testing. Data reported here is from individual analyses. Table 10 displays the Beta signal intensity for each subject in each region. The anterior cingulate functional region was not used in this analysis as it was defined on different anatomical images. Visual assessment, however, indicated activity in the left anterior cingulate gyrus for both subjects, only when tracking with the right ankle. No right ACG activity was noted.

Table 9. Physical Performance and Accuracy Index Results for the Two Left-involved fMRI Subjects.

		Subject S109	Subject S133
Physical Performance			
Balance (s)		60	60
right			
	left	49.27	60
Toe rises (#)		30	40
right			
	left	36	40
Heel rises (#)		40	40
right			
	left	40	23
Stairs (s)		19.83	17.03
Accuracy Index (%)			
	right	59	62.14
	left	49.23	50.34

Table 10. Mean Beta Signal Intensity in All Regions for the Two Left-involved fMRI Subjects Tracking with Both Ankles.

	Tracking with right ankle		Tracking with left ankle	
	Subject S109	Subject S133	Subject S109	Subject S133
Right M1	1.18	0.81	1.57	1.84
Left M1	1.80	0.93	1.25	2.24
Right PCL	0.67	0.68	1.49	2.00
Left PCL	1.79	1.24	1.20	1.74
Right S1	0.69	0.78	1.19	2.05
Left S1	0.21	0.75	0.99	1.98
Right PMC	1.16	0.86	1.50	1.89
Left PMC	1.45	0.82	1.31	2.40
Right SMA	0.84	1.24	1.24	1.96
Left SMA	2.06	1.43	1.84	2.40
Right PSMA	0.82	0.54	0	1.35
Left PSMA	0.84	0.80	0.60	1.67

CHAPTER V - DISCUSSION

This study investigated differences in motor control between subjects with complaints of functional instability and subjects without such complaints. Previous studies have supported a change in motor control within the central nervous system as contributing to FI (Beckman and Buchanan, 1995; Caulfield and Garrett, 2002; Hertel and Olmsted-Kramer, 2007; Hiller et al., 2004; Ross and Guskiewicz, 2004), but have not examined cortical activation as a possible source of this change. As well, fMRI analyses were used as an exploratory measure to evaluate which sensorimotor cortices might show activation changes during an accuracy-demanding task performed with the ankle. While the scores on the accuracy task were unable to discriminate between healthy control and FI subjects, different patterns of cortical activation were observed with the corresponding fMRI data. This study also used a kinematic analysis of a potentially vulnerable position (accepting weight on a plantarflexed foot – step down task) to assess the variability in motor performance between FI and control subjects. Differences were demonstrated in timing and speed parameters of performance of the step down task between FI and control groups. These findings complement the currently available literature suggesting that impaired motor control, not just local tissue damage, is associated with functional instability.

Physical Performance Measures

The results suggest that two of the four Test Protocol items chosen (heel and toe rises) were able to distinguish between FI and control subjects, and a third (time to descend stairs) showed a trend to performance differences between groups. Similar positive finding in the smaller fMRI group may suggest a more robust difference in the toe rise activity. The Test Protocol developers (Kaikkonen et al., 1994) suggested that the toe and heel rise tasks measured strength. While it is true that strength is a component of these tasks, one must also acknowledge that that toe and heel rises are activities requiring dynamic balance in potentially challenging positions. The balance requirement interpretation of these tasks coincides more convincingly with past research results (Hertel et al., 2006; Hiller et al., 2004; Perrin et al., 1997; Ryan, 1994). In previous studies strength deficits, tested in more stable positions with more stringent protocols, were not consistently demonstrated in FI subjects (Hubbard et al., 2007a; McKnight and Armstrong, 1997). As no relationship was found between calf tightness and limited number of

heel rises performed, local soft tissue restriction does not appear to be a reasonable explanation for the disparity between FI and control subjects on this measure. Perhaps both strength and flexibility are independent factors contributing to FI.

The trend towards a slower time for stair descent in the FI group at a minimum suggests less self-confidence during this activity and possibly a weakness or deconditioning issue. A slower time may also represent a safety need for closer cognitive attention due to impaired motor control. Kaikkonen et al. (1997) did not report specific time parameters for the time to descend stairs, instead reporting categories of performance and total scores for the entire instrument. As stair number and dimensions in the present study differ from that used in the Kaikkonen study, a conversion to their scoring system was not performed.

Kinematic Analysis of Step Down Task

The initial hypothesis was that variability of performance of the ten single-step cycles on a stair would be greater in the FI group compared to the control group, and in the involved compared to uninjured ankle within the FI group. The sub-hypothesis related to the inversion/eversion and dorsiflexion/plantarflexion was not supported. However, while no between-group differences were noted, between-motion comparisons indicated greater variability for the inversion/eversion cycles than the dorsiflexion/plantarflexion cycles. Similar conclusions were found for healthy subjects on stairs (Yu et al., 1997) and level-surface walking (Kadaba et al., 1989; Leardini et al., 1999). Direct comparison of actual values for repeatability is not appropriate as these authors (Kadaba et al., 1989; Leardini et al., 1999; Yu et al., 1997) did not normalize the CMC values as was done in the present study. Moseley (1996), however, reported greater between-subject variability for dorsiflexion/plantarflexion than inversion/eversion, and very similar within-subject variability for all three planes of motion, when the subjects walked on a level surface. The observed variability of inversion/eversion may be linked to flexibility in motor control to allow for online corrections as required by unexpected perturbations or foot placement errors (MacKinnon and Winter, 1993). Findings congruent with past research support the methodology used in this study. However, the results of no differences between groups diminish the expectation that increased kinematic variability under the current test conditions is associated with FI. Manipulating the test conditions to

detect differences in the repeatability of the step down task would be a reasonable progression of this research.

The investigation of discrete variables, however, does offer some insight into the function on stairs of individuals with functional instability. The hypothesis of differences in time for swing and weight acceptance phase was not supported, although a trend towards a more rapid full contact during weight acceptance was seen in the FI group. One might speculate on the meaning of this trend, should it be confirmed with another, larger sample. It is reasonable to suggest that either the gastrocnemius/soleus complex was unable to function adequately in energy absorption (Reiner et al., 2002) or the risk of loss of balance in a plantarflexed position was avoided by rapid descent to the more stable foot-flat position. The FI subjects in this study were limited in performance of toe rises, supporting the former interpretation. The later interpretation, however, is better supported by past research findings of impaired postural control (Hiller et al., 2004; Ross and Guskiewicz, 2004; Van Deun et al., 2007).

The instantaneous angular speed of the ankle on stair contact was different between ankles, but not groups. This finding does not fully support the hypothesis of differences between ankles in the FI subjects, or between the ankles of the FI and control groups. While the interaction did not reach significance, this main effect was primarily due to the greater speed of the uninvolved ankle of the FI group. This would suggest a deficit in control on the uninvolved ankle, given that this speed is not reflected on either ankle of the control group. An inability to effectively stabilize on the involved support limb while simultaneously preparing a stable weight acceptance position on the uninvolved limb may present in this manner. Monaghan et al. (2006) did report increased angular velocity in the frontal plane at heel strike during level surface walking in the involved ankle of FI subjects compared to the left ankle of controls. The uninvolved ankle was not monitored.

A trend to reversal of instantaneous linear velocity of the foot at the end of swing phase for the FI group suggests a hesitation with foot placement, possibly allowing more time to plan or execute the best projected foot placement on contact. This point in the stride cycle for stair descent corresponds to the “preparation for foot placement” as described by McFadyen and Winter (1988). One might reasonably speculate that a velocity reversal on approaching the step reflects less automatic processing, and could potentially influence stability depending on the

speed of forward progression of the head, arms and trunk. However, no overt loss of balance was recorded during the conditions of this study. As well, phase timing differences, if present, were subtle, as no between-group differences in swing time were found as might be expected if greater attention were required in the FI group when approaching the step. This finding could also be an indication of poor control, not a compensatory strategy. If so, the deficit would be in control of more proximal joints, such as at the knee or hip. Here, as well, the initial hypothesis of differences between ankles with this parameter was not supported, but a trend partially supports the difference between groups portion of the hypothesis.

Tracking Task

The tracking task did not discriminate between healthy control and FI subjects under either of the conditions (standing or supine in the magnet). As well, the correlations between the Beta signal intensity and the AI offered no further information. The original hypothesis that there would be differences between ankles in the FI group and between FI and control groups was not supported. A similar task has been used effectively in the hand in prior research (Carey et al., 1998; Carey et al., 1994; Lungu et al., 2007). This study used the tracking task with a new population in a new movement (inversion/eversion) of the ankle. Use of this task at the ankle have been reported only for one neurologically impaired subject performing dorsiflexion/plantarflexion (Carey et al., 2004). Based on the results of the current study, it is possible to assume that this task, at least with the parameters used here, is not an appropriate measure for the FI population or this paradigm. However, the possibility remains that modification of the tracking task, such as increasing the velocity of the movement or using a more familiar movement such as dorsiflexion/plantarflexion, may be more effective in revealing differences in skilled movements between FI subjects and healthy controls. Increasing the velocity of tracking may make the task more similar to functional activities where accurate foot placement is required. Use of a more familiar movement in addition to manipulating other task parameters may differentially reduce variability in the control group, should real between-group differences in performance exist. The addition of force parameters to the task may also more closely simulate the common weight bearing functional environment of the foot and ankle.

fMRI Analyses

Differences in cortical activation were demonstrated between ankles of each group and between groups. The original hypothesis of differences for this measure is supported. The paucity of research using brain imaging to examine lower extremity orthopedic conditions allows, and invites, speculation on the meaning of the results from this study. These findings can then stimulate further research to confirm or refute such speculations, and expand understanding of motor function in functional instability.

