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EFFECTIVENESS OF A FOOT ORTHOSIS ON MUSCULAR ACTIVITY IN FUNCTIONAL ANKLE INSTABILITY –

A RANDOMIZED CONTROLLED TRIAL

An academic thesis submitted to
the Faculty of Human Sciences of the University of Potsdam

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by

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Hereby, I declare that this thesis, entitled "Effectiveness of a foot orthosis on muscular activity in functional ankle instability - a randomized controlled trial" or parts of the thesis, submitted to the Faculty of Human Sciences (Research Focus Cognition Sciences, Department of Sports and Health Sciences) of the University of Potsdam, have not yet been submitted for a doctoral degree to this or any other institution neither in identical nor in similar form. The work presented in this thesis is the original work of the author, created under guidance and mentoring of the responsible supervisors. I did not receive any help or support from commercial consultants. All parts or single sentences, which have been taken analogously or literally from other sources, are identified as citations. I am aware of the publicly accessible promotion regulation of the Faculty of Human Sciences of the University of Potsdam. In particular, I have noted the importance of § 18 and § 19. I am aware of the consequences with regard to false affidavits.

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TABLE OF CONTENTS

ABSTRACT

BACKGROUND: A majority of studies documented a reduced ankle muscle activity, particularly of the peroneus longus muscle (PL), in patients with functional ankle instability (FI). It is considered valid that foot orthoses as well as sensorimotor training have a positive effect on ankle muscle activity in healthy individuals and those with lower limb overuse injuries or flat arched feet (reduced reaction time by sensorimotor exercises; increased ankle muscle amplitude by orthoses use). However, the acute- and long-term influence of foot orthoses on ankle muscle activity in individuals with FI is unknown.

AIMS: The present thesis addressed (1a) acute- and (1b) long-term effects of foot orthoses compared to sensorimotor training on ankle muscle activity in patients with FI. (2) Further, it was investigated if the orthosis intervention group demonstrate higher ankle muscle activity by additional short-term use of a measurement in-shoe orthosis (compared to short-term use of “shoe only”) after intervention. (3) As prerequisite, it was evaluated if ankle muscle activity can be tested reliably and (4) if this differs between healthy individuals and those with FI.

METHODS: Three intervention groups (orthosis group [OG], sensorimotor training group [SMTG], control group [CG]), consisting of both, healthy individuals and those with FI, underwent one longitudinal investigation (randomised controlled trial). Throughout 6 weeks of intervention, OG wore an in-shoe orthosis with a specific “PL stimulation module”, whereas SMTG conducted home-based exercises. CG served to measure test-retest reliability of ankle muscle activity (PL, M. tibialis anterior [TA] and M. gastrocnemius medialis [GM]). Pre- and post-intervention, ankle muscle activity (EMG amplitude) was recorded during “normal” unperturbed (NW) and perturbed walking (PW) on a split-belt treadmill (stimulus 200 ms post initial heel contact [IC]) as well as during side cutting (SC), each while wearing “shoes only” and additional measurement in-shoe orthoses (randomized order). Normalized RMS values (100% MVC, mean±SD) were calculated pre- (100-50 ms) and post (200-400 ms) - IC.

RESULTS: (3) Test-retest reliability showed a high range of values in healthy individuals and those with FI. (4) Compared to healthy individuals, patients with FI demonstrated lower PL pre-activity during SC, however higher PL pre-activity for NW and PW. (1a) Acute orthoses use did not influence ankle muscle activity. (1b) For most conditions, sensorimotor training was more effective in individuals with FI than long-term orthotic intervention (increased: PL and GM pre-activity and TA reflex-activity for NW, PL pre-activity and TA, PL and GM reflex-activity for SC, PL reflex-activity for PW). However, prolonged orthoses use was more beneficial in terms of an increase in GM pre-activity during SC. For some conditions, long-term orthoses intervention was as effective as sensorimotor training for individuals with FI (increased: PL pre-activity for PW, TA pre-activity for SC, PL and GM reflex-activity for NW). Prolonged orthoses use was also advantageous in healthy individuals (increased: PL and GM pre-activity for NW and PW, PL pre-activity for SC, TA and PL reflex-activity for NW, PL and GM reflex-activity for PW). (2) The orthosis intervention group did not present higher ankle muscle activity by the additional short-term use of a measurement in-shoe orthosis at re-test after intervention.

CONCLUSION: High variations of reproducibility reflect physiological variability in muscle activity during gait and therefore deemed acceptable. The main findings confirm the presence of sensorimotor long-term effects of specific foot orthoses in healthy individuals (primary preventive effect) and those with FI (therapeutic effect). Neuromuscular compensatory feedback- as well as anticipatory feedforward adaptation mechanism to prolonged orthoses use, specifically of the PL muscle, underpins the key role of PL in providing essential dynamic ankle joint stability. Due to its advantages over sensorimotor training (positive subjective feedback in terms of comfort, time-and-cost-effectiveness), long-term foot orthoses use can be recommended as an applicable therapy alternative in the treatment of FI. Long-term effect of foot orthoses in a population with FI must be validated in a larger sample size with longer follow-up periods to substantiate the generalizability of the existing outcomes.

ZUSAMMENFASSUNG

HINTERGRUND: Eine Mehrzahl an Studien konnte bei Patienten mit funktioneller Sprunggelenksinstabilität (FI) eine reduzierte Muskelaktivität der Sprunggelenksmuskulatur, besonders des M. peroneus longus (PL), zeigen. Es gilt als valide, dass Schuheinlagen als auch sensomotorische Trainingsformen einen positiven Effekt auf die Muskelaktivität der Sprunggelenksmuskulatur bei Gesunden und Personen mit Überlastungsreaktionen der unteren Extremität oder flachem Fußgewölbe haben (reduzierte Reaktionszeit durch sensomotorisches Training; erhöhte Muskelamplitude durch den Gebrauch von Einlagen). Jedoch ist der Akut-und Langzeiteinfluss von Schuheinlagen auf die Muskelaktivität der Sprunggelenksmuskulatur bei Personen mit FI unbekannt.

ZIELE: Die vorliegende Arbeit befasste sich mit Akut (1a)- und Langzeiteffekten (1b) von Schuheinlagen im Vergleich zu sensomotorischem Training auf die Muskelaktivität der Sprunggelenksmuskulatur bei Patienten mit FI. (2) Des Weiteren wurde untersucht, ob eine Einlageninterventionsgruppe eine höhere Muskelaktivität durch den zusätzlichen kurzzeitigen Einsatz einer In-Schuh-Messeinlage (im Vergleich mit dem kurzzeitigen „nur Schuheinsatz“) nach der Intervention zeigt. (3) Als Voraussetzung wurde bewertet, ob die Muskelaktivität der Sprunggelenksmuskulatur zuverlässig (reproduzierbar) erfasst werden kann und (4) ob sie sich zwischen gesunden Personen von der bei Personen mit FI unterscheidet.

METHODEN: Drei Interventionsgruppen (Einlagengruppe [OG], Sensomotorische Trainingsgruppe [SMTG], Kontrollgruppe [CG]), bestehend aus je Gesunden und Personen mit FI, wurden einer Längsschnittuntersuchung (Randomisierte kontrollierte Studie) unterzogen. In der 6 wöchigen Interventionsphase trug die OG eine In-Schuh-Einlage mit einem spezifischen „PL Stimulationsmodul“, während die SMTG heimbasierte Übungen durchführte. Die CG diente dazu, die Test-Retest-Zuverlässigkeit der Muskelaktivität der Sprunggelenksmuskulatur (PL, M. tibialis anterior [TA] and M. gastrocnemius medialis [GM]) zu messen. Vor- und nach der Intervention wurde die Muskelaktivität der Sprunggelenksmuskulatur (EMG-amplitude) während „normalem“ unperturbiertem (NW) und perturbiertem Gehen (PW) auf einem „split-belt“-Laufband (Reiz 200 ms nach initialem Fersenkontakt [IC]) und während eines „Seitschrittes“ (SC) als Antäuschmaneuver, jeweils mit Tragen von „Nur-Schuhen" und mit zusätzlichen In-Schuh-Messeinlagen (randomisierte Reihenfolge), aufgezeichnet. Die normalisierten RMS-Werte (100% MVC, mean±SD) wurden vor (100-50 ms) und nach (200-400 ms) dem IC berechnet.

ERGEBNISSE: (3) Die Test-Retest Zuverlässigkeit zeigte eine hohe Streuung der Werte bei Gesunden und Personen mit FI. (4) Verglichen mit den Gesunden, zeigten Patienten mit FI eine geringere PL Voraktivität beim SC, jedoch eine höhere PL Voraktivität beim NW und PW. (1a) Der akute Einlagengebrauch beeinflusste die Muskelaktivität des Sprunggelenkes nicht. (1b) Für die meisten Konditionen war das sensomotorische Training effektiver bei Personen mit FI als die langfristige Einlagenintervention (erhöhte Aktivität: PL and GM Voraktivität und TA Reflexaktivität beim NW, PL Voraktivität und TA, PL und GM Reflexaktivität beim SC, PL Reflexaktivität beim PW). Jedoch war der langfristige Einlagengebrauch vorteilhafter im Sinne einer erhöhten GM Voraktivität beim SC. Für einige Konditionen war die langfristige Einlagenintervention genauso effektiv wie das sensomotorische Training bei Personen mit FI (erhöhte Aktivität: PL Voraktivität beim PW, TA Voraktivität beim SC, PL and GM Reflexaktivität beim NW). Langanhaltender Einlagengebrauch war auch bei gesunden Personen vorteilhaft (erhöhte Aktivität: PL und GM Voraktivität beim NW und PW, PL Voraktivität beim SC, TA und PL Reflexaktivität beim NW, PL und GM Reflexaktivität beim PW). (2) Die Einlageninterventionsgruppe wies keine höhere Muskelaktivität der Sprunggelenksmuskulatur durch den zusätzlichen kurzzeitigen Einsatz einer In-Schuh-Messeinlage beim Re-test nach der Intervention auf.