Level of Cortical Activation

The first notable observation from the fMRI analyses is the large volume of activation present for all subjects, most evident with the within-group analyses. Although possible to use tighter thresholds to limit significant intensity, this may then also have obscured real differences and been less informative. The large extent of activation may be viewed in light of the task requirements during tracking. Moving the ankle in an inversion/eversion motion for accuracy is a novel task. As subjects were not selected to be athletes for whom precision with skilled foot and ankle tasks was required, it is reasonable to assume that they had not previously attended to this motion with any regularity during daily activity. This can be contrasted to the more frequent need to attend to skilled movements of the hand while manipulating objects. As well, interlimb coordination is more tightly coupled in lower extremities in activities such as gait, where support on one leg and movement with the other are simultaneously required. The task for this study was unilateral. In addition, there was an element of stimulus response incompatibility in that the sine wave was oriented in a vertical direction, yet the required motion was performed in the frontal plane while the patient was horizontal. Such incompatibility may have increased the cortical processing required while accomplishing the tracking task (Dassonville et al., 2001).

Numerous authors have identified increased extent of activation with complex finger activities. Lotze et al.(2000), in a study of the somatotopy of M1 using finger movements, reported increased intensity of activation with more complex tasks. This included a disseminated pattern of activation in M1 and S1, activation in SMA, PMC, and ipsilateral M1. Gordon et al. (1998) reported similar results with more complex simulated typing activities in their study. Rao et al.

(1993) added variations in pacing to simple and complex finger movements and also reported a greater spatial range of activation with the complex tasks. While no simpler task was used in this study for comparison, task complexity was likely to have contributed to the broad areas of activation observed.

The subjects were able to perform the tracking task with apparent isolation of movement to the ankle when observed outside the magnet; however, no EMG values were obtained to rule out stabilizing activity of other lower limb muscles. Increased muscular activity of a level not appreciated during the pre-scan practice may have contributed to the observed distribution of activation. Monitoring the motion of the opposite, non-tracking ankle was performed during the fMRI session, and no significant mirror movement activity was recorded. Should contraction of other musculature have been a factor in the volume of cortical activation observed, it is unlikely that a bias between groups or limbs was introduced. While an argument may be made that the FI subjects would actively stabilize the involved limb to a greater extent, the outcome would then be greater activation while tracking with that ankle; this was not found to be the case. Tracking with both ankles in each group showed extensive activation.

Within-group Comparisons

For both groups, tracking with the involved/right ankle produced greater contralateral than ipsilateral activation in the PCL, while no difference was found between hemispheres with the uninvolved/left ankle. The PCL region was identified in this study to ensure analysis of all potential foot and ankle motor representation (Luft et al., 2002; Penfield and Rasmussen, 1950). In M1, also while tracking with the right ankle, the FI subjects demonstrated greater contralateral activation, while a trend to significance was found in control subjects. The region identified here as PCL is often descriptively included with M1 (Roland and Zilles, 1996). General descriptions of the role of M1 in motor function include movement execution (Gerloff et al., 1998; Roland and Zilles, 1996), movement sequence organization (Gerloff et al., 1998), and spatial and temporal processing for accuracy (Carey et al., 2006).

Bilateral activation was present in all regions investigated a priori in this study, and so comparisons were made between hemispheres for differences in relative activation. No other lower extremity studies compared the activity between subjects' limbs as was done for this

study. The available comparison literature generally recorded only the presence or absence of ipsilateral activation. DeBaere et al. (2001) reported primarily contralateral M1 activation during isolated dorsiflexion/plantarflexion using a group analysis and p-value, 0.05 corrected. Dobkin (2004) used a voxel count method to report contralateral S1/M1 activation with a corrected probability of 0.01 based on individual analyses. Sayhoun et al. (2004) reported relatively bilateral sensorimotor cortex activation with a similar task but a less stringent activation threshold of $p < 0.05$ corrected for individual analyses. Alkadhi et al. (2002), using an individual analyses, showed a small percentage (17%) of subjects demonstrated ipsilateral activation during dorsiflexion/plantarflexion of the ankle. No prior studies have used inversion/eversion of the ankle as a movement task. If one considers inversion/eversion in the presence of stimulus-response incompatibility to be a complex task, then greater ipsilateral activation than has been previously been reported would be expected with this study. Therefore the relatively greater contralateral activation in the FI subjects tracking with the involved ankle, compared both to the uninvolved ankle and both ankles of control subjects, suggests an alteration of motor control. Alternatively, it could suggest a pre-existing pattern that identifies those likely to develop FI following ankle trauma. However, differences between studies based on individual versus groups analyses and varying thresholds for significance may also influence study outcomes.

More symmetrical activation in the non-dominant limb for both groups may reflect the effect of lateralization of function such as a preference to perform skilled movements with the dominant limb. Higher correlations with hand preferences were found for skilled than for unskilled foot movements (Kalaycioglu et al., 2008), and it is reasonable to speculate that some corollaries exist between the extent of cortical lateralization found for skilled hand tasks in right-handed individuals and that for skilled foot tasks in right-footed individuals. Using a paced simple movement of flexion and extension of finger, knee, ankle, and toe, Kapreli et al. (2006) reported greater bilateral activation with movement of non-dominant limbs. Similar results have been reported for the upper extremity (Kim et al., 1993; Singh et al., 1998; Verstynen et al., 2005). Kim et al. (Kim et al., 1993) used fMRI to investigate hemispheric lateralization of the motor cortex during sequential opposition of the thumb and remaining four fingers (pacing/speed was not specified). Ten right-handed and five left-handed subjects were used. They concluded that hemispheric asymmetry was more pronounced in right- than left-handed subjects, and that the asymmetry was primarily when using the dominant, right hand. It should be noted that they

recorded activity in the precentral gyrus, which in the present study was divided into anterior (PMC) and posterior (M1) portions. Singh et al. (Singh et al., 1998) reported on the degree of ipsilateral activation from the Kim et al. study. These authors noted greater ipsilateral activation in the precentral gyrus in right-handed subjects when tracking with the left than right hand. Use of the left (non-dominant) hand in a sequence task resulted in bilateral M1 activation (Johansen-Berg and Matthews, 2002).

Conversely, in a study of right handed healthy subjects, Haaland et al. (Haaland et al., 2004) found no significant differences in the sensorimotor cortex (SMC) regarding hemispheric asymmetry between hands or tasks of varying complexity. These authors compared simple repetitive single finger movements with more complex sequence and chord movements between left and right hands. They did, however, find greater left PMC activity with the more complex sequence and chord (simultaneous button pressing of three of the four medial digits) activities independent of which hand performed the task, concluding the left PMC was involved in control of more complex activities and the SMC was involved only in execution. The lack of such a finding for left PMC for any of the within-group comparisons may be related to differences in the task requirements, as a continuous activity was employed in the present study, with consistent performance requirements.

Using control subject activation patterns as the norm, then, one could reasonably speculate that superimposed upon a normal difference in lateralization of activation between dominant and non-dominant ankles, the involved ankle of FI subjects showed an increased lateralization effect in M1. Kapreli et al. (Kapreli et al., 2006) reported greater contralateral than ipsilateral activation in M1 with healthy subjects performing dorsiflexion/plantarflexion without a skill component, also noting a greater lateralization effect with the dominant versus nondominant limb. The disparity between this finding and the trend in the current study may have resulted from the difference in task, speed (1.2 Hz versus 0.4Hz), or variability and subject number (18 versus 8 and 10). These authors also reported, however, that there was less of a lateralization effect for ankle movements than observed with finger movements, supposing that the differing functional requirements of hand versus ankle were represented by different activation patterns. A reasonable supposition, then, is that a greater degree of hemispheric lateralization in M1 of the FI group does represent a pertinent alteration of motor control, and may possibly be linked to the findings with the step task of speed differences suggesting greater difficulty with bipedal control.

Inter-hemispheric differences in S1 and SMA regions when tracking with the right ankle were found in the control group. The absence of these differences in the FI group is also of interest. The S1 region is described as the initial processing area for somatosensory information (Legon and Staines, 2006; Pollok et al., 2004). In S1 more symmetrical activation was found when tracking with the left ankle in both groups. Ciccarelli et al. (2005) studied right and left ankle movements and Dobkin et al. (2004) studied just right ankle movements; both reported only contralateral S1 activation. Sayhoun et al. (2004), Ashe and Ugurbil (1994), and Mattay and Weinberger (1999) all reported results of a combined primary sensorimotor region (S1/M1) which showed the addition of ipsilateral activation with more complex activities; however, statistical comparisons of the relative amount of activation between hemispheres were not reported. One may propose, then, based on the results for control subjects in this study, that a more contralaterally weighted activation of S1 is the norm in the dominant compared to the non-dominant limb. The absence of this finding in the FI subjects may reflect either altered sensory processing for the tracking task or less sensory input from the involved ankle.

Descriptions of the role of SMA in motor function describe activity with preparation and execution of sequential movements (Cunnington et al., 2002; Gordon et al., 1998; Rao et al., 1993; Roland and Zilles, 1996). In this study, activity in SMA with ankle motions showed no asymmetry in the FI subjects when tracking with either ankle, and a predominance of left SMA activity tracking with either ankle in the control group. This left SMA predominance in healthy subjects has been reported by several authors studying finger activity ((Babiloni et al., 2003; Rogers et al., 2004). Rogers et al. (Rogers et al., 2004) used fMRI to study 11 right-hand dominant subjects performing an auditorily paced finger extension movement. They analyzed the data using signal intensity changes and a path analysis to link SMA to sensorimotor cortex (SMC) activation to investigate the role of SMA in this activity. They reported a dominant role of left SMA in controlling these unilateral finger movements, as the level of left SMA activation was equal between left and right hand movements, whereas the right SMA was more active during left hand movement. They also observed a “pattern of connectivity” only between left SMA and the SMC of each hemisphere. Similar conclusions were drawn by Babiloni et al. (Babiloni et al., 2003) using a self-paced finger extension activity in 8 right-handed subjects. A similar left SMA activation was reported by Dassonville et al. (Dassonville et al., 1998) in an

investigation that added a condition of a predictable versus unpredictable sequence to the finger task demonstrated greater left hemisphere activation of SMA with use of either hand.

In contrast, Ciccarelli et al. (2005), found activation in the right SMA with activity in either ankle of their healthy subjects. Sayhoun et al. (2004) reported bilateral SMA activation during active right ankle movement, and relatively symmetrical (based on Z-scores presented) bilateral SMA activation when comparing active to passive motion conditions. Kapreli et al. (Kapreli et al., 2006) also reported no asymmetry in SMA with ankle movements. In the current study, task complexity may play a role in the difference between the present results and those of Ciccarelli et al., Sayhoun et al., and Kapreli et al., who used simple dorsiflexion/plantarflexion movements. Dobkin (2004) reported left SMA activation for his subjects, tracking with presumably the right ankle (not clearly stated but implied) but did not study left ankle movement. Left SMA activation has been reported with a wrist and ankle movement coordination task of the right extremities that was not present with isolated movements (Debaere et al., 2001). A decrease in left SMA activation was reported in the presence of a distracting cognitive task during a left finger task (Johansen-Berg and Matthews, 2002). It does not appear that a right finger task was tested, .

The lack of a left SMA predominance in the FI subjects may represent a failure to recruit appropriate resources for the complexity of the task. Whether this is a predisposition of those likely to develop FI, or a consequence of the injury remains unclear. The ability to perform as well on the task as the healthy subjects invites further investigation of the significance of this finding.

Qualitative comparisons of patterns of hemispheric lateralization in the regions investigated suggest that cortical activation associated with the uninvolved non-dominant left ankles of the FI subjects is not substantially different from that associated with the non-dominant left ankle of healthy control subjects, with the exception of a lack of predominance in left SMA for left ankle activity. However, when tracking with the involved dominant right ankle compared to the dominant right ankle of controls, both a greater lateralization effect in M1 and a lesser effect in S1 and SMA were seen in the FI subjects. This most likely is due to multiple factors, only some of which may be postulated from other reports in the literature. Varying sensory processing and lack of appropriate recruitment of available resources may be two such factors.

Between-group Comparisons

The question with these analyses was which voxels showed greater activation in the control group during track, and then which voxels showed greater activation in the FI group during track during the same task. Therefore, regions similarly activated in both groups were not identified. The total area identified for each comparison, based on voxel count, is considerably less in these comparisons than the significant voxels found in the within-group analyses (Appendices Z and AD). While intriguing to consider how these regions of activation relate to those found with the within-group analyses, caution must be used. It is important to recall that different statistical thresholds were used in the within- and between-group analyses. As well, the data were extracted for the regions of interest defined based on anatomic boundaries. Localization of activation within each area is limited by the spatial smoothing and application of multiple subjects' functional data to one subject's anatomical image. Some differences in location of cluster center of mass were reported for regions showing increased activation in each group (Table 8) and in the FI group for each ankle (Table 6), but it was not possible with this analysis to specifically identify and compare the voxels found with each analysis. Instead, this discussion focuses on the functions attributed to the ROIs where differences in activation were identified.

In general, more regions of greater signal intensity were found in the control group during tracking than in the FI group in most brain regions analyzed. The finding of more robust activation in the control group suggests a diminished response in the FI group as the abnormal finding. There is no other fMRI literature to assist with interpretation which addresses motor function in a presumably neurologically intact population with an orthopedic complaint. Possibly less global activation is a marker for those who develop FI. Conversely, a pattern of diminished activity could reflect a decreased connectivity across cortical regions that is somehow triggered by poor recovery from the initial sprains. Two regions, however, did show greater activation in the FI group than controls when tracking with either ankle.

The left PMC showed voxels of greater activity in the FI group than in the control group when tracking with either ankle. The role of the PMC in motor activity guided by sensory information and during planning of newly learned sequences before movement initiation has been described (Roland and Zilles, 1996). Ashe and Ugurbil (1994) summarized that the PMC

was particularly active during movement in response to visual stimuli, which is the case with the motor task in this study. Perhaps the FI group is more attentive to visual stimuli due to inaccurate or diminished sensory input from the ankle or due to the inability to effectively process sensorimotor information. Dassonville et al. (2001) reported increased activity when their subjects needed to respond to a stimulus in an incongruent manner. Their task was a right hand task in right-handed individuals. The incompatibility of the ankle tracking task in the present study has already been discussed, and may play a role in the observed activation. However, the right PMC was consistently activated in the Dassonville study. An fMRI study of the steps in a mental rotation task (encode, indicate, rotate, match and respond) demonstrated significant bilateral activity in the dorsal premotor cortex during the rotation portion of the task (Lamm et al., 2007). The Lamm et al. study further noted greater left PMC activation during the matching step whereby the subjects compared their mental rotation with another figure. As only right-handed subjects responding with the right hand were studied, further clarification of hemispheric localization is not available.

Sayhoun et al. (2004) reported bilateral PMC activation with simple active ankle motion, but statistical comparisons between right and left hemisphere intensities were not provided. Ciccarelli, however, did not identify PMC activation when studying cortical processing during ankle movements (2005). Lotze et al. (2000) reported increased PMC activation with increasing complexity of a finger task, but did not report on lateralization. Lafleur et al. (2002) noted bilateral PMC activation with the execution of left foot dorsiflexion and plantarflexion movements in response to an auditory stimulus. Right foot movement was not tested. This activation was present during the early, but not later, learning phase of an explicitly taught sequence. These authors used positron emission tomography (PET) as the imaging modality. The most appealing and congruent previous finding is increased activation in the left PMC with attention compared to distraction during right finger tasks of varying complexity (Rowe et al., 2002). As the left fingers were not tested, it remains unclear whether the attention function resides in the left PMC for tasks with either extremity or simply in the contralateral hemisphere. However, the study of Haaland et al. (Haaland et al., 2004), comparing both right and left finger tasks of varying complexity, did find greater left PMC activation for the more complex tasks regardless of which hand was performing. The possibility exists that for the FI subjects, the tracking task for the involved ankle was more difficult, and recruitment of the voxel group not utilized by the control subjects resulted in comparable performance to the control group.

The primary somatosensory cortex also showed voxels in the left hemisphere of the FI subjects with greater activation than control subjects, regardless of which ankle was tracking. Attention to the task may have influenced activation here, although the localization to the left hemisphere cannot be explained. Meyer et al. (1991), in a PET study, reported a significant influence of attention on blood flow in the somatosensory cortex during presentation of a sensory stimulus to a finger. During a coordination activity of wrist and ankle movement, an increase in contralateral sensorimotor activity, beyond that found with isolated wrist and ankle movements, has been reported (Debaere et al., 2001). Activation of S1 in both hemispheres was recorded during sequential, but not repetitive, simulated typing tasks, including a task with only the right index finger (Gordon et al., 1998). Both the coordination task of Debaere et al. and the sequential tasks of Gordon et al. appear to require greater attention by the subject than more simple movements, although this was not specifically measured.

The third region showing greater activation in the FI subjects was the anterior cingulate cortex (ACC). This region was more active only in the left hemisphere while tracking with the right ankle, and showed no activity in the control group with the within-group analysis. Activation in the ACC with attentional requirements has been reported by several authors. A decrease in anterior cingulate activity was reported when a distraction task was added during a sequential button-pressing task (Johansen-Berg and Matthews, 2002) and an increase was observed when learning a new finger movement sequence compared to attending to a previously learned automatic sequence (Jueptner et al., 1997). Anterior cingulate cortex activity was related to learning a continuous finger tracking task under conditions of stimulus-response incompatibility, and diminished as the task was mastered (Lungu et al., 2007). Others have indicated, however, that this region is also active with simple ankle movements (Dobkin et al., 2004; Kollias et al., 2001).

While localization to the left hemisphere for SI and PMC activation when tracking with either the right or left ankle cannot be fully explained, greater activation of these regions in the FI group may be linked to greater attention to the task in this group. The ACC region has a greater body of research implicating its role in attention to challenging tasks, and combined with the findings from SI and PMC, supports the conclusion that attention is a significant factor in the differences in cortical activity between the FI and control groups. The task used in this study

was novel for the subjects and contained a component of stimulus-response incompatibility, making it a challenging task. While achieving similar performance levels, the FI subjects displayed differences in cortical processing that suggest the tracking task was more difficult for them to accomplish than it was for the control subjects. It is not clear whether or not this increased attention was an explicit choice on the part of the FI subjects. Future studies could ask subjects to rate task difficulty.

Summary of Outcomes for Hypotheses

1. There will be significant differences in the movement parameters of a step cycle when repeatedly descending a stair, between involved and uninvolved FI ankles and between FI subjects and healthy controls.
 - a. There will be greater trial to trial variability in the excursion of inversion/eversion and dorsiflexion/plantarflexion as measured by the coefficient of multiple correlations.
 - b. There will be a difference in the time for swing and weight acceptance phases.
 - c. There will be a difference in linear velocity in preparation for foot placement phase of swing and in the angular speed on step contact.

No differences were found for the variability in excursion in inversion/eversion or dorsiflexion/plantarflexion between ankles within the FI group, or between the FI and control groups. No differences were found in swing time, and a trend to faster weight acceptance phase in the FI subjects compared to control subjects. While not significant, there was a trend to a reversal of linear velocity at 80% of swing phase for the FI subjects compared to control subjects. An unexpected finding of a significant difference for ankle, but not group or interaction, was present for the instantaneous angular speed at forefoot contact, with the uninvolved/left ankles being faster than the right. Inspection of the means suggested that this was largely due to the speed of the FI uninvolved ankle, with a low probability for the interaction effect.

2. The accuracy of ankle movement, measured by an accuracy index while tracking a sine wave, will be less during inversion and eversion for involved versus uninvolved ankles and for FI versus healthy control subjects.