SCHLUSSFOLGERUNG: Große Variationen für die Reproduzierbarkeit spiegeln die physiologische Variabilität der Muskelaktivität während des Gehens wider und werden daher als akzeptabel erachtet. Die Hauptergebnisse bestätigen das Vorhandensein von sensomotorischen Langzeiteffekten von spezifischen Schuheinlagen bei Gesunden (primär-präventiver Effekt) und Personen mit FI (therapeutischer Effekt). Der neuromuskuläre kompensatorische Feedback- als auch der antizipatorische Feedforward-Anpassungsmechanismus auf die langfristige Einlagennutzung, insbesondere des M. peroneus longus, untermauert die Schlüsselrolle des PL in der Bereitstellung von essentieller dynamischer Sprunggelenksstabilität. Aufgrund seiner Vorteile gegenüber sensomotorischem Training (positives subjektives Feedback hinsichtlich des Komforts, Zeit- und-Kosteneffektivität), kann der langanhaltende Einlagengebrauch als geeignete

Therapiealternative in der Behandlung von FI empfohlen werden. Der Langzeiteffekt von Schuheinlagen in einer Population mit FI bedarf einer Validierung mittels höherer Stichprobengrößen und längerer Follow-up-Perioden, um die Verallgemeinerbarkeit der existierenden Studienergebnisse zu belegen.

List of Figures

List of Tables

Abbreviations

FI	functional ankle instability/functional instable participants/ ankles/group
H	healthy participants/ankles/group
EMG	electromyography/electromyographic
EMG-A	EMG-amplitude
TA	M. tibialis anterior
PL	M. peroneus longus
GM	M. gastrocnemius medialis
NW	normal (unperturbed) walking
PW	perturbed walking
SC	side cutting
pre	100-50 ms before IC
post/reflex	200-400 ms following IC
OG	orthosis group
SMTG	sensorimotor training group
CG	control group
Shoe	“shoe only” condition (without imbedded orthosis)
Orthosis	in-shoe orthosis condition (with imbedded orthosis)
M1	pre-test
M2	post-/re-test
ICC	intraclass correlation coefficient
CV	coefficient of variation
TRV	test-retest variability
SD	standard deviation
MVC	maximum voluntary (isometric) contraction
SLR	short latency response
MLR	medium latency response
LLR	late latency response
IC	initial heel contact
AMI	arthrogenic muscle inhibition
H-reflex	Hoffmann-reflex
TMS	transcranial magnetic stimulation
COP	center of pressure
SEBT	star excursion balance test
ACC	accelerometer
CAIT	Cumberland Ankle Instability Tool (Questionnaire)
FAAM	Foot and Ankle Ability Measure (Questionnaire)

CHAPTER I: INTRODUCTION

1. Theoretical Background/Preliminary Considerations

1.1 Clinical relevance of functional ankle instability

Epidemiology of ankle sprains and functional ankle instability

Injuries to the ligaments of the ankle complex are among the most common orthopaedic injuries in recreational activities and competitive sports, accounting for 10-30% of all sports trauma (Zöch, Fialka-Moser, & Quittan, 2003). Most ankle injuries are lateral ankle sprains (85%) (Zöch et al., 2003). In a systematic review of sports injuries sustained from 1977 to 2005, ankle sprain was the major ankle injury in 33 of 43 sports (Fong, Hong, Chan, Yung, & Chan, 2007). Another previous report, summarizing 16 years of National Collegiate Athletic Association injury surveillance data for 15 sports, indicated high injury rates for basketball, soccer, volleyball and gymnastics (1.01-1.30/1000 athlete-exposure)(Kobayashi & Gamada, 2014). Lateral ankle sprains have an incidence of about 2.15 per 1000 person-years and a lateral ankle sprain is estimated to occur per 10.000 person-days (Gutierrez et al., 2012; Hubbard & Wikstrom, 2010). The annual medical cost of treating lateral ankle sprains was found to be $1.1 billion in the United States' high school soccer and basketball programs (Kobayashi & Gamada, 2014). Approximately 55% do not seek injury treatment from a medical service (Gribble et al., 2013). The severity of ankle sprains may often be underestimated by athletes and health care professionals. Additionally, there is evidence that there is a two-fold increased risk for injury recurrence for at least one year after an acute ankle sprain (Janssen, van Mechelen, & Verhagen, 2011). The recurrence rate is varying according to the referred literature (32-74% (Gribble et al., 2013), 40-75% (Huang, Lin, Kuo, & Liao, 2011; Sefton et al., 2009), 30-80% (Palmieri-Smith, Hopkins, & Brown, 2009; Rosen et al., 2013)). In sports such as basketball, up to 70-80% of individuals with an initial ankle sprain could have injury recurrence (Delahunt et al., 2010; Delahunt, Monaghan, & Caulfield, 2007; Hertel, 2002). Typically, patients with functional ankle instability (FI) suffer from persistent residual symptoms or functional limitations as pain, swelling or weakness. They affect 30-72% of patients and 13-15% of patients remain occupationally handicapped (Arnold, Linens, De La Motte, & Ross, 2009; Hamlyn, Docherty, & Klossner, 2012; Morrison et al., 2010; O'Driscoll & Delahunt, 2011). Up to 72 % of individuals are unable to return to their previous level of activity (Hiller, Kilbreath, & Refshauge, 2011).

Injury mechanism

Most frequently, lateral ankle sprains occur during landing, cutting and sidestepping in sports activities with or without contact (Delahunt et al., 2007; Kobayashi & Gamada, 2014; Zöch et al., 2003). Typically, they appear following lateral movement that produces an excessive supination of the rearfoot about an externally rotated lower leg after initial contact of the foot (Cordova & Ingersoll, 2003; Hertel, 2002)(see Figure 1). Increased plantar flexion of the ankle joint may also be involved in the inversion injury mechanism (Zöch et al., 2003).

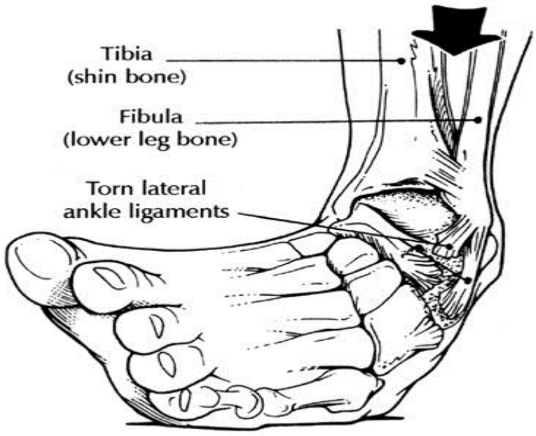

Figure 1: Ankle sprain mechanism (excessive supination [combined inversion, adduction and plantarflexion of the rear foot])

Terminology of functional ankle instability

In general, a universally approved definition (gold standard) of FI does not exist (Delahunt et al., 2010). FI is a clinical syndrome that may develop after suffering from several recurrent episodes of lateral ankle sprains (Santilli et al., 2005). It has been linked to an increased risk of developing ankle osteoarthritis (Koshino et al., 2015). There is no consensus about the definition of FI concerning the frequency and the timing of ankle sprains; the indications of authors vary (frequency of 1 to >3 sprains within the past (half) year, year before testing or in last 2 years) (Mitchell, Dyson, Hale, & Abraham, 2008; Munn, Sullivan, & Schneiders, 2010; Steib, Hentschke, Welsch, Pfeifer, & Zech, 2013). However, most authors refer to a minimum of 2 sprains within the past 2 years (Brown, Padua, Marshall, & Guskiewicz, 2008; Fu & Hui-Chan, 2005; Mitchell et al., 2008). FI is commonly characterized by the subjective sensation of giving way or feeling of joint instability in the absence of pathological ligament laxity during dynamic situations (Delahunt et al., 2010; Gutierrez, Kaminski, & Douex, 2009).

The development of residual symptoms after the initial ankle sprain has been initially termed “chronic ankle instability” (Hertel, 2002). Chronic ankle instability has been reported to be the most frequent and serious residual disability after initial sprains to the ankle lateral ligament complex (Delahunt, Monaghan, & Caulfield, 2006a; Hertel, 2002). In the widely accepted model of Hertel et al. (2002), “mechanical instability” and “FI” build together part of a continuum (Figure 2)(Hertel, 2002). Mechanical instability is thought to result from various anatomical changes (pathologic ligamentous laxity, arthrokinematic changes or degenerative changes that may exist in isolation or in combination). FI is proposed to result from functional insufficiencies such as impaired proprioceptive and neuromuscular control. According to Hertel et al. (2002), recurrent sprains occur in the presence of mechanical and functional insufficiencies (Hertel, 2002). These changes predispose the person to further episodes of chronic ankle instability. However, it is becoming more evident that CAI patients are quite a heterogeneous population regarding their impairments. Subsequently, for some patients this model is not adequate. One exemplary scenario is that some individuals report residual feelings of instability, but have not reinjured their ankle. This led to the consideration of a possible conglomeration of subgroups. Therefore, Hiller and colleagues (2011) refined the model by separating recurrent sprain from the presence of both instabilities (Figure 3)(Hiller et al., 2011). They expanded the number of subgroups from 3 to 7 to incorporate the unique sets of impairments characterising a specific subgroup (1. mechanical instability, 2. “perceived instability” [corresponding to “FI”], 3. recurrent sprain alone or 4.-7. these 3 groups in combinations). This homogeneity of subgroups helped determine more adequately the presence/absence of impairments, relationships among impairments, activity limitations and participant restrictions (Hiller et al., 2011).

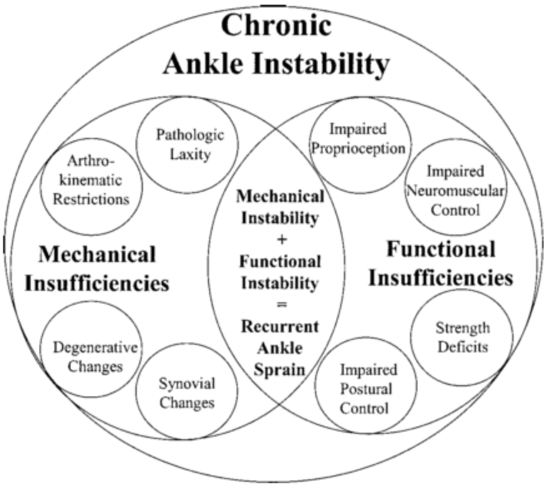

Figure 2: Paradigm of mechanical and functional insufficiencies contributing to "chronic ankle instability" (Hertel et al., 2002)

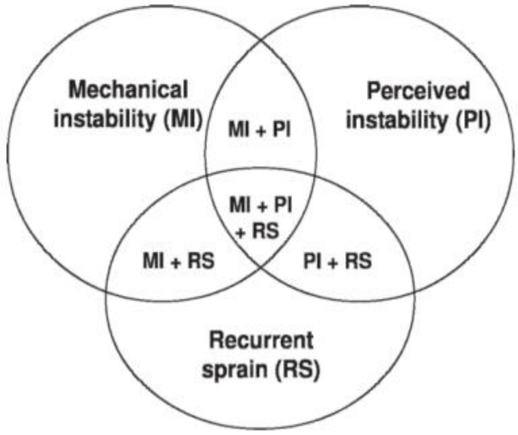

Figure 3: Model of "chronic ankle instability" demonstrating 7 possible sub-groups (Hiller et al., 2011)