This hypothesis was not supported between ankles of the FI group or between groups.

3. There will be a difference in cortical activation measured during the tracking task between involved and uninvolved ankles of FI subjects and control subjects measured.

This hypothesis was supported with differences between ankles of the FI group and differences between the FI and control groups.

Study Limitations

The small N, for both the kinematic and brain imaging investigations, was a limitation. The fact that some significance was found even with small numbers, however, supports that real differences exist.

The results of this study can be generalized to persons meeting the inclusion criteria of FI, ages 18-50, and both sexes. Given the broad range of acceptable incidence of giving-way and recurrent sprains in the FI subjects, as well as the potential inclusion of control subjects with a history of sprain, it is possible that true differences between groups were masked. Sufficient time may not have elapsed following an initial sprain for the manifestation of FI to be apparent in control subjects who had experienced a sprain, resulting in possible group misclassification.

Designed as an exploratory investigation, the broad scope of this study prevented specific comparisons of tracking task characteristics needed to confirm or refute issues raised by the brain imaging results. However, differences were found supporting the basic premise of the study. While it was expected that performance accuracy differences would be demonstrated with the tracking task, this was not found. Advances in statistical comparisons such as group analysis (e.g. using only right-involved subjects), and design complexity (e.g. collecting data from both ankles within the same scanning session) that have occurred since the inception of the study would have strengthened the fMRI analysis. In addition, the issue of fMRI reliability must be mentioned. Between session and between run baseline and activation variability have been reported. However, the Beta signal intensity method of analysis used in this study has been found to be the most reliable (Kimberley et al., 2008). A technology limitation is the

potential for imprecise localization of SMA due to the close proximity of each hemisphere along the mesial walls.

As previously described for the tracking task, the orthosis did not dictate the position of dorsiflexion/plantarflexion assumed by the subject either standing or supine. Therefore the available range of inversion/eversion for each subject was influenced by this self-selected position. Those assuming a more plantarflexed position would then have had a larger excursion in inversion/eversion available to them. However, as the excursion was individually determined, and the Accuracy Index standardized for each subject, this would not have influenced comparisons between subjects.

Recording only one step in sequence, rather than several in the midst of a sequence in the step down task, may have impacted the type of variability seen, as initiation of an activity from a stationary position could have different control requirements than continuous activity. Also, the anatomic coordinate system used to define ankle/rearfoot motion was unique to this investigation, thereby limiting direct comparison to other studies. However, as no standardized system was established that included calcaneal landmarks, the system used was a reasonable choice. Technical limitations include the possibility of skin motion artifact resulting in extraneous movement of the sensors within a data collection period, the question of accuracy and repeatability when digitizing surface landmarks, and the difficulty of correctly orienting axes with the close proximity of the calcaneal landmarks.

Finally, no specific self-report or functional performance measures were used to categorize the relative degree of perceived disability or objective limitations. These measures may have helped to stratify subjects or enabled correlation with outcome measures to investigate a potential continuum of functional instability.

Future Research

To build upon these exploratory results, future investigations using a cognitive distraction task and possibly fatigue as components during the step down task are suggested. These added elements may mimic natural occurrences during functional activities that contribute to circumstances of instability. Pacing and varying the self-selected speed of descent, as well, may

be instructive to further clarify velocity and phase differences in FI subjects. Capturing multiple steps in sequence could also be used to magnify variability in the frontal plane ankle motions by eliminating preparation time between steps. Simultaneous capture of the kinematics of both limbs would further clarify the control demands between limbs for stability and foot placement, and might further explain the increased angular speed of the uninvolved FI ankle.

Determination of appropriate standardized self-report and objective functional performance measures for use in categorizing the spectrum of disability related to FI may be useful. Correlations could then be investigated between laboratory measured variables and functional limitations, potentially making more subtle relationships evident.

Modification of the tracking task to make it more sensitive to performance differences between FI and control subjects could further clarify factors related to motor skill. Use of a more familiar motion such as dorsiflexion/plantarflexion may make the task easier to better illustrate differences between groups that a more complex, unfamiliar task does not. Another modification could be to increase the velocity of tracking to better simulate functional ankle speeds. A different approach would be the addition of a force component, either through resistance or having a force target, to simulate the control requirements in weight bearing. Use of a random wave form, as a proxy for response to the unique foot placement and balance requirements of each step may also be informative.

In addition, manipulation of the tracking task and inclusion of distraction tasks during brain imaging could be used to investigate the particular regions most associated with attentional differences that potentially exist between groups. Incorporating increased sensory stimuli from the ankle, such as was done with a simple piece of tape to improve balance performance (Matsusaka et al., 2001) may also reveal differences in S1 processing between healthy and control subjects, and be a method of exploring the effect of attention on performance and cortical activation. If modifications of the tracking task resulted in performance differences between groups, than training to improve performance while monitoring cortical activation patterns may indicate key factors in therapeutic interventions to improve ankle stability. Alternatively, exploration of a different movement paradigm for use with fMRI could be beneficial. Inclusion of plantar surface contact and targeted foot placement might better simulate the functional requirements of the ankle while eliminating the influence of motion of

the entire lower extremity and trunk which occurs when performing the step down task. Concurrent activation pattern changes in S1, PMC, and ACG would then further support the present speculation of these regional changes as markers of differential attentional requirements in FI.

Monitoring of multiple lower limb muscles with EMG, and training to localize muscle recruitment to the prime movers of the desired ankle motion may also influence the extent of activation and allow more discreet cortical localization to those areas most critical to ankle function.

Clinical Implications

Extension of this research offers several potential clinical benefits. First, identification of clinical markers of the alteration in motor control suggested by these laboratory findings could be used for prospective research to determine whether the differences between FI and healthy subjects are solely a result of the ankle sprain and inadequate recovery or a likely precipitating factor with sprain occurrence in predisposed individuals. Should it be determined that a pre-existing finding is a significant predictor of FI, screening in sports, particularly early in athletic participation, may be useful in curtailing the prevalence of this condition. Validated preventative measures could then be employed, such as taping or bracing, balance training or yet to be determined motor skill training.

A second, related benefit may be in the early identification of those most likely to develop FI following a first-occurrence ankle sprain. Whether this identification is based on a predisposition to development of recurrent complaints, or is related to the nature of the specific injury and acute rehabilitation is yet to be determined. However, it is not likely to be effective and cost efficient to invest intensive rehabilitation in all ankle sprain sufferers to address that portion of the population who will become chronic. Identification of those most likely to benefit from services may then decrease overall healthcare costs while improving individual well-being or more effectively targeting the current healthcare expenditures related to ankle sprain.

A third potential benefit of better understanding of the nature of FI is the development of enhanced treatment strategies for those already affected by instability. Balance training has been shown to decrease injury rates in soccer players with a history of instability (Tropp et al., 1985a) and to improve postural control in FI subjects (Gauffin et al., 1988; Rozzi et al., 1999). It may be that other interventions incorporating factors yet to be studied could also be employed to improve skill and motor control in those with FI. These factors may include distraction, fatigue, and rapid response to changing surface or target foot placement conditions while in weight bearing. Other methods of skill training, such as a modification of the tracking task may also prove beneficial. It would be hoped that the addition of other effective treatment components would further improve outcomes in individuals with FI by addressing all contributing elements.

Conclusion

In summary, differences in cortical processing during a skilled ankle movement task were identified in sensorimotor areas relating to hemispheric lateralization, potentially linked to the bilateral functional control requirements at the ankle and possibly attention to movement between subjects with functional instability and healthy controls. The results also suggest that while activity performance on a skilled task was comparable between groups, the FI group experienced that task as more difficult. Physical performance differences were also identified in the ability to rise onto toes and heels and in time for rapid stair descent. Kinematic differences between FI subjects and healthy controls were found for instantaneous angular speed at contact with the stair when stepping down, and for the time while progressing from forefoot contact in plantarflexion to full weight bearing. These findings confirm alterations in motor control, and invite further investigation of the nature of the alterations and the environmental and task factors that contribute to functional instability.

APPENDIX A

LATERAL PREFERENCE INVENTORY – FOOT SUBSCALE

Choose “right”, “left”, or “either” in response to the following questions:

1. With which foot would you kick a ball to hit a target?
2. If you wanted to pick up a pebble with your toes, which foot would you use?
3. Which foot would you use to step on a bug?
4. If you had to step up on a chair, which foot would you place on the chair first?

Scoring:

One point per question, positive for “right”, negative for “left”, and no score for “either”.

Coren, S., (1993). A lateral preference inventory for measurement of handedness, footedness, eyedness, and earedness: norms for young adults. *Bulletin of the Psychonomic Society*, 31 (1), 1-3

APPENDIX B

Diabetic Foot Screen for Loss of Protective Sensation

Gillis W. Long Hansen's Disease Center, LEAP Program, 5445 Point Clair Road, Carville, LA 70721

Filament Application Instructions:

- 1) Show the filament to the patient and touch it to his/her hand or arm so that he/she knows it does not hurt.
- 2) Use the 10 gram filament to test sensation at the indicated sites on each foot as shown. Apply the filament along the perimeter of and NOT on an ulcer, callous, scar, or necrotic tissue.

- 3) Hold the filament perpendicular to the skin and use a smooth motion when testing. Use a 3 step sequence that includes (1) touch the skin, (2) bend the filament, and (3) lift from the skin (See Figures 1-3). Do not use rapid movement. The approach, skin contact, and departure of the filament should be approximately 1½ seconds duration.

- 4) Ask the patient to respond "yes" when the filament is felt. If the patient does not respond when you touch a given point on the foot, continue on to another site. When you have completed the sequence, REPEAT the area(s) where the patient did not indicate feeling the filament.
- 5) Use the filament in a random sequence.
- 6) On the form, indicate with a minus sign, "—", the areas where the patient did not respond to the filament. LOSS OF PROTECTIVE SENSATION AT ANY ONE OF THE EIGHT SITES INDICATES A FOOT AT HIGH RISK.
- 7) If you wish to clean the filament, use sodium hypochlorite (household bleach) 1:10 solution or follow the infection control disinfecting guidelines in your facility.

<http://bphc.hrsa.gov/leap/Screening.htm>

APPENDIX C

Edinburgh Handedness Inventory

Subject number _____

Date _____

Please indicate your preferences in the use of hands in the following activities by putting a √ in the appropriate column. If in any case you are really indifferent, mark both columns. Some of the activities require both hands. In these cases the part of the task, or object, for which hand preferences is wanted is indicated in brackets.

	Task	Right	Left
1	Writing		
2	Drawing		
3	Throwing		
4	Scissors		
5	Toothbrush		
6	Knife (without fork)		
7	Spoon		
8	Broom (upper hand)		
9	Striking match		
10	Opening box (lid)		
TOTAL			
Determination			

Oldfield, R. C. (1971). The assessment and analysis of handedness: the Edinburgh inventory. *Neuropsychologia* 9, 97-113.

APPENDIX D

Sports and Leisure Activity Scale*

Highest performance level is chosen for rating.

1. International level contact sports	Soccer, handball, basketball, volleyball, football
2. College Competition level contact sports	Soccer, handball, basketball, volleyball
3. Non-contact sports (a)	tennis, badminton, squash, gymnastics, hockey
4. Non-contact sports (b)/leisure activities	track and field, soccer, handball, basketball, volleyball, tennis, squash, badminton, orienteering
5. sports/leisure activities	cross country skiing, running on uneven surfaces >5 times per week
6. leisure activities	jogging on uneven surfaces >2 times per week
7. leisure activities	occasional jogging on uneven surfaces
8. leisure activities	walking on uneven surfaces
9. leisure activities	walking on even surfaces
10. sedentary	no consistent exercise activity

* adapted from Konradsen L, Bech, L, Ehrenberg, M, Nickelson T (2002). Seven years follow-up after ankle inversion trauma. Scandinavian Journal of Medicine & Science in Sports, 12, 129-135

APPENDIX E

Subject Demographic Comparison Statistics

Factor	All		Right-involved fMRI	
	t statistic (df = 38)	p-value	t statistic (df = 16)	p-value
Age	1.069	0.292	0.057	0.955
Height	-0.253	0.802	0.364	0.720
Weight	0.873	0.388	1.925	0.072
	Φ	p-value	Φ	p-value
Sex	-0.056	0.740	0.040	1.000
Hand preference	0.280	0.182	0.271	0.446
Anterior drawer + involved/right ankle	-0.651	<0.001*	-0.671	0.015*
uninvolved/left ankle	-0.197	0.407	-0.200	0.559

Φ = Fisher's Exact Correlation Coefficient

* - significant at $\alpha = 0.05$

APPENDIX F

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PARTICIPANT CONSENT FORM

Movement Accuracy and Cortical Activation in Functional Ankle Instability

You are invited to be in a research study examining control of ankle movements and which areas of the brain are active during these movements. The ankle movements are those of descending steps and also following a cursor on a computer screen. The study will examine the performance of people with continuing problems with an ankle after an ankle sprain (repeated sprains under “normal” conditions which probably wouldn’t cause a first time sprain, or feelings of the ankle “giving way”) compared to people without such complaints. You were selected as a possible participant because (1) you have sustained an ankle sprain which limited weight bearing at the time of injury and are experiencing continuing incidences with the same ankle or (2) you are a non-affected person of similar age and sex to the symptomatic subjects and you choose your right foot kicking a ball, and other activities. We ask that you read this form and ask any questions you may have before agreeing to be in this study.

This study is being conducted by Kathleen Anderson, MBA, PT, James Carey, PhD, PT, and Paula Ludewig, PhD, PT, in the Physical Therapy Department at the University of Minnesota.

Procedures:

If you agree to be in this study, we would ask you to do the following things:

Undergo manual testing of your ankle mobility and strength, and to check for swelling and tenderness. If you have had knee or hip injuries or surgeries, you will be asked to squat as far to the floor as possible pain free.

Answer questions to determine which foot you prefer to use for activities.

Answer questions about how you originally injured your ankle, and under what conditions you have experienced additional problems.

Descend two flights of stairs, walking, while timed. Rise on the toes of each foot up to 45 times, and rise on the heel of each foot up to 45 times (to check strength and endurance).

Wear sensors taped to your heel and shin, and have bony landmarks on your leg and foot touched with a device to record their position. A pad will also be taped to the bottom of your foot to indicate exactly when you touch the step. The sensors are connected to a computer which tracks your foot position using small magnetic signals. You will then descend two steps barefoot while a computer records how you placed your foot as you stepped down. You will be asked to keep your eyes focused on a marker directly in front

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of you. You will repeat this ten times on the same ankle, then rest for five minutes, and repeat the process on the other ankle. You will also walk 5 feet on level surface 10 times for each ankle. You will balance on each foot up to one minute standing on a beam 4 inches high. This will take up to one and one-half hours.

Wear an ankle motion measuring device (goniometer) while you move your ankle in and out to move a cursor on a computer screen, tracing a figure. The ankle tracking task may be performed while you are lying in the MRI scanner, which will take about an hour. This will be done on a day separate from the step activity in the scanner, and on the same day if not in the scanner. Time to complete the tracking task if you are not in the scanner will be about one half hour.

Some subjects will be randomly assigned to the scanner, with your chances being slightly less than 1 in 2. Magnetic Resonance Imaging (MRI) is a technique used to look at the brain, and is commonly used in hospitals and clinics. During the MRI scan, a strong magnet attached to the computer creates pictures of the brain that tell which parts were active when the scan was performed. The magnetic strength of this device has been approved by the Food and Drug Administration; however, the long term risks of this strength are not yet known.

During the scan, you will be able to communicate with the researchers and leave the scanner if you wish. You will also have a few minutes before the start of the experiment to experience being in the MRI machine.

Risks and Benefits of Participating:

There are no risks beyond those of normal daily life for descending the steps, and no known risks for using the electromagnetic sensors in the step task, as the magnetic field for this particular test is weak. There is a minor risk of skin irritation from the tape used to secure the sensors, such as that from removing a bandage. There could be adverse effects that we do not yet know about.

With regard to the MRI, most people experience no ill effects from the large magnetic field of the MRI, but some people report dizziness, mild nausea, headache, a metallic taste in their mouth, or a sensation of flashing lights. These symptoms, if present, subside shortly after leaving the magnet. If you have had any surgeries or have any metal implants such as aortic valve replacements, joint implants, metal sutures, or a cardiac pacemaker, we need to know about them as they may be contraindicated for the MRI. If you have any metal implants in your head, receiving the MRI may result in death or injury (dental fillings are ok). See Medical History Appendix. There could be adverse effects we do not yet know about. You will be in a semi-enclosed, dark, and humid environment for about an hour. This may be very difficult for you if you have

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claustrophobia. The scanner is also noisy. You will be given ear plugs to muffle the sound, and wear headphones and a microphone which will allow you to communicate with the researchers.

There are no anticipated benefits to participating in the study.

Costs:

You will not receive payment for participation in this study.

Research Related Injury:

In the event that this research activity results in an injury, treatment will be available, including first aid, emergency treatment and follow-up care as needed. Care for such injuries will be billed in the ordinary manner, to you or your insurance company. If you think you have suffered a research related injury let Kathy Anderson (612-626-3554) or Jim Carey (612-626-2746) know right away.

Confidentiality:

The records of this study will be kept private. In any sort of report we might present or publish, we will not include any information that will make it possible to identify you as a subject.

Voluntary Nature of the Study:

Your decision whether or not to participate will not affect your current or future relations with the University. If you decide to participate, you are free to withdraw at any time without affecting those relationships.

New Information:

If during the course of this research study there are significant new findings which might influence your willingness to continue, the researchers will inform you of those developments.

Contacts and Questions:

You may ask any questions you have now. If you have question later, you may call Kathy Anderson (612-626-3554), James Carey (612-626-2746) or Paula Ludewig (612-626-0420).

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If you have any questions or concerns regarding this study and would like to talk to someone other than the researchers, contact the Patient Relations Department, University of Minnesota, Mayo Mail Code-310, B310 Mayo Memorial Building, 420 Delaware Street SE, Minneapolis, MN 55455; telephone 612-273-5050.

You will be given a copy of this form to keep for your records.

Statement of Consent:

I have read the above information. I have asked questions and received answers. I consent to participate in the study.

Signature _____ Date _____

Signature of Investigator _____ Date _____

Medical History Appendix
Screening Form With Exclusionary Criteria

1. Have you had any other injuries or surgeries to either leg, apart from your ankle sprain? If so, please explain.	YES NO
2. Do you have any visual problems?	YES NO
3. Do you have any heart or breathing problems?	YES NO
4. Are you claustrophobic?
(afraid of enclosed places)	YES NO
5. Have you had any surgeries?	YES NO
6. Do you have Diabetes?	YES NO
7. Are you able to ascend and descend steps pain free?	YES NO
8. Have you had any problems with seizures?
If so, please specify:	YES NO
9. Are you on any medication? Please list.	YES NO
10. Do you have any difficulties with balance or dizziness?	YES NO
11. Do you have any allergies to adhesive tape, or skin sensitivities?	YES NO
12. Are you or do you suspect you may be pregnant?	YES NO
13. Are you feeling in good health today?	YES NO

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The following items may be hazardous and can not be allowed in the MRI

Please indicate if you have any of the following:

YES	NO	
_____	_____	Cardiac pacemaker
_____	_____	Aneurysm clip
_____	_____	Implanted cardiac defibrillator*
_____	_____	Any type of electrodes (eg. Brain, heart or spinal cord stimulator)
_____	_____	Cochlear implant
_____	_____	Implanted insulin pump
_____	_____	Catheter
_____	_____	Halo vest or cervical fixation device
_____	_____	Hearing aid
_____	_____	Implanted drug infusion device (eg. Baclofen. pump)
_____	_____	Any foreign body eg; shrapnel, bullet
_____	_____	Artificial heart valve
_____	_____	Any type of ear implant
_____	_____	Eye prosthesis*
_____	_____	Any type of implant
_____	_____	Any surgical clips or staples
_____	_____	Vascular access port
_____	_____	Intraventricular shunt*
_____	_____	Artificial limb or joint
_____	_____	Dental Hardware i.e.; braces, retainer
_____	_____	IUD
_____	_____	Wire mesh
_____	_____	Any orthopedic implants: pins, rods, screws, nails, etc.
_____	_____	Non-removable body piercing

The above information is correct to the best of my knowledge. I have read and understand the entire contents of this form and have had the opportunity to ask questions regarding the information on this sheet.