The underlying neurophysiologic mechanism of the pathology FI is still unknown (Wikstrom, Bishop, Inamdar, & Hass, 2010), nevertheless numerous contributing factors to the development of FI have been presented in the literature. FI can be caused by proprioceptive, neuromuscular or postural control deficits and muscle weakness (Arnold et al., 2009; Hertel, 2002; Kobayashi & Gamada, 2014; Witchalls, Newman, Waddington, Adams, & Blanch, 2012). The individual causes of FI do not occur in isolation, but are more likely components of a complex pathoetiologic paradigm. The main causative factor attributing to FI is proprioceptor damage to mechanoreceptors in the lateral ligaments at the time of injury with subsequent partial de-afferentation of proprioceptive reflexes (Konradsen, 2002; Pintsaar, Brynhildsen, & Tropp, 1996). This famous theory was originally developed by Freeman et al. (Freeman, Dean, & Hanham, 1965). Consequently, the ligamentous mechanoreceptors never regenerate or regain normal functional capacity (McVey, Palmieri, Docherty, Zinder, & Ingersoll, 2005; Palmieri-Smith et al., 2009). A lack of proprioceptive information from partial de-afferentation (continual altered or interrupted peripheral afference from cutaneous receptors and joint mechanoreceptors) could chronically suppress the γ-motoneuron system and desensitize the muscle spindle, thus resulting in inhibition of the recruitment of type II α-motoneurons (McVey et al., 2005; Palmieri-Smith et al., 2009). This subsequently contributes to a diminished muscle function/efferent motor drive of the muscle due to the decreased ability to voluntarily activate musculature (Hopkins, Brown, Christensen, & Palmieri-Smith, 2009; McVey et al., 2005; Palmieri-Smith et al., 2009). This results in the presence of arthrogenic muscle inhibition (AMI), which denotes neurological shutdown of the muscles surrounding an injured, previously damaged joint (McVey et al., 2005; Palmieri-Smith et al., 2009). The presence of AMI has not been established yet in patients with functional ankle instability, but it there is preliminary evidence that it is present in the PL muscles of those patients. Other authors attribute damage to the deep branch of the peroneal nerve at time of initial injury to the development of FI (Hertel, 2002).

Stabilizing role of ankle muscles

During dynamic activities, stability of the ankle joint depends on passive structures and muscle reactions of voluntary and reflexive nature to prevent inversion sprains (Cordova & Ingersoll, 2003; Granacher, Gruber, Förderer, Strass, & Gollhofer, 2010; Hopkins et al., 2009). Neuromuscular (reflexive) activity of ankle musculature is theorized to play a pivotal role in individuals with FI (Feger, Donovan, Hart, & Hertel, 2015). The ankle muscles tibialis anterior (TA), peroneus longus (PL) and gastrocnemius medialis (GM) act as the most important ankle joint stabilizers. The TA and PL are crucial in protecting the ankle joint complex against unexpected destabilization (McVey et al., 2005). In particular, the PL muscle, as an evertor and plantarflexor of the foot, serves to maintain correct foot position in medio-lateral direction during heel contact and especially foot flat/mid-stance phase of the gait cycle (Hopkins et al., 2009; Suda, Amorim, & Sacco, 2009)(see Figure 4).

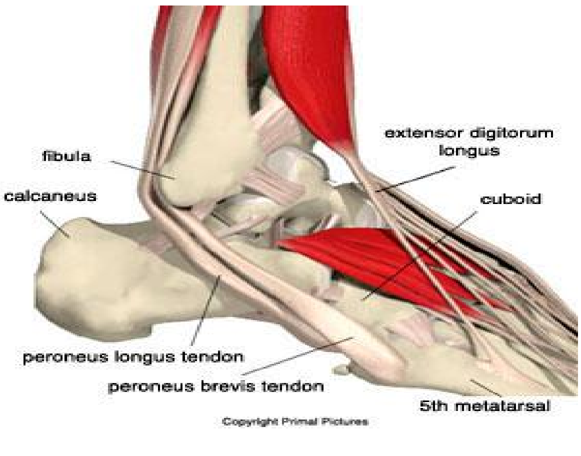

Figure 4: Course of the PL tendon (origin: proximally from lateral condyle of tibia and head of fibula, attachment: plantar lateral aspect of the first metatarsal and medial cuneiform)

In weight-bearing conditions, the primary role of the PL is to provide dynamic musculotendinous stability to the first ray (medial cuneiform, first metatarsal, and great toe) (Bellew, Frilot, Busch, Lamothe, & Ozane, 2010). Considering gait cycle (IC to IC), the PL is active during whole stance phase (Sutherland, 2001). Peak PL activity occurs during latter half/terminal stance phase when the weight of the body is plantar flexed onto and transferred over the forefoot, where propulsion of body weight occurs (Bellew et al., 2010). GM muscle is active at a similar phase, shortly after the PL, whereas TA muscle, as the antagonist, is active from IC (eccentric work) until the PL and GM take over the stabilizing role during the mid-stance phase (Sutherland, 2001). The TA is again active after toe off until the next IC (Sutherland, 2001). The PL muscle plays an integral role in controlling the amount of inversion occurring at the ankle joint by preventing a lateral heel strike (Hopkins et al., 2009; Hopkins, Coglianese, Glasgow, Reese, & Seeley, 2012; Palmieri et al., 2004). However, it has become evident that reflexive factors may not act quickly enough to prevent an ankle injury on their own, implying that pre-activity of ankle musculature before IC is essential to protect the joint against an unexpected event in a feedforward manner (Gutierrez et al., 2012; Hertel, 2002). Proper functioning of both, the open-loop (feedforward/preparatory) and closed-loop (feedback/reactive) neuromuscular control systems, is crucial for the maintenance of dynamic ankle joint stability (Gutierrez et al., 2012). An impaired activation of ankle muscles can result in uncontrolled rearfoot supination and inadequacies in the dynamic defence mechanism (Delahunt, Monaghan, & Caulfield, 2006b; Hopkins et al., 2009). Hence, it may leave the ankle vulnerable to injurious loads, which increases the risk of ankle sprains (Hertel, 2008; Palmieri-Smith et al., 2009).

Function and origin of reflex responses in FI

Individuals with FI have the potential to correct a possible inversion and prevent further damage by help of stretch reflex responses. The function of these responses might lie in balance control and/or in reduction of loading of the ankle in period after perturbation (inversion) moment (Nieuwenhuijzen & Duysens, 2007). Physiologically, the initial compensatory reflex response activity following perturbation/postural disturbance is a relatively unspecific immutable pattern, derived from spinal α-motoneurons activated by the stretch of muscle spindles. Those monosynaptic spinal stretch (short latency) reflexes (SLR) are mediated by Ia afferents and are highly involved 40-70 ms after stimulus, particularly of the TA muscle (Schillings, van Wezel, Mulder, & Duysens, 2000; Taube et al., 2006). The medium latency stretch reflex responses (MLR, 70-100 ms post stimulus) could be attributed to cutaneous responses and proprioceptive group I and II afferents, but also are mediated by transcortical influences (Schillings et al., 2000; Taube et al., 2006). The later part of the response during perturbed walking might be an appropriate strategy for final behavioural decision (e.g. to avoid the obstacle), which might be modified by external factors and can be adjusted to fit the actual nature/demands of the task (Schillings et al., 2000). Donahue et al. (2014) reported evidence of long-latency components of stretch reflex responses (LLR, >100 ms after stimulus) being independent on the level of background EMG activity (muscle activity before ground contact or perturbation), meaning that the LLR is a more voluntary, corrective response (Donahue, Docherty, & Riley, 2014). At least the LLR above 160 ms are partially under voluntary control and particularly those responses in later perturbation trials are much more selective (Nieuwenhuijzen & Duysens, 2007; Schillings et al., 2000). LLR were exclusively seen in the PL muscles and were greater and more consistent than the other reflex responses (Nieuwenhuijzen & Duysens, 2007).

1.2. Neuromuscular deficits in individuals with functional ankle instability

There exists evidence for neuromuscular control deficits predisposing individuals to the development of repeated episodes of the ankle giving way (Gutierrez et al., 2012; Wikstrom et al., 2010). The term neuromuscular control defines the unconscious activation of dynamic restraints occurring in preparation for and in response to joint motion and loading for the purpose of maintaining and restoring functional joint stability (Riemann & Lephart, 2002). Neuromuscular deficits can be deficiencies in cutaneous sensation, neuromuscular firing/recruitment patterns, muscle-spindle activity (mediated through the γ-motoneuron system) or nerve-conduction velocity (Hertel, 2002). The most common reported deficiency is an impaired balance control with postural instability in patients with FI (Delahunt et al., 2006a; Hertel, 2002; Munn et al., 2010). FI has also been associated with deficiencies in sensorimotor function in terms of impaired feedback and feedforward mechanisms of motor control strategies (Gutierrez et al., 2009; Hertel, 2008; Hopkins et al., 2009; Munn et al., 2010). This leads to a delayed and diminished reflex response in the ankle joint evertors. Subsequently, the reflex response of the ankle joint evertors (PL) does not respond fast, nor strong enough to prevent a sudden unexpected inversion perturbation. Recent research has shown that the PL muscle does not adequately prepare the ankle joint complex for expected contact with the ground during landing (Akhbari, Ebrahimi Takamjani, Salavati, & Ali Sanjari, 2007; Holmes & Delahunt, 2009). Recent studies additionally identified a decreased sensitivity on the plantar surface of the foot in individuals with chronic ankle instability (Hoch, McKeon, & Andreatta, 2012). Hoch et al. (2012), as well as Powell et al. (2014), found individuals with chronic ankle instability had significantly higher detection thresholds during the vibrotactile stimulation of the plantar cutaneous mechanoreceptors/afferents at the head of the first metatarsal (p=0.01, base of the fifth metatarsal (p<0.001 and the heel (p=0.01)(Hoch et al., 2012; Powell, Powden, Houston, & Hoch, 2014). They additionally demonstrated postural control deficits with eyes open for mean of time-to boundary (TTB) minima (=magnitude of TTB measure)(p=0.01) and the standard deviation of TTB minima (variability of TTB measure) in the anterior-posterior direction (p=0.02) tested by the Balance Error Scoring System (Powell et al., 2014). TTB measurements quantify double-and single-limb stance postural steadiness deficits. They predict the time it takes the spatiotemporal COP to reach the limits of the base of support. Lower TTB measures are associated with greater postural unsteadiness, that is, less time is available to recover from a balance perturbation (Cobb, Joshi, Bazett-Jones, & Earl-Boehm, 2012; Knapp, Lee, Chinn, Saliba, & Hertel, 2011). Hoch et al. (2012) and Powell et al. (2014) have indicated these alterations in plantar cutaneous somatosensation may help explain the underlying mechanisms associated with the sensorimotor system impairments in individuals with chronic ankle instability (Hoch et al., 2012; Powell et al., 2014). Electromyography (EMG) has also been used in the assessment of neuromuscular control as it allows the timing and degree of muscle activity to be determined during functional tasks (O'Driscoll & Delahunt, 2011). Several studies have investigated ankle muscle activity deficits during normal walking on a treadmill (Barlow, Donovan, Hart, & Hertel, 2014; Feger, Donovan, Hart, & Hertel, 2014; Feger et al., 2015; Maclellan et al., 2014; Santilli et al., 2005). An impaired magnitude of ankle muscle activity and of reflex responses during simulated unexpected stumbling while standing or walking on split-belt treadmills has also been documented. In various experimental studies, it could be shown reaction times or latencies of the PL muscle are delayed in individuals with FI during different movements (standing, walking, sudden inversion perturbations)(Hopkins et al., 2009; Knight & Weimar, 2011; Mitchell et al., 2008;

Munn et al., 2010). Less studies could refute these outcomes (Ebig, Lephart, Burdett, Miller, & Pincivero, 1997; Munn et al., 2010). Arampatzis et al. (2005) observed that rather than the instant/timing of activity, it is more likely the level of muscle activity plays the lead role in joint stabilization (Arampatzis et al., 2005). Considering level/magnitude of muscle activity (amplitudes), literature produces conflicting results. Some studies presented that ankle muscle activity was not different or even higher in individuals with FI compared to healthy controls (Delahunt et al., 2006a, 2007; Gutierrez et al., 2012; Hopkins et al., 2012; Koshino et al., 2015; Suda et al., 2009). Authors hypothesized that the observed increases in PL activity may be the result of a change in the pre-programmed feedforward motor control (Delahunt et al., 2006a; Gutierrez et al., 2012). Contrary to these results, several studies identified a reduced ankle muscle activity in individuals with FI, particularly for the PL (Delahunt et al., 2006b; Donahue et al., 2014; Levin et al., 2015; Lin, Chen, & Lin, 2011; Palmieri-Smith et al., 2009; Rosen et al., 2013; Suda & Sacco, 2011). A summary of the recent literature concerning ankle muscle activity in FI individuals can be found in Table 1.

Table 1: Overview of studies investigating electromyographic activation of ankle musculature in FI

Authors	**Participants**	**Methods**	**Outcome measures**	**Muscles**	**Significant findings**
Feger et al. (2015)	Healthy individuals, those with CAI	Walking	Pre-and post-initial contact (IC) amplitude	TA, PL, M. Gastroc-nemius lateralis	no differences between groups in EMG amplitude pre-and post-initial contact (*p*>0.05)
Koshino et al. (2015)	Participants with CAI and healthy controls	Side cutting task, side-turn while walking	Mean of normalized EMG, pre IC (200 ms) and every 10 % windows of stance phase (IC to toe off)	TA, PL, GM, other muscles of upper thigh	No difference while side-turn during walking between healthy and CAI; significantly higher mean activity of GM than control group during 10–30 % of stance phase (*p*<0.05, ESs = 1.04–1.73)
Gutierrez et al. (2012)	Healthy individuals, those with FI and copers	Landing from jump on ankle supinating device	EMG areas and ensemble EMG 200 ms pre-and post IC	PL	Increased preparatory (*p*=0 .01) and reactive (*p*=0.02) EMG activation in FI
Hopkins et al. (2012)	Healthy individuals, those with FI	Forward lunge	EMG amplitude entire stance of lunge	TA, PL	FI less TA activity at begin and end of stance; higher TA activity in FI at loading portion of stance (25%)

Authors	Participants	Methods	Outcome measures	Muscles	Significant findings
Suda et al. (2009)	Healthy volleyball players	Landing from a jump	EMG amplitude (RMS) 200 ms pre-and post IC	PL	Lower RMS 200 ms pre-landing for FI (26.2±8.4%; controls: 43.0±22.0%; *p*<0.05); higher RMS 200 ms post-landing for FI (55.8±21.6%, controls: 47.5±13.3%; *p*<0.10)
Delahunt et al. (2007)	Healthy individuals and those with FI	Lateral hopping	Integral EMG during two separate linear envelops 200 ms pre-and post IC	PL, TA	No difference pre- and post-IC (67±28 % ms FI, 65±28 % ms controls) for PL; increased pre-and post TA activation in FI (203±101% ms; controls: 173±72% ms)
Delahunt et al. (2006)	Healthy individuals and those with FI	Treadmill walking	Integral EMG (2 separate linear envelops 200 ms pre-and post IC)	PL	Increase in EMG post-heel strike in FI (107.9% ms; controls: 64.53% ms; *p*<0.01)
Levin et al., (2015)	Healthy individuals, those with CAI	Sudden ankle inversion (trapdoor) while landing	SLR (short latency reflex response)	PL, GM	Decreased SLR responses following touchdown in CAI for PL and GM (*p*<0.05)
Donahue et al. (2014)	Healthy individuals and those with FI	Perturbation task on a walkway	SLR and LLR (late latency reflex response)	PL	Decreased amplitude of SLR and LLR in FI (*p*<0.01)
Rosen et al. (2013)	Healthy individuals and those with FI	Landing from a lateral jump	Peak EMG activity pre IC	TA, PL	Reduced peak EMG of TA in FI (30.8±47.2%, controls:20.7±20.7, *p*=0.03) and PL (19.2±20.4%, controls: 54.3±94.6%, *p*=0.03)
Suda et al. (2011)	Volleyball players with FI	Lateral shuffle manoeuvre	EMG amplitude 50 ms pre IC, EMG peak magnitude	PL	Decreased PL muscle activity 50 ms before IC and lower PL peak magnitude in FI
Lin et al. (2011)	Healthy individuals, those with CAI	Stop-jump landing task	EMG (RMS) amplitude pre (200-100 ms, 100 ms-IC) and post landing (200-100 ms, 100 ms-IC)	PL	Smaller RMS of EMG signal in post-landing phase in CAI (CAI: 0.73 ± 0.32; controls: 0.51 ± 0.22; *p*= 0.04)

Authors	Participants	Methods	Outcome measures	Muscles	Significant findings
Palmieri-Smith et al. (2009)	Healthy individuals and those with FI	Sudden ankle inversion perturbation while walking	EMG amplitudes (normalized linear envelopes [%MVC]) 100 ms post onset activity	PL	Reduced EMG amplitude in pathological ankle (1.7±1.3%) compared to healthy ankle in FI (3.3±3.1%) (*p*<0.001); no differences between ankles of controls (0.4±0.2% and 0.4±0.2%; *p*<0.05)
Delahunt et al. (2006)	Healthy individuals and those with FI	Drop jumping	Integral EMG (2 separate linear envelops 200ms pre- and post IC)	PL	Decreased EMG activation 200 ms prior initial contact in FI (54.0±2.7% FI group, controls: 81.3±8.7%; *p*<0.01)

Complete study outcomes are not presented within this table; the focus was on EMG amplitude data of lower leg muscle activity; CAI = chronic ankle instability

As previously mentioned patients with FI might suffer from AMI. AMI manifests after the initial ankle sprain and the effects of the sprain persist even after the injury has healed (McVey et al., 2005). Further, AMI has been suggested to dampen neuromuscular protective mechanisms and lead to future injury. Whether it contributes to ongoing ankle dysfunction, remains unknown. However, the arthrogenic muscle response does not only manifest as inhibition, but also as facilitation of joint musculature (McVey et al., 2005). A common technique used to evaluate the presence or absence of arthrogenic muscle response is the Hoffman Reflex (H-reflex), the electrical analogue of the stretch reflex. Some studies have even shown that the PL excitability (measured by transcranial magnet stimulation [TMS] or H-reflex) is reduced during sitting and standing in individuals with FI compared to asymptomatic individuals (p=0.04)(Futatsubashi, Sasada, Tazoe, & Komiyama, 2013; McVey et al., 2005; Pietrosimone & Gribble, 2012).

In the end, comparability between these studies should also be critically examined since most of them were conducted with varying methodologies (static or dynamic measurement setups, time windows of muscle activation, leg muscles investigated). They also differ in the inclusion criteria for participants with FI, test positions and perturbation characteristics (e.g. intensity of perturbation, nociceptive or mechanical stimuli)(Hiller et al., 2011; Holmes & Delahunt, 2009; Schillings et al., 2000). This could explain some of the discrepancy in the reviewed studies. Literature is still conflicting regarding whether the neuromuscular deficits entail a decreased or increased muscular activity in individuals with FI. However, when surveying all the existing studies, a clear tendency for reduced EMG amplitude of ankle musculature, especially when investigating PL muscle, is distinct.