Subject's signature _____ **Date** _____

Investigator _____

***Definitions:**

- A defibrillator is any agent or measure, eg. an electric shock that stops fibrillation of the heart muscle and restores the heart beat to normal.
- A prosthesis is a man-made substitute for a diseased or missing part of the body.
- A shunt is a tube that redirects fluid from one part of the body to another.

APPENDIX G

HIPAA¹ AUTHORIZATION TO USE AND DISCLOSE INDIVIDUAL HEALTH INFORMATION FOR RESEARCH PURPOSES

- 1. Purpose.** As a research participant, I authorize Kathleen Anderson, James Carey, Paula Ludewig and the researchers' staff to use and disclose my individual health information for the purpose of conducting the research project entitled "Movement Control and Cortical Activation in Functional Ankle Instability", Human Subjects Code Number 0209M32681.
- 2. Individual Health Information to be Used or Disclosed.** My individual health information that may be used or disclosed to conduct this research includes: Age, gender, height, weight, occupation, hand and foot dominance, history of orthopedic injuries, functional limitations related to these injuries, medical history related to safety in the MRI and ability to repeatedly climb stairs, current sporting/recreational activity level, and skin allergies to adhesive tape.
- 3. Parties Who May Disclose My Individual Health Information.** The individual health information will be obtained only from measurement during the research or by my report.
- 4. Parties Who May Receive or Use My Individual Health Information.** The individual health information disclosed by parties listed in item 3 and information disclosed by me during the course of the research may be received and used by Kathleen Anderson, James Carey, Paula Ludewig and the researchers' staff.
- 5. Right to Refuse to Sign this Authorization.** I do not have to sign this Authorization. If I decide not to sign the Authorization, I will not be allowed to participate in this study or receive any research related treatment that is provided through the study. However, my decision not to sign this authorization will not affect any other treatment, payment, or enrollment in health plans or eligibility for benefits.
- 6. Right to Revoke.** I can change my mind and withdraw this authorization at any time by sending a written notice to Kathleen Anderson, Program in Physical Therapy, University of Minnesota, MMC 388, 420 Delaware Street S.E., Minneapolis, MN 55455, to inform the researcher of my decision. If I withdraw this authorization, the researcher may only use and disclose the protected health information already collected for this research study. No further health information about me will be collected by or disclosed to the researcher for this study.
- 7. Potential for Re-disclosure.** My individual health information disclosed under this authorization may be subject to re-disclosure outside the research study and no longer protected. Examples include potential disclosures for law enforcement purposes, mandated reporting of abuse or neglect, judicial proceedings, health oversight activities and public health measures.

This authorization does not have an expiration date.

¹ HIPAA is the Health Insurance Portability and Accountability Act of 1996, a federal law related to privacy of health information.

I am the research participant or personal representative authorized to act on behalf of the participant.

I have read this information, and I will receive a copy of this authorization form after it is signed.

Page 2, HIPAA Authorization

“Movement Control and Cortical Activation in Functional Ankle Instability”

University of Minnesota Human Subjects Code number 0209M32681

signature of research participant or research participant's
personal representative

date

printed name of research participant or research participant's
personal representative

description of personal representative's authority to act on behalf
of the research participant

APPENDIX H

STABILITY OF SENSOR SIGNAL/EFFECT OF METAL IN FLOOR

Sensor readings with transmitter at 11 inches above the floor, sensors secured to a board and stabilized at the specified distance above the floor. Transmitter reference frame is +X forward (tested at approximately 24 inches) from transmitter, +Z is towards floor (height varied per platform and step height), and +Y to right. Position of sensor 2 in relation to sensor 3 was recorded, and maintenance of this positional relationship is monitored in the Y direction.

Height from floor	Trial #	Rotation One	Rotation Two	Rotation Three
4 inches	1	142.5	33.7	166.2
	2	142.5	33.7	166.2
	3	142.5	33.7	166.2
11 inches	1	142.4	33.5	166.4
	2	142.3	33.6	166.5
	3	142.4	35.6	166.4
18 inches	1	142.6	33.3	166.3
	2	142.7	33.3	166.3
	3	142.7	33.3	166.3

APPENDIX I

DIGITIZATION POINTS USED TO ESTABLISH 3-D COORDINATE SYSTEMS

	Localization of point	Rationale/Information provided
Shank		
1	Medial most point of medial tibial plateau	Midpoint used
2	Lateral most point of the lateral tibial plateau	
3	Medial most point of medial malleolus	Midpoint used
4	Lateral most point of lateral malleolus	
1	Medial most point of medial tibial plateau	Non-collinear point
5	Most anterior point of tibial tuberosity	Indicator of positive direction
Foot		
6	Medial most point of proximal calcaneal tuberosity	Midpoint used
7	Lateral most point of proximal calcaneal tuberosity	
8	Medial most point of distal calcaneal tuberosity	Midpoint used
9	Lateral most point of distal calcaneal tuberosity	
10	Dorsal aspect of 2 nd metatarsophanlangeal joint	Non-collinear point
11	Dorsal aspect of 5th metatarsophanlangeal joint	Indicator of positive direction

APPENDIX J

Calculation of Angular Data

The initial kinematic data recorded was the position of the sensors relative to the transmitter as the subject moved. Prior to motion recording, the position of the selected anatomic landmarks were recorded relative to the respective local sensor. To make use of the defined anatomical coordinate systems, and to describe the movements as motion of the calcaneus relative to the tibia, matrix algebra was used.

1. A transformation matrix (4x4) was used to convert the anatomic landmarks' positions to be relative to the local sensors rather than the transmitter. Tibial landmarks are related to sensor 2 on the distal shin, and calcaneal landmarks were related to sensor 3 on the medial posterior calcaneus.
2. Local coordinate systems are established relative to the local sensor. The Z axis of the tibia was established by taking the midpoint of the tibial plateau landmarks and the malleolar landmarks, and describing a unit vector directed superiorly as positive. The intermediate X axis was established by taking the midpoint of the malleolar landmarks, and the lateral malleolus landmark, and describing a unit vector directed laterally as positive. The cross product of these vectors was used to establish the Y axis, directed anteriorly as positive. The X axis was then created to be orthogonal by the cross product of Z and Y axes. The right hand rule determined the order of computing the cross product, to ensure the desired positive direction. These were described for the right tibia. For the left, Y was positive facing posteriorly. For the Z axis of the calcaneus, the midpoints of the proximal and distal landmarks were used to describe the positive axis superiorly directed. The intermediate Y axis was calculated from the orthogonal intersection of a line from the dorsal surface of the second metatarsophalangeal joint landmark with the Z axis, positive anteriorly, and the X axis from the cross product of the Z and Y. The Y axis was created to be orthogonal by the cross product of Z and X.
3. A transformation matrix was used to convert motion description of the local coordinate system from local sensor reference to transmitter reference.
4. A transformation matrix was used to describe the orientation of the calcaneal axes relative to the tibial axes, from the previous orientation in relation to the transmitter.
5. The final rotation matrix was in the form of direction cosines.
6. The Cardan sequence chosen to describe the data was Z-Y-X. The rotation angle can be derived from the matrix using the following formulae:

- a. Angular rotation about Z = $\tan^{-1} (R_{21}/R_{11})$
 - b. Angular rotation about Y = $\tan^{-1} (-R_{31} / \sqrt{R_{11}^2 + R_{21}^2})$
 - c. Angular rotation about X = $\tan^{-1} (R_{32}/R_{33})$
- R11 R12 R13
Where $R_{C/T} = \begin{matrix} R21 & R22 & R23 \\ R31 & R32 & R33 \end{matrix}$

APPENDIX K

Summary of Missing Kinematic Data.

Group	Ankle	Deviation	# steps
Control	Left	No heel contact	1
Control	Right	No heel contact	1
FI	Involved	No heel contact	1
FI	Involved	No heel contact	1
FI	Involved	No heel contact	2
FI	Uninvolved	No heel contact	6 §
FI	Uninvolved	No toe contact	2
FI	Involved	No heel contact	8 §
FI	Uninvolved	No heel contact	1
FI	Involved	No toe contact	3

§ - not used in analysis of weight acceptance phase

APPENDIX L

Descriptive Statistics for Physical Performance Single Leg Balance.

		Time (s) Median (IQR)	Within-group Comparisons			Between-group Comparisons			
			Wilcoxon Signed-rank*	n	p- value	Mann- Whitney U*	n ₁	n ₂	p- value
FI	all (N = 20)								
	involved ankle	60 (0)	1.378	10	0.168	-0.563	20	20	0.573
	uninvolved Ankle	60 (0)				0.95	20	20	0.342
	fMRI (N = 8)								
	involved ankle	60 (0)	0.875	8	0.382	-1.006	8	10	0.314
	uninvolved ankle	60 (0)				‡	8	10	‡
Control	all (N = 20)								
	right ankle	60 (0)	0.000	10	1.00				
	left ankle	60 (0)							
	fMRI (N = 10)								
	right ankle	60 (0)	0.000	10	1.00				
	left ankle	60 (0)							

FI – Functional instability

• - Z-value approximation with continuity correction

‡ - all scored perfectly, unable to compute

not significant at $\alpha = 0.05$

APPENDIX M

Descriptive Statistics for Physical Performance Heel Rises

		Number Median (IQR)	Within-group Comparisons			Between-group Comparisons				
			Wilcoxon Signed- rank*	n	p- value	Mann- Whitney U	n ₁	n ₂	p- value	
FI	all (N = 20)									
	involved ankle	32.5 (24.5)	0.919	20	0.358	-2.018	20	20	0.041	* }
	uninvolved ankle	36.5 (15.8)				-1.604	20	20	0.109	
	fMRI (N = 8)									
	involved ankle	28 (32.0)	1.207	8	0.228	-1.443	8	10	0.149	
	uninvolved ankle	35.5(14.8)				-0.683	8	10	0.494	
Control all (N = 20)										
	right ankle	40 (9.8)	0.42	20	0.674					
	left ankle	40 (5.3)								
	fMRI (n= 10)									
	right ankle	40 (12.8)	0.661	10	0.509					
	left ankle	40 (8)								

FI – Functional Instability

• Z-value approximation with continuity correction

* significant at $\alpha = 0.05$

APPENDIX N

Descriptive Statistics for Physical Performance Toe Rises

		Number Median (IQR)	Within-group Comparisons			Between-group Comparisons			
			Wilcoxon Signed- rank*	n	p- value	Mann- Whitney U	n ₁	n ₂	p- value
FI	all (N = 20)								
	involved ankle	40 (4)	0.597	20	0.551	-3.081	20	20	0.002
	uninvolved ankle	40 (3)				-1.627	20	20	0.104
	fMRI (N = 8)								
	involved ankle	36 (18.0)	0.798	8	0.425	-2.757	8	10	0.006
	uninvolved ankle	37.5(8.8)				-2.381	8	10	0.018
Control all (N = 20)									
	right ankle	40 (0)	1.388	20	0.168				
	left ankle	40 (0)							
	fMRI (n = 10)								
	right ankle	40 (0)	0.000	10	1.000				
	left ankle	40 (0)							

*

*

*

FI – Functional instability

• Z-value approximation with continuity correction

* significant at $\alpha = 0.05$

APPENDIX O

Descriptive Statistics for Physical Performance Stair Descent.

		Time (s) Median (IQR)	Mann Whitney U	$n_1 = n_2$	p-value
All Subjects					
	FI	17.42 (3.57)	1.907	20	0.056
	control	15.14 (1.95)			
fMRI					
		Mean ($\pm$ SD)	t statistic	df	
	right-involved FI	18.88 (3.16)	0.735	16	0.473
	control	17.42 (4.8)			
FI – Functional instability					
Not significant at $\alpha = 0.05$					

APPENDIX P

Correlation of Calf Tightness and Reduced Heel Rises

		Φ	p-value
Functional Instability	All		
	involved ankle	0.167	0.642
	uninvolved ankle	0.208	0.650
	fMRI		
	right-involved ankle	0.500	0.429
	uninvolved ankle	0.500	0.486
Controls	All		
	right ankle	0.250	0.549
	left ankle	0.250	0.549
	fMRI		
	right ankle	0.750	0.133
	left ankle	0.750	0.133

Φ – Fisher's Exact Test Correlation Coefficient

Not significant at $\alpha = 0.05$

APPENDIX Q

Mixed Model ANOVA Results for Fisher Z-transformed Coefficients of Multiple Correlations for Step Down Task.

Factor	df	F-ratio	p-value
Group – FI or control	1/38	0.00	0.972
Ankle – involved/right or uninvolved/ left	1/38	1.07	0.307
Group x ankle interaction	1/38	0.16	0.691
Motion – IV/EV or PF/DF	1/38	117.11	0.00*
Group x motion interaction	1/38	0.02	0.888
Ankle x motion interaction	1/38	1.26	0.269
Group x ankle x motion interaction	1/38	0.72	0.402

FI – Functional instability, IV – inversion, EV-eversion, PL – plantarflexion, DF – dorsiflexion

*significant at $\alpha = 0.05$

APPENDIX R

Mixed Model ANOVA Results for Time of Swing Phase.

Factor	df	F-ratio	p-value
Group – FI or control	1/38	1.20	0.250
Ankle – involved/right or uninvolved/left	1/38	0.01	0.926
Group x ankle interaction	1/38	0.00	0.946
FI – Functional instability			
Not significant at $\alpha = 0.05$			

APPENDIX S

Mixed Model ANOVA Results for Weight Acceptance Phase.

Factor	df	F-ratio	p-value
Group – FI or control	1/38	2.98	0.092
Ankle – involved/right or uninvolved/left	1/35	1.93	0.173
Group x ankle interaction	1/35	1.49	0.230
FI – Functional instability			
Not significant at $\alpha = 0.05$			

APPENDIX T

Mixed Model ANOVA Results for Ankle Instantaneous Angular Speed.

Factor	df	F-ratio	p-value
Group – FI or control	1/37	0.35	0.559
Ankle – involved/right or uninvolved/left	1/35	4.63	0.038 *
Group x ankle interaction	1/35	2.42	0.129

FI – Functional Instability

* - significant at $\alpha = 0.05$

APPENDIX U

Mixed Model ANOVA Results for Instantaneous Linear Velocity of the Foot in the Forward (Y) Progression at 80 % of Swing Phase

Factor	df	F-ratio	p-value
Group – FI or control	1/38	3.34	0.075
Ankle – involved/right or uninvolved/left	1/36	2.77	0.105
Group x ankle interaction	1/36	0.82	0.370

FI – Functional instability

APPENDIX V

Scatter plot of instantaneous angular speed at forefoot contact of individual subjects. FI – Functional instability.

APPENDIX W

Scatter plot of instantaneous linear velocity of the foot in the forward (Y) direction at 80% of swing phase of individual subjects. FI – Functional instability.

APPENDIX X

Descriptive Statistics for Instantaneous Angular Speed at Forefoot Contact and Instantaneous Linear Velocity in the Forward Progression (Y), Including Outliers.

	Functional Instability		Controls	
Ankle	Involved	Uninvolved	Right	Left
Median Angular Speed (IQR) (°/s)	97.4 (51.4)	116.0 (50.9)	100.0 (25.1)	94.7 (55.2)
Median Linear Velocity (IQR) (m/s)	-0.08 (0.14)	-0.03 (0.13)	0.03 (0.28)	0.00 (0.26)

APPENDIX Y

Descriptive and Comparison Statistics for the Ankle Tracking Task.

		AI (%) Median (IQR)	Within-group Comparisons			Between-group Comparisons			
			Wilcoxon Signed- rank ^a	n	p- value	Mann- Whitney U ^a	n ₁	n ₂	p- value
FI	all (N = 20)								
	involved ankle	51.11 (30.92)	0.878	20	0.38	-1.768	20	20	0.239
	uninvolved ankle	50.74 (35.34)		20		-0.176	20	20	0.86
	fMRI (N = 8)								
	right-involved ankle	47.63 (36.33)	0.35	8	0.726	0.222	8	10	0.824
	uninvolved ankle	44.26 (50.8)		8		-0.222	8	10	0.824
Control	all (N = 20)								
	right ankle	59.97 (23.82)	0.728	20		0.467			
	left ankle	50.71 (24.33)		20					
	fMRI (N = 10)								
	right ankle	50.25 (51.12)	0.714	10	0.476				
	left ankle	54.41 (64.25)		10					

AI – Accuracy Index; FI – Functional Instability

^a Z-value approximation with continuity correction

APPENDIX Z

Scatter plots of Accuracy Indices for the ankle tracking task of individual subjects using inversion and eversion movements. A -10-second standing task performed by all 40 subjects, B - 60 second supine ankle tracking task performed by 8 right-involved and 10 control fMRI subjects. FI – Functional instability.

APPENDIX AA

Scatter plots of Beta signal intensity of individual right-involved FI subjects while tracking with A – the involved (right) ankle and B – the uninvolved (left) ankle. Ipsi – hemisphere ipsilateral to the tracking ankle, contra – hemisphere contralateral to the tracking ankle. M1 – primary motor cortex, PCL – paracentral lobule, S1 – primary sensory cortex, PMC – premotor cortex, SMA – supplementary motor area, PSMA – pre-supplementary motor area.

APPENDIX AB

Scatter plots of Beta signal intensity of individual control subjects while tracking with A – the right ankle and B – the left ankle. Ipsi – hemisphere ipsilateral to the tracking ankle, contra – hemisphere contralateral to the tracking ankle. M1 – primary motor cortex, PCL – paracentral lobule, S1 – primary sensory cortex, PMC – premotor cortex, SMA – supplementary motor area, PSMA – pre-supplementary motor area.

APPENDIX AC

Beta Signal Intensity for Both Groups Tracking with Each Ankle in the Anatomically Defined Cortical Regions.