1.3 Test-retest reproducibility of ankle muscle activity in individuals with functional ankle instability

It has been shown in several studies that ankle muscle activity differs between healthy individuals and those with FI (Donahue et al., 2014; Lin et al., 2011; Rosen et al., 2013; Suda & Sacco, 2011). Before distinguishing muscle activity of healthy individuals from those of FI and evaluating changes (ankle EMG activity) after a treatment program (orthoses intervention), it is crucial to identify whether the measurement of ankle muscle activity is accurate and consistent between testing days. Thus, the test-retest reproducibility of these measures was demonstrated first. Although treadmill walking is a cyclical, consistent movement with given speed, it is affected by individual stride length and frequency (Danion, Varraine, Bonnard, & Pailhous, 2003; Hausdorff, 2005). The fact, that gait characteristics vary between and within subjects, must to be considered when evaluating the consistency of ankle muscle activity between test sessions. Despite the wide use of surface electromyography (EMG) during dynamic exercises, the reproducibility of ankle muscle activity had not been established during stumbling on a split-belt treadmill in individuals with FI. Additionally, some reliability studies considered EMG parameters other than amplitude (Gupta, Mudie, & Clothier, 2014; Hopper, Allison, Fernandes, O'Sullivan, & Wharton, 1998). ICC values of 0.91 (left leg) and 0.82 (right leg) could be demonstrated for peroneal latency during sudden inversion perturbations while standing (Hopper et al., 1998). Another study found muscle onset of the GM (which is defined as the instant in which the muscle increases its level of activity above baseline) during single leg hopping to yield ICC values of 0.72 to 0.95 (Gupta et al., 2014). Conflicting findings exist between studies evaluating the reproducibility of EMG amplitudes as outcome parameter. During maximum dynamic contractions on an isokinetic dynamometer, the reproducibility of surface EMG amplitudes of knee extensors revealed ICC values of 0.83 to 0.98 (Larsson et al., 1999). In individuals with patellofemoral pain syndrome, EMG amplitude of the GM during stance phase of a stair descent task presented ICC values of ≥0.70 (Bolgla, Malone, Umberger, & Uhl, 2010). Earlier studies published ICC values ranging from 0.72 to 0.89 (GM) and 0.95 to 0.96 (soleus [S]) for EMG amplitudes during standing, backwardly directed perturbations of upright stance, running, hopping and drop jumping in healthy individuals (Gollhoferl, Horstmann, Schmidtbleicher, & Schönthall, 1990; Horstmann, Gollhofer, & Dietz, 1988). A more recent study noted within-day repeatability of TA, PL and GM EMG waveform data were good to excellent during walking (coefficient of multiple correlation [CMC]: 0.77-0.92), during a side-turn movement (CMC: 0.73-0.92) and side cutting (CMC: 0.71-0.97) in participants with chronic ankle instability and healthy controls (Koshino et al., 2015). Contrary to these outcomes, another current study found ICC values of 0.47 (GM), 0.51 (S), 0.09 (TA) and 0 (PL) for peak amplitude in patients with lower leg pathologies (pes planovalgus, rheumatoid arthritis) during walking (Barn, Rafferty, Turner, & Woodburn, 2012). During pedalling exercises, a CV of 15.8-43.1% was determined for EMG amplitude of the GM and GL, S and TA (Jobson, Hopker, Arkesteijn, & Passfield, 2013). Other study groups identified a high range in CV values (7-88%) for EMG amplitudes of lower leg muscles between test sessions in healthy individuals during walking (Barn et al., 2012; Kadaba et al., 1989; Murley, Menz, Landorf, & Bird, 2010). Karamanidis and colleagues (2004) presented that the reproducibility of several lower limb muscle EMG parameters (amplitude, latency, mean power frequency) during running (2.5 m/s) is dependent on the muscle studied and time window analyzed. In this study, EMG amplitude ICC values of 0.85 (TA) and 0.78 (GM) during pre-activation and 0.71 (TA) and 0.92 (GM) during contact phase were found (Karamanidis, Arampatzis, & Brüggemann, 2004). Reproducibility criteria used in the available studies were very diverse. In addition, most of the studies presented a high range of muscle amplitudes variability, which may be simply a critical factor in EMG analysis of ankle musculature during walking. In addition, the mentioned reliability studies differed in methodology, for example leg muscles considered (e.g. m. tibialis posterior [TP], m. vastii [V]), pathologies included (e.g. knee osteoarthritis (Hubley-Kozey, Robbins, Rutherford, & Stanish, 2013), rheumatoid arthritis (Barn et al., 2012)) and setups used (fine-wire EMG; cycling, running, isokinetic exercises). Moreover, very few studies directly compared the influence of pathology (FI ankles) on reproducibility of muscle activity during walking with healthy ankles.

1.4 Treatment regimen for individuals with functional ankle instability

1.4.1 Effect of sensorimotor training in individuals with functional ankle instability

The neuromuscular deficits in patients with FI can be addressed with conservative therapy modalities to avoid or reduce the risk of injury recurrence (secondary prophylaxis). Training programs often use neuromuscular/sensorimotor (sensorimotor corresponds to neuromuscular) exercises to treat patients with FI. The term neuromuscular training is used to describe a combination of functionally based exercises, including postural stability, proprioceptive and strength training as part of a rehabilitation regimen (Lin, Delahunt, & King, 2012).

Some studies examined the effects of neuromuscular training on the response times of lower leg musculature to sudden inversion perturbations. Clark and Burden (2005) investigated the effects of a 4-week wobble-board training program (3x/week) on the onset of the TA and PL muscle activity in subjects with FI (Clark & Burden, 2005). The exercise group showed a significant decrease in both the TA (29.9%) and PL (31.2%) onset latencies following completion of the program, which was not observed in the control group. According to the authors, the identified decrease in latency could signify an intrinsic stiffening of the muscles, which would enhance muscle spindle activation via feedforward neuromuscular control, resulting in a quicker reflex response initiation. Akhbari et al. (2007) showed a specific balance training program on a Biodex Stability System (3x/week for 4 weeks) reduced the TA and PL onset times and peak latencies during sudden ankle inversion in subjects with FI (Akhbari et al., 2007). A 6-week multi-station proprioceptive exercise program in patients with chronic ankle instability also yielded significant improvements in joint position sense, postural sway and muscle reaction times (non-significant increase in muscle response of PL)(Eils & Rosenbaum, 2001). Although no long-term effect of an ankle training intervention was conducted, Bellew et al. (2010) provided evidence for an increased activity of PL muscle ($p<0.05$) during exercises that more accurately reflect its biomechanical function compared to conventional exercises (unidirectional, non-weight bearing) (Bellew et al., 2010). Training of ankle musculature, specifically of the PL, may be used to increase the sensitivity of the proprioceptive afferent input response and serve as a preventative measure against inversion ankle sprains (Bellew et al., 2010). Systematic reviews have found limited to moderate evidence of the effectiveness of neuromuscular training for static and dynamic postural stability, active/passive joint position sense and muscle onset latencies in subjects with chronic instable ankles (Hupperets, Verhagen, & van Mechelen, 2009; Lin et al., 2012; O'Driscoll & Delahunt, 2011). Limited proof was explained by few studies, small sample sizes and risks of bias (Lin et al., 2012). Other studies have shown increases in functional joint stability of individuals with FI after neuromuscular training programs (de Vries, Krips, Sierevelt, & Blankevoort, 2006; Lee & Lin, 2008; Lin et al., 2012). Additionally, balance training interventions of varying durations (4-12 weeks) led to better performance on static or dynamic postural stability (e.g. reduced mean radius of COP and joint position sense when compared to healthy controls) (Lee & Lin, 2008; Mettler, Chinn, Saliba, McKeon, & Hertel, 2015; Sefton, Yarar, Hicks-Little, Berry, & Cordova, 2011). The authors speculate that their training programs may have partially repaired the damaged sensorimotor system pathways, resulting in a more effective functioning of the neuromuscular system (Mettler et al., 2015). Another study demonstrated isokinetic strength training in combination with proprioception training shortens rehabilitation, allowing an earlier return to activities of daily life as well as serving as a secondary prophylaxis (Zöch et al., 2003). A further systematic review summarized that balance, proprioceptive and muscle strengthening exercises are effective for patients with FI in decreasing the incidence of giving-way episodes, improving balance stability and function (Loudon, Santos, Franks, & Liu, 2008). A beneficial effect of supervised neuromuscular training (conducted over 20-30 minutes for 4 weeks) in terms of short-term functional outcomes (evaluated by "Foot and Ankle Disability Index" questionnaire) could also be demonstrated in other studies (Lin et al., 2012)(de Vries et al., 2006). In a recent study by Mc Criskin et al. (2015), prophylactic bracing and combined neuromuscular and proprioceptive training programs were recommended as preventive treatment in athletic cohorts, minimizing the risk of FI development (McCriskin, Cameron, Orr, & Waterman, 2015). In summary, there are contradictory findings in regards to the effect of sensorimotor training in individuals with FI. This could be explained by varying therapy programs, their durations as well as their functional outcomes (self-reported instability, postural stability, joint position sense, muscle latency). The majority of studies investigated the effect of sensorimotor training on different outcome parameters other than the ankle musculature (EMG amplitude).

1.4.2 Neuromuscular effect of foot orthoses in individuals with functional ankle instability

Although active exercises seem to be the first choice therapy, neuromuscular deficits in individuals with FI can also be improved by using passive therapy methods, like braces or orthoses. During the last decade, the use of foot orthoses as treatment option has received great attention next to sensorimotor training, as widely accepted therapy form. However, the effectiveness of foot orthoses in subjects with FI is still the subject of much debate in many studies (Gerstner Garces, 2012). The advantage of wearing foot orthoses over other treatment modalities, such as sensorimotor training of the ankle musculature, is the time-effectiveness. By itself or in combination with active exercises, foot orthoses may beneficially affect the neuromuscular deficiencies in individuals with FI. An additional advantage of orthoses is they are more affordable than physiotherapy (Landorf & Keenan, 2000). Landorf et al. (2000) stated there is a need for high quality evidence-based studies to convince stakeholder of the effectiveness of foot orthoses as a therapy approach (Landorf & Keenan, 2000). Literature shows that orthoses can serve as a passive therapy option next to physiotherapy and proprioceptive training because they are effective in treatment and prevention of lower limb overuse injuries (Kilmartin & Wallace, 1994; Nawoczenski & Janisse, 2004; Nurse & Nigg, 2001; Tomaro & Burdett, 1993). In a prospective, randomised, controlled clinical trial by Hirschmueller et al. (2011), wearing semi-rigid customized running shoe orthoses for 8 weeks was determined to be an effective conservative therapy strategy for chronic running injuries. In these injured runners, pain was reduced and overall comfort of the orthoses were high (Hirschmüller et al., 2011).

However, the particular effect mechanism of foot orthoses is not clarified in detail. In the past, foot orthotics treatment aimed mainly to balance biomechanical malposition or incorrect loading. One major concern, regarding FI, is the partially unknown aetiology of the pathology and its risk factors. Single mal-positions are associated with several kinds of pathologies. Therefore, an evidence-based prescription of foot orthoses counteracting the risk factors of the pathology is difficult. The same orthotic or insert is often proposed for different lower limb pathologies (Nigg, Khan, Fisher, & Stefanyshyn, 1998)(Landorf & Keenan, 2000), however different types of orthotic modifications provoke different peripheral sensory influences (Bruhn, Gollhofer, & Gruber, 2001).

Biomechanical control paradigm

According to the biomechanical approach, foot orthoses optimize the mechanical alignment of the lower extremity skeleton. Reduced rearfoot eversion, internal rearfoot inversion moment, peak impact force and peak rate of loading were found during the stance phase of walking and running (Baker, Taunton, McKenzie, & Beauchamp, 2006; Dixon, 2007; McMillan & Payne, 2008; Mills, Blanch, Chapman, McPoil, & Vicenzino, 2010). Mills et al. (2010) systematically reviewed the literature to improve the understanding of the physiological basis for orthoses in terms of a kinematic and shock attenuation paradigm (Mills et al., 2010). The main findings of the kinematic paradigm were that posted, non-moulded orthoses systematically reduced peak rearfoot eversion (2.12°) and tibial internal rotation (1.33°) in non-injured cohorts (Mills et al., 2010). The shock attenuation paradigm concluded that non-posted and posted, moulded orthoses produced larger reductions in loading rate and vertical impact force compared to posted, non-moulded orthosis (Mills et al., 2010). Also, after short-term treatment with orthoses (semi-rigid, custom made)(6 weeks), decreases in maximum eversion angle and velocity, ankle inversion moment and impact peak and vertical loading rate were found during running in a group of runners with a history of overuse knee injury (MacLean et al., 2008). In their study, Stacoff et al. (2000) demonstrated medial foot orthoses generate small kinematic effects on the calcaneus and tibia (measured with bone pins) during the stance phase of running in healthy subjects (Stacoff et al., 2000). These results also showed orthotic effects were subject-specific and unsystematic across conditions (Stacoff et al., 2000). Thus, the idea that the major function of orthotics was to exclusively align the original structure of the skeleton was questioned (Nigg et al., 1998). Impact cushioning with shoe inserts or orthotics was found to be below 10% and it was thought that such small reductions may not be relevant for injury reduction (Nigg et al., 1998). Generally, kinetic and kinematic studies explaining the effect of foot orthotics by means of a single mechanical mechanism do exist but according to the unsystematic and inconclusive findings, as well as methodological weaknesses of these studies, the mechanical approach of foot orthoses should be critically questioned. Studies speculate that orthotic effects can in part be attributed to proprioceptive mechanisms (Stacoff et al., 2000)(Nigg et al., 1998). Therefore, it is recommended that more studies consider a sensorimotor control mechanism following orthoses intervention as a possible effect mechanism (Baur, Hirschmuller, Muller, & Mayer, 2003).

Sensorimotor control paradigm

Overall, there is no evidence showing a sensorimotor effect on ankle musculature after wearing foot orthoses (Baur, Hirschmüller, Müller, & Mayer, 2011; Ebig et al., 1997; Hirschmüller et al., 2011; Mills et al., 2010). There is limited knowledge regarding muscular responses to foot orthoses interventions or the specific functioning/effect mechanism of foot orthoses (Baur et al., 2011; Nigg et al., 1998; Vicenzino et al., 2008). In a systematic review by Mills et al. (2010), the neuromotor control paradigm (neuromotor is analogous to sensorimotor) had less conclusive substantiation compared to the biomechanical paradigm. The authors stated there is a need for further research focusing on the role of neuromotor control modification and long-term adaptation to orthoses (Mills et al., 2010). According to the sensorimotor approach, foot orthoses modify the afferent input of cutaneous mechanoreceptors at the plantar foot sole. Therefore, it is assumed that reflective compensatory reactions (sensory afferent feedback mechanism) of the ankle muscles are enabled or supported (Nurse & Nigg, 2001). Altering sensory feedback signals with an orthotic intervention modifies sensorimotor integration mechanisms in a subject-specific manner (Burke et al., 2006). Nigg et al. (1998) described in detail the sensorimotor adaptation mechanisms due to foot orthoses application (Nigg et al., 1998). The foot has various sensors detecting input signals with subject-specific thresholds. A force signal acts as an input variable on the shoe (shoe sole as first filter, orthoses as second filter and plantar surface of foot as third filter). The sensory feedback is processed and the filtered information, namely magnitude of pressure, velocity and direction of the mechanical stimulus, is transferred to the central nervous system (Enoka & Duchateau, 2008). Several studies have shown that manipulation of plantar input at the sole of the foot, thus to joint- or muscle receptors in the ankle joint, may lead to changes in plantar pressure distribution beyond the midfoot (Fallon, Bent, McNulty, & Macefield, 2005; Nurse & Nigg, 2001; Wu & Chiang, 1996). Due to modified plantar pressures, the central nervous system modulates the activation of a muscular innervation pattern by producing subject-specific reflex responses in the leg muscles (Nigg, Nurse, & Stefanyshyn, 1999; Stacoff et al., 2000). Stimulation of cutaneous afferences through different surfaces changes (e.g. material properties of foot orthoses) or electrical stimuli might alter muscular activity of the ankle muscles, either in terms of facilitation or inhibition (Duysens, Tax, Trippel, & Dietz, 1992). Cutaneous afferences contribute to human balance control and provide neutral alignment for proper muscle activation (Mattacola & Dwyer, 2002). Thus, orthoses are thought to affect the sensorimotor system (Baur et al., 2003; Murley, Landorf, Menz, & Bird, 2009; Stacoff et al., 2001). The whole sensorimotor control loop with proprioceptors (afferences), process control at the spinal or supraspinal level (CNS) and the resulting sensorimotor movement control (efferences) must be considered (Bruhn et al., 2001). Strong synaptic coupling between tactile afferences and spinal motoneurons could emphasize the potential importance of cutaneous inputs from the sole of the foot in the control of gait and posture (Fallon et al., 2005). According to Burke et al. (2006), it is essential to understand the connection between modified sensory feedback and the resulting modulation of motoric output to incorporate the role of sensorimotor integration mechanisms as a benefit of orthopaedic interventions (Burke et al., 2006). Chen et al. (1995) recommended a more detailed look into the relationship between pressure beyond the longitudinal arch and increased stability of the foot (Chen, Nigg, Hulliger, & de Koning, 1995). In this context, recent studies are investigating the effect of foot orthoses on muscle activity using surface EMG. Initially, due to some literature the proposed benefit of foot orthotics may be related to decreases in muscle activity required to minimize muscle work and reduce muscle fatigue, thus improve comfort and performance (Nawoczenski & Ludewig, 1999; Nigg et al., 1999). However, current studies are interpreting increased ankle muscle activation due to an orthotic use as positive findings in terms of supporting the joint stability. O'Connor & Hamill (2004) could not demonstrate any neuromuscular adaptations (EMG on-off pattern) or systematic muscle responses of the S, TA, PL, GM and GL after foot orthoses application during perturbed walking on treadmill in healthy individuals (O'Connor & Hamill, 2004). Nurse et al. (2005) found a reduced muscular activity of S and TA after wearing orthoses in asymptomatic adults (Nurse, Hulliger, Wakeling, Nigg, & Stefanyshyn, 2005). Another study identified ankle bracing resulted in a lower pre-contact amplitude (100 ms pre IC) of the PL (p=0.02) compared to a no-brace condition during treadmill walking in a population with chronic ankle instability (Barlow et al., 2014). Concerning the long-term use of orthosis, Midgley et al. (2007) demonstrated that the use of external ankle support (tape and brace) over one entire season (4-5 months) did not induce neuromuscular changes in terms of onset times of the PL muscle during inversion perturbation while walking in healthy volleyball players (no significant interaction for electromechanical delay [determined by the onset of force contribution after artificial activation] between groups over time: p=0.79 nor for reaction time: p=0.09)(Midgley et al. 2007). Nevertheless, a majority of studies have witnessed an increase in EMG activity of the ankle musculature during different dynamic test situations after both acute- and long-term use of foot orthotics in asymptomatic individuals and those with lower limb overuse injuries or flat arched feet (Baur et al., 2011; Mündermann, Wakeling, Nigg, Humble, & Stefanyshyn, 2006; Murley & Bird, 2006; Murley, Menz, & Landorf, 2009). A systematic review evaluated the literature with reference to the effect of foot posture, foot orthoses and footwear on lower limb muscle activity during walking and running. Some evidence supports the idea that foot orthoses increase activation of the TA and PL muscles, however literature is inconclusive and highly variable (Murley, Landorf, et al., 2009). Although muscle onset times instead of amplitudes were considered, Dingenen et al. (2015) could reveal earlier onset times of the PL, among other leg muscles, with a standardized (p>0.001) and customized (p=0.03) orthosis condition compared to a barefoot condition during transition from double to single leg stance (Dingenen et al., 2015). Two studies could present an increased ankle muscle activity with the use of particular ankle destabilizing devices/orthoses. Significantly increased muscle amplitudes of the PL, TA (moderate to large effect sizes) could be revealed in individuals with chronic ankle instability when wearing ankle destabilizing devices compared to shoes during functional exercises, specifically a unipedal eyes-closed balance test, the Star Excursion Balance Test (SEBT), lateral hops and walking (Donovan, Hart, & Hertel, 2015). The mechanical device induced subtalar joint destabilization by which ankle muscle initiation was controlled (Donovan et al., 2015). Mündermann et al. (2006) presented similar findings. Posting and custom-moulded foot orthoses increased the global EMG intensity (EMG intensities in two frequency bands averaged for pre-and-post heel-strike intervals and for 30-100% of stance phase) of the PL and GM during the stance phase of running (p<0.05) in recreational runners with pronating foot type (Mündermann et al., 2006). According to the authors, there is a greater need to stabilize the ankle joint with orthoses because ankle musculature attempted to compensate during all produced instability tasks (Mündermann et al., 2006). Ludwig et al. (2013) investigated the effect of imbedded pressure points within specific sensorimotor insoles on PL muscular activity during walking in healthy individuals

(Ludwig, Quadflieg, & Koch, 2013). The defined pressure areas (8 mm distal of retinaculum inferius, soft foam lateral element) imposed pressure at the site of the peroneal tendon (Figure 5). Results indicated that PL activity was significantly increased during mid-stance phase (significant change in muscle activation at 17.51±4.3% of stance phase, maximum values of 21.56±10.03% MVC when wearing sensorimotor insoles compared to “dummy-insoles” (dummy 16.09±7.06%)($p<0.001$). The authors explained the effectiveness of the insole by the soft foam sensorimotor wedge which imposed pressure on the skin above the peroneal tendon. This then would induce changes in afferent information (e.g. muscle spindles) when the body weight was transferred to the foot. This pressure stimulus most likely help stabilize the foot position and may modify ankle muscle activation pattern in a selective matter by reducing inhibiting mechanisms at the spinal level (Ludwig et al., 2013).