	Tracking Right		Tracking Left	
	FI	Control	FI	Control
	Mean Beta ($\pm$ SD)	Mean Beta ($\pm$ SD)	Mean Beta ($\pm$ SD)	Mean Beta ($\pm$ SD)
IM1	0.428 (0.374)	0.445 (0.350)	0.600 (0.270)	0.434 (0.220)
CM1	0.753 (0.345)	0.584 (0.260)	0.751 (0.275)	0.464 (0.394)
IPCL	0.619 (0.445)	0.358 (0.722)	0.671 (0.269)	0.837 (0.301)
CPCL	0.780 (0.376)	0.744 (0.338)	0.781 (0.353)	0.872 (0.495)
IS1	0.510 (0.325)	0.360 (0.350)	0.478 (0.309)	0.393 (0.221)
CS1	0.544 (0.296)	0.524 (0.323)	0.620 (0.224)	0.439 (0.360)
IPMC	0.657 (0.359)	0.546 (0.559)	0.782 (0.309)	0.296 (0.439)
CPMC	0.796 (0.519)	0.622 (0.402)	0.770 (0.370)	0.413 (0.624)
ISMA	0.626 (0.381)	0.525 (0.318)	0.774 (0.285)	0.737 (0.411)
CSMA	0.731 (0.368)	0.662 (0.269)	0.707 (0.255)	0.618 (0.407)
IPSMA	0.369 (0.254)	0.299 (0.339)	0.403 (0.322)	0.343 (0.197)
CPSMA	0.378 (0.260)	0.264 (0.380)	0.379 (0.186)	0.311 (0.315)
ACG	0.262 (0.288)	0 (0)	0 (0)	0 (0)

FI – Functional instability, IM1 and CM1 – ipsilateral and contralateral primary motor cortex, IPCL and CPCL – ipsilateral and contralateral paracentral lobule, IS1 and CS1 – ipsilateral and contralateral primary sensory cortex, IPMC and CPMC – ipsilateral and contralateral premotor cortex, ISMA and CSMA – ipsilateral and contralateral supplementary motor area, IPSMA and CPSMA – ipsilateral and contralateral pre-supplementary motor areas, ACG – anterior cingulate gyrus.

APPENDIX AD

Paired Test Statistics for Right-involved Functional Instability Subjects Tracking with Each Ankle (df = 7, n = 8).

	Involved (Right) Ankle		Uninvolved (Left) Ankle	
	t or Z Statistic (df or n)	p-value	t or Z Statistic (df or n)	p-value
M1	4.57 (9)	0.003*	1.69 (7)	0.135
PCL	-2.48 (9)	0.042*	-1.12 (7)	0.301
S1	0.67 (9)	0.525	-1.74 (7)	0.126
PMC	0.63• (8)	0.529	-0.13 (7)	0.902
SMA	1.33• (8)	0.183	-1.06 (7)	0.326
PSMA	0.15 (9)	0.888	-0.32 (7)	0.759

M1 – primary motor cortex, PCL – paracentral lobule, S1 – primary sensory cortex, PMC – premotor cortex, SMA – supplementary motor area, PSMA – pre-supplementary motor area, ACG – anterior cingulate gyrus. • Wilcoxon Signed-rank Z-value approximation with continuity correction, *significant at $\alpha = 0.05$.

APPENDIX AE

Paired Test Statistics for Control Subjects Tracking with Each Ankle.

	Right Ankle		Left Ankle	
	T or Z Statistic (df or n)	p-value	T or Z Statistic (df or n)	p-value
M1	-2.25 (9)	0.051	0.41 (8)	0.690
PCL	2.65• (10)	0.008*	0.36 (8)	0.725
S1	3.92 (9)	0.004*	-0.60 (8)	0.562
PMC	0.49 (9)	0.639	1.11 (8)	0.299
SMA	3.69 (9)	0.005*	-3.47 (8)	0.008
PSMA	0.92• (10)	0.359	0.71• (9)	0.478

M1 – primary motor cortex, PCL – paracentral lobule, S1 – primary sensory cortex, PMC – premotor cortex, SMA – supplementary motor area, PSMA – pre-supplementary motor area, ACG – anterior cingulate gyrus. •Wilcoxon Signed-rank Z-value with continuity correction, *significant at $\alpha = 0.05$.

APPENDIX AF

Number of Significant Voxels ((p(Bonf) < 0.05)) per Region from Within-group fMRI Analyses.

	FI Right ankle	FI Left ankle	Control Right ankle	Control Left ankle
IM1	2292	2708	4811	446
CM1	3195	2640	6589	4849
IPCL	765	1479	880	1852
CPCL	1489	804	1853	882
IS1	3776	4114	8439	7189
CS1	4413	6776	9402	8888
IPMC	8619	7145	10632	3759
CPMC	8029	8172	10629	7189
ISMA	3596	3029	3658	3249
CSMA	3114	3470	3142	2657
IPSMA	2421	985	1971	811
CPSMA	1648	1255	2807	1061
ACG	304	0	0	0

FI - functional instability, IM1 and CM1 – ipsilateral and contralateral primary motor cortex, IPCL and CPCL – ipsilateral and contralateral paracentral lobule, IS1 and CS1 – ipsilateral and contralateral primary sensory cortex, IPMC and CPMC – ipsilateral and contralateral premotor cortex, ISMA and CSMA – ipsilateral and contralateral supplementary motor area, IPSMA and CPSMA – ipsilateral and contralateral pre-supplementary motor area, ACG – anterior cingulate gyrus.

APPENDIX AG

Correlations Between Mean Beta Signal Intensity of the fMRI Within-group Analyses and the Accuracy Index Calculated from Tracking with the Right Ankle.

Region	Functional Instability (n = 8)		Control (n = 10)	
	r_s	p-value	r_s	p-value
IM1	0.57	0.139	-0.15	0.700
CM1	0.43	0.289	-0.10	0.798
IPCL	0.26	0.531	0.08	0.831
CPCL	0.45	0.260	0.17	0.668
IS1	0.26	0.531	-0.08	0.831
CS1	0.38	0.352	-0.13	0.732
IPMC	0.19	0.651	0.02	0.966
CPMC	0.24	0.570	0.05	0.899
ISMA	0.19	0.651	-0.1	0.798
CSMA	0.12	0.779	-0.22	0.576
IPSMA	0.14	0.736	-0.42	0.265
CPSMA	0.43	0.289	-0.48	0.187
ACG	0.33	0.420	0.0	0.0

IM1 and CM1 – ipsilateral and contralateral primary motor cortex, IPCL and CPCL – ipsilateral and contralateral paracentral lobule, IS1 and CS1 – ipsilateral and contralateral primary sensory cortex, IPMC and CPMC – ipsilateral and contralateral premotor cortex, ISMA and CSMA – ipsilateral and contralateral supplementary motor area, IPSMA and CPSMA – ipsilateral and contralateral pre-supplementary motor areas, ACG – anterior cingulate gyrus.

APPENDIX AH

Correlations between Mean Beta Signal Intensity of the fMRI Contrast between Track and Rest and the Accuracy Index Calculated from Tracking with the Left Ankle.

Region	Functional Instability (n = 8)		Control (n = 9)	
	r_s	p-value	r_s	p-value
IM1	-0.38	0.352	-0.65	0.058
CM1	-0.60	0.120	-0.40	0.286
IPCL	-0.21	0.610	-0.35	0.356
CPCL	-0.10	0.823	0.10	0.798
IS1	-0.45	0.260	-0.63	0.067
CS1	-0.48	0.233	-0.65	0.058
IPMC	-0.31	0.456	-0.07	0.865
CPMC	-0.70	0.058	-0.02	0.967
ISMA	-0.19	0.651	-0.28	0.460
CSMA	-0.33	0.420	-0.13	0.732
IPSMA	0.14	0.736	-0.53	0.139
CPSMA	-0.14	0.736	-0.32	0.406

IM1 and CM1 – ipsilateral and contralateral primary motor cortex, IPCL and CPCL – ipsilateral and contralateral paracentral lobule, IS1 and CS1 – ipsilateral and contralateral primary sensory cortex, IPMC and CPMC – ipsilateral and contralateral premotor cortex, ISMA and CSMA – ipsilateral and contralateral supplementary motor area, IPSMA and CPSMA – ipsilateral and contralateral pre-supplementary motor area, ACG – anterior cingulate gyrus.

APPENDIX AI

Paired Comparisons of Mean Beta Signal Intensity from the Same Brain Region While Tracking with Each Ankle.

	t or Z Statistic (df or n)	p-value
Region - control		
Left M1	1.532 (8)	0.164
Left PCL	0.890• (9)	0.399
Left S1	1.494 (8)	0.173
Right S1	-1.251 (8)	0.246
Left PMC	3.555 (8)	0.007*
Left SMA	-1.697 (8)	0.128
Right SMA	-1.010 (8)	0.341
Region – functional instability		
Left S1	0.484 (7)	0.643
Left PMC	1.019 (7)	0.342

• Wilcoxon signed-rank Z-value approximation with continuity correction

* significant at $\alpha = 0.05$

APPENDIX AJ

Number of Significant Voxels Showing Beta Greater Signal Intensity for One Group Compared to the Other Group during Tracking

	Tracking with right ankle		Tracking with left ankle	
	FI	Control	FI	Control
Right M1	†	663	†	1563
Left M1	†	1491	†	1645
Right PCL	†	†	†	354
Left PCL	†	531	†	1230
Right S1	†	455	†	1066
Left S1	100	1535	121	1093
Right PMC	†	613	†	†
Left PMC	1167	989	352	130
Right SMA	†	51	†	272
Left SMA	†	77	†	241

FI – Functional instability, $p < 0.001$, minimum cluster size = 50, † - no activation present

M1 – primary motor cortex, PCL – paracentral lobule, S1 – primary sensory cortex, PMC – premotor cortex, SMA – supplementary motor area

APPENDIX AK

Talaraich Coordinates for the Center of Mass of the Voxels Significantly* More Active in the Control Group Compared to Functional Instability Group Tracking with Each Ankle.

Tracking with right ankle							Tracking with left ankle					
	Right Hemisphere			Left Hemisphere			Right Hemisphere			Left Hemisphere		
	x	y	x	x	y	z	x	y	z	x	y	z
M1	33	-20	46	-34	-18	47	34	-19	43	-32	-19	43
PCL							2	-31	51	-3	-31	52
S1	34	-22	42	-37	-27	46	37	-21	41	-33	-25	43
PMC	36	-8	52	-33	-9	48						
SMA	2	-14	52	-1	-14	50	2	-19	55	-1	-19	55

* p < 0.001.

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