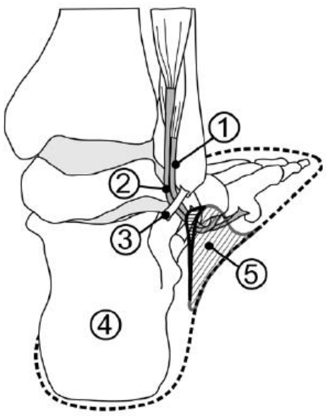

Figure 5: Schematic positioning of lateral insole element:

1. tendon of M. peroneus brevis
2. tendon of M. peroneus longus
3. retinaculum peroneum superius
4. calcaneus
5. sensorimotor element (hatched)

Baur et al. (2003) could confirm those findings. They examined the effect of functional elements of insoles on plantar pressure distribution and muscular activity in healthy runners on a treadmill (Baur et al., 2003). Insoles with longitudinal arch wedges showed subject-specific increases in PL amplitude during the stance phase of walking which might indicate an improved ankle joint stability. Analysis of peak pressure and maximum mean pressure in areas of functional elements showed changes towards higher loads as a result of medial longitudinal wedges (+31%). As pressure at medial arch increased, so did the PL activation (r=0.62-0.72). However, Baur et al. (2003) concluded that high pressure below the longitudinal arch was not forcefully a result of the high longitudinal arch support, but was individual specific (Baur et al., 2003). Altering sensory input, by changing shoe, orthotic and/or surface constructions are also methods by which abnormal gait patterns can be treated (Nurse & Nigg, 2001). Another group investigated whether orthoses change muscle activity in people with flat arched feet towards a pattern observed in people with normal arched feet (Murley, Landorf, & Menz, 2010). In detail, during mid-stance/propulsive phase, the PL amplitude increased significantly with a prefabricated orthosis, compared with the shoe-only condition (peak amplitude: 21% increase, p=0.02; RMS amplitude: 24% increase, p=0.02) and customized orthosis condition (peak amplitude: 16% increase, p=0.03) (Murley, Landorf, et al., 2010). Nawoczenski et al. (1999) studied the effects of semi-rigid foot orthotics on mean electromyographic amplitudes of the proximal and distal lower extremity muscle groups during the first 50% of stance phase during treadmill running in recreational runners with lower extremity pain (Nawoczenski & Ludewig, 1999). Statistically significant changes (p<0.05) in biceps femoris (BF)(11.1% decrease) and TA amplitude (37.5% increase) for the orthotic condition could be identified. In another study by Murley et al. (2006), asymptomatic participants with a pronated foot type wore 0°, 15°and 30° inverted custom-made foot orthoses (Murley & Bird, 2006). A statistically significant increase in TA maximum EMG amplitude occurred for "shoe only" (30% increase), 0° (33% increase), 15° (38% increase) and 30° (30% increase) inverted orthoses compared to barefoot walking (p<0.01). Additionally, PL maximum EMG amplitude increased significantly with 15° inverted orthosis compared to barefoot walking (21% increase, p=0.04) and to footwear alone. However, level of medial rearfoot posting did not significantly alter maximum EMG amplitude. In addition, Nawoczenski and Murley stated that subjects' electromyographic responses to orthotic use are highly variable and individualized (Murley & Bird, 2006)(Nawoczenski & Ludewig, 1999). Only one available study has noted a rise in ankle musculature EMG amplitude after long-term application of foot orthoses. Baur et al. (2011) could show that after 8 weeks of orthotic use in runners with overuse injuries, pre-activity of the PL muscle was increased in an orthoses group compared to controls during walking (orthoses group: 1.18±0.43, 95% confidence interval=1.08-1.28; p=0.003; control group: 0.97±0.32, 95% confidence interval= 0.90-1.05) (Baur et al., 2011). This finding suggests an altered pre-programmed activity, which might lead to improved ankle joint stability, providing a possible effect mechanism for foot orthoses therapy (Baur et al., 2011). Other studies tested the neurophysiological effect of foot orthoses using spinal reflex measures. Nishikawa et al. (2002) found increased PL motoneuron excitability (H_{max}/M_{max}-ratio measured by H-reflex) by application of braces or foot orthoses (semi-rigid, medial wedge) during sitting and standing in healthy individuals

(Nishikawa, Ozaki, Mizuno, & Grabiner, 2002). These findings were explained by the protective mechanism improving ankle joint stiffness against vulnerable situations (Baur et al., 2011). It was assumed that braces/foot orthoses offered a proprioceptive stimulation to cutaneous mechanoreceptors and an improved sensory feedback (Nishikawa et al., 2002). However, some studies refuted these findings, particularly when braces were used over long-term (no effect on stretch reflex amplitude) or during sudden inversion perturbations (Kernozek, Durall, Friske, & Mussallem, 2008; Midgley et al., 2007; Sefton, Hicks-Little, Koceja, & Cordova, 2007). These conflicting results were explained by the task dependence of muscles and cutaneous reflexes and their dependence on postural position (Chalmers & Knutzen, 2000; Zehr & Stein, 1999). Additionally, during the step cycle of walking, a phase dependence of amplitude of reflex responses is present (Zehr & Stein, 1999). There is grade B evidence that foot orthotics can help improve postural control in people with chronic ankle instability (Gabriner, Braun, Houston, & Hoch, 2015). Several studies have shown improved balance/postural control after wearing foot orthoses (soft and semi-rigid, custom-fitted, different number of foam bases) over short- or long-term periods (1-4 weeks) (Hadadi et al., 2011; Holmes & Delahunt, 2009; Lee & Lin, 2008; Sesma, Mattacola, Uhl, Nitz, & McKeon, 2008). Decreases in COP, sway velocity and increases in reach distance were demonstrated by several study groups (Hadadi et al., 2011, 2014; Hamlyn et al., 2012; Sesma et al., 2008).

In general, the mentioned results are hardly comparable due to different methodological setups (e.g. static/dynamic test situation, cross-sectional/longitudinal investigations), participant groups (e.g. healthy/FI) and their foot form, characteristics of therapy orthoses (braces, semi-rigid, longitudinal arch, other devices), lower limb muscles and time windows of EMG analysis investigated. Although there is limited knowledge on the effectiveness of foot orthoses in terms of ankle muscle neuromuscular activity, most studies explained neuromuscular adaptations by modified proprioceptive/afferent feedback of mechanoreceptors at the foot's sole (Baur et al., 2003; Mündermann, Nigg, Humble, & Stefanyshyn, 2003a; Stacoff et al., 2000). In the majority of studies, these adaptation mechanisms were confirmed by an increased ankle muscle activation (amplitude), which might contribute to an improved ankle joint stability in individuals with FI.

1.4.3 Effect of foot orthoses in comparison to sensorimotor training in individuals with functional ankle instability

In general, there is a lack of studies comparing foot orthotics and sensorimotor training interventions as treatment modalities, even more so in individuals with FI. In a chronic ankle instability group, Lee et al. (2013) found no significant differences in static or dynamic balance abilities between those provided with orthoses and those who underwent rehabilitation exercises (balance training, neuromuscular training, strength training, plyometric training; 1 hour per day; 3 days per week) with foot orthoses (p>0.05)(Lee, Lim, Jung, Kim, & Park, 2013). Athletes with chronic ankle instability, who had foot orthotics applied for 4 weeks, improved their proprioceptive and balancing abilities (improvement in joint reposition sense by -1.07±1.64), but did not show additional treatment effects compared to 4 weeks of rehabilitation exercise treatment (Lee et al., 2013). Kim et al. (2014) combined muscle strengthening and proprioceptive exercises (3 days/week for 4 weeks) and found an increased effectiveness in individuals with FI due to increased strength of all ankle muscles compared to only applying muscle strengthening exercises (Kim et al., 2014). Another study demonstrated the added value of vibration to 6 weeks of wobble board training compared to only wobble board training in football players with FI (Cloak, Nevill, Day, & Wyon, 2013). The combined therapy approach led to an improved center of mass distribution (p≤0.001, effect size (ES) = 0.66) and increased SEBT reach distances (p≤0.01 and p≤0.002, ES = 0.19 and 0.29, respectively) (Cloak et al., 2013).

Most studies compared other types of treatment modalities or compared combined therapy programs with isolated training exercises for their effectiveness in individuals with FI. Particularly, few studies focused on the interventions' effects on the ankle muscle activity (Cloak et al., 2013; Janssen et al., 2011; Kim et al., 2014; Lee et al., 2013; Prado et al., 2014).

Lack of knowledge

In summary, it is still not fully clarified whether ankle muscle activity differs between healthy individuals and individuals having FI. There has not been enough scientific research evaluating the effectiveness of acute foot orthosis application on ankle muscle activity, specifically in patients with FI. A combined investigation of ankle health status (healthy individuals/those with FI) and shoe condition ("shoe only" or in-shoe orthosis) in terms of ankle muscle activation has rarely been conducted. There is no proof for the effectiveness of long-term foot orthoses use (compared to sensorimotor training) on the exact neuromotor control modification and sensorimotor adaptation mechanisms of ankle musculature in individuals with FI related to a healthy control group (Baur et al., 2011; Hirschmüller et al., 2011; Mills et al., 2010; Vicenzino et al., 2008). Furthermore, the majority of studies, which have evaluated the influences of orthoses on ankle muscle neuromuscular activity, focused on PL muscle. However, the role of other ankle stabilizing muscles (as TA and GM) needs clarification as well (Grüneberg, Nieuwenhuijzen, & Duysens, 2003; Louwerens, van Linge, de Klerk, Mulder, & Snijders, 1995). It is necessary to consider the flexible state of the sensorimotor system since ankle injuries occur during dynamic activities (Grüneberg et al., 2003). While the effects of static constraints in stabilizing the ankle joint are relatively well understood, those of dynamic constraints are less clear and require further investigation (Gehring et al., 2013; Hopkins, McLoda, & McCaw, 2007). Thus, a walking model may be a more functional approach in evaluating dynamic response characteristics of ankle musculature (Hopkins et al., 2007). Walking on a treadmill also has the advantage of transferring an everyday situation into a laboratory setting. There is little study work available concerning pre-active and reflexive muscle responses to sudden (inversion) perturbations in individuals with FI (Delahunt et al., 2006a)(Delahunt, 2007). Neuromuscular control of ankle muscles is required during different sport-specific loading situations. One typical situation could be a reflexive reaction to an unexpected foot displacement (e.g. body check) of ankle musculature. This can be simulated during application of perturbations during the loading phase of the foot on the treadmill (Gutierrez et al., 2009). By removing the walkway or dropping the supportive surface, split-belt treadmills can simulate unexpected slipping and stumbling under highly standardized conditions (e.g. controlling timing of perturbation) and evoking significant and sizable ankle muscle reflex responses (Nieuwenhuijzen, Grüneberg, & Duysens, 2002). Another potential situation would be a plant-and-cut movement which is common in court sports and characterized by anticipatory activity of ankle musculature. Cutting manoeuvres are very closely related to ankle ligament ruptures (Koshino et al., 2015; Oliveira, Silva, Lund, Farina, & Kersting, 2014). Thereby, an inversion to the lateral ankle ligaments can be used to assess functional performance deficits in subjects with FI (Hopkins et al., 2007). Muscle activity during side cutting has been extensively studied mostly in the context of knee musculature and ACL injury, but rarely in individuals with FI (Besier, Lloyd, & Ackland, 2003; Colby et al., 2000; Koshino et al., 2015).

Both sport-specific situations could provoke the injury mechanism of an ankle sprain by placing stress on the lateral ankle ligaments, requiring adequate dynamic stabilization by ankle muscles (Docherty, Arnold, Gansneder, Hurwitz, & Gieck, 2005; Hertel, 2002). Evaluating pre- and reflexive activity of ankle muscles, while simulating the described scenarios with a combined foot orthoses application, is a new scientific approach and may provide insights into ankle stability control in individuals with FI. Additionally, through treating FI patients with foot orthoses, which might be a promising treatment option, important knowledge concerning the specific effect mechanism, might be gained.

1.5 Objective

The aim of the presented study work was to investigate the effectiveness of a foot orthotic intervention on ankle muscle activity in individuals with FI. Specifically, the following research objectives were defined (Table 2):

Table 2: PhD-Questions with Hypotheses

Main Question (MQ) 1:
Is there a difference in ankle muscle activity between healthy participants and those with FI at M1?
Auxiliary/Side Question (SQ) 1a: Can ankle muscle activity be measured reproducibly in healthy individuals and those with FI between two test sessions (M1, M2)?
Main Question (MQ) 2: **Do participants with FI respond with a different ankle muscle activity to a measurement in-shoe orthosis (related to "shoe only") compared with healthy participants at M1 (Acute effect orthosis)?**
Main Question (MQ) 3: **Is there a difference in ankle muscle activity between an orthosis intervention group and a control group (no intervention) from M1 to M2 (Long-term effect orthosis)?**
Auxiliary/Side Question (SQ) 3a: Do participants in the orthosis group show (even) higher ankle muscle activity by additional short-term application of a measurement in-shoe orthosis compared to short-term application of "shoe only" after intervention at M2 (="transmission-effect")?
Main Question (MQ) 4: **Is there a difference in ankle muscle activity between an orthosis intervention group and a sensorimotor training group from M1 to M2 (Long-term effect orthosis)?**
Main Question (MQ) 5: **Do participants with FI respond with a different ankle muscle activity to a measurement in-shoe orthosis compared with healthy participants from M1 to M2 (Long-term effect orthosis)?**

Main Question (MQ) 1:

This study investigates if ankle muscle activity differs between healthy participants and those with FI during perturbed treadmill walking (normal unperturbed walking as control condition) and during side cutting at M1 (cross-sectional effect). The results provide information as regards to possible differences in neuromuscular activity in individuals with FI in relation to healthy individuals. Subsequently, different baseline effects can be considered for long-term investigations.

Hypothesis:

Individuals with FI will show a decreased ankle muscle activity compared with healthy individuals (Delahunt et al., 2006b; Donahue et al., 2014; Levin et al., 2015; Lin et al., 2011; Palmieri-Smith et al., 2009; Rosen et al., 2013; Suda & Sacco, 2011).

Auxiliary/Side Question (SQ) 1a:

Test-retest reproducibility of ankle muscle activity (pre- and post-test [M1 and M2]) is investigated in individuals with FI and compared with a healthy cohort during perturbed treadmill walking (normal unperturbed walking as control condition) and during side cutting. During perturbed walking, it is also asked if ankle muscle activity differs between healthy individuals and those with FI, and between unperturbed and perturbed walking (possible influence of ankle status, as well as walking condition, on reproducibility of ankle muscle activity measures). During side cutting, it is also assessed if ankle muscle activity differs between healthy individuals and those with FI.

Hypothesis:

Ankle muscle activity during perturbed treadmill walking and side cutting in individuals with and without FI will be reproducibly measured between test sessions (M1, M2), however will be affected by some variability (Barn et al., 2012; Danion et al., 2003; Hausdorff, 2005; Kadaba et al., 1989; Murley, Menz, et al., 2010). Further, ankle muscle activity will be different between healthy individuals and those with FI and between unperturbed and perturbed walking.

Main Question (MQ) 2*:*

Further, the study investigates if healthy participants would respond differently to an in-shoe-orthosis condition compared with FI participants during perturbed treadmill walking (normal unperturbed walking as control condition) and during side cutting at M1. Therefore, it is assessed whether ankle muscle activity differs between healthy participants and those with FI under "shoe only" and a measurement in-shoe orthosis condition at M1 (acute effect orthosis). This outcome provides data on the immediate effect of a foot orthosis related to a shoe condition (short-term adaptation). Consequently, differences in baseline ankle muscle activity between these conditions can be considered for long-term investigations.

Hypothesis:

Participants will show increased ankle muscle activity with a measurement in-shoe orthosis compared to a "shoe only" condition (particularly participants with FI)(Baur et al., 2003; Donovan et al., 2015; Ludwig et al., 2013; Murley, Landorf, et al., 2010).

Main Question (MQ) 3:

Orthotic intervention influences on ankle muscle activity are assessed and compared to a control group (no intervention) during perturbed treadmill walking (normal unperturbed walking as control condition) and during side cutting from M1 to M2 (longitudinal effect orthosis, any effect at all?). Differences in ankle muscle activity between foot orthotic intervention group and control group from M1 to M2 are also investigated.

Hypothesis:

Ankle muscle activity will be enhanced by the orthosis intervention compared to a control group (no intervention; decrease in ankle muscle activity)(Baur et al., 2011; Murley & Bird, 2006).

Side Question (SQ) 3a:

Participants in the orthosis intervention group are evaluated to see if they would present (even) higher ankle muscle activity by additional short-term use of a measurement in-shoe-orthosis (="transmission effect", meaning the effect of an increased ankle muscle activity got intensified by the short-term orthosis use) after intervention phase at M2. Therefore, differences in ankle muscle activity are assessed between a "shoe only" and a measurement in-shoe orthosis condition in the orthosis group (related to control group) at M2.

Hypothesis:

A "transmission effect" (intensified effects by short-term orthosis application at M2) will exist in the orthosis intervention group.

Main Question (MQ) 4:

Orthotic intervention influences on ankle muscle activity is compared to sensorimotor training intervention during perturbed treadmill walking (normal unperturbed walking as control condition) and during side cutting from M1 to M2 (longitudinal effect orthosis).

Differences in ankle muscle activity between foot orthosis intervention group and sensorimotor training group from M1 to M2 are analyzed. Findings might give insight into possible adaptation mechanisms due to the long-term foot orthoses use.

Hypothesis:

The orthosis intervention will be as effective as sensorimotor training (Lee et al., 2013) in increasing ankle muscle activity or will be even more effective compared with a sensorimotor training intervention in terms of a more pronounced increase in ankle muscle activity.

Main Question (MQ) 5:

Finally, it is considered and tested if healthy participants would react differently to a measurement in-shoe orthosis condition after intervention phase compared with FI participants during perturbed treadmill walking (normal unperturbed walking as control condition) and during side cutting at M2. Thus, differences in ankle muscle activity between healthy participants and those with FI in the intervention groups from M1 to M2 are examined (longitudinal effect orthosis). This could help yield new strategies when prescribing adequate treatment/therapy intervention for individuals with FI and serve as the starting point when planning tailored treatment programs.

Hypothesis:

Individuals with FI will show an increased ankle muscle activity after both interventions (and more pronounced) compared with healthy individuals.

CHAPTER II- METHODS

2. Methods

2.1 Study Design

This study (randomized controlled trial) was approved by the ethical committee of the University of Potsdam and conducted following the European Community of Good Clinical Practice (EC-GCP) Note for Guidance and the Consolidated Standards of Reporting Trials (CONSORT) guidelines for randomised controlled trials (www.consort-statement.org)(see flow chart according to CONSORT 2010 Flow Diagram and Checklist in section "Participants-Group assignment and randomization procedure"). All experiments were conducted at the Outpatient Clinic of the University of Potsdam (Germany).

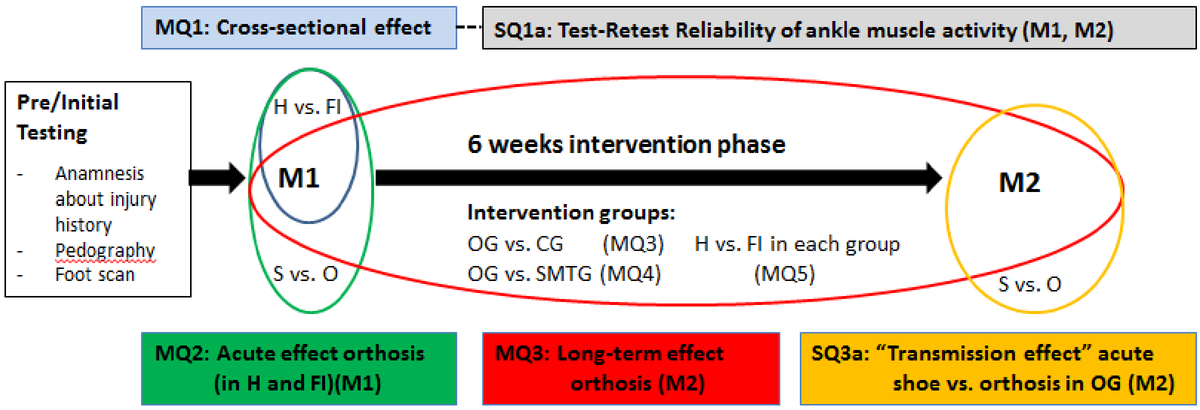

Figure 6: Schematic representation of study design; *SQ = side question, MQ = main question; H = healthy participants, FI = participants with functional instable ankles, S = "shoe only", O = (measurement in-shoe) orthosis, OG = orthosis intervention group, SMTG = sensorimotor training group,*

Participants underwent an intervention study (longitudinal study design) with two identical measurement protocols on 2 different days (M1, M2), separated by 6 weeks. Questions 1 to 5 were answered by this single intervention study (Table 1). The schematic representation (flow chart) in brief outlines the study design with the intervention phase and groups involved (Figure 6).

2.2 Participants

Recruitment of study population and inclusion criteria

Individuals responding to a study flyer were recruited from August 2012 to April 2013. Each participant signed a written informed consent prior to the first measurement. Inclusion criteria for participants consisted of an age of 18-35 and performing physical activity at least 3 times per week for 60 minutes. Participants with healthy ankles, functionally instable ankles or both (one side healthy, the other functionally instable) were recruited. After, participants' ankles were categorized into 2 groups - healthy (H) and FI. Separate ankles, independent from side, were considered for classification into the 2 groups. A possible scenario was that a participant could have a healthy ankle unilateral and FI ankle contralateral, whereby the healthy ankle was designated into the healthy ankle group and the FI ankle into the FI ankle group. Criteria for H group were a frequency of no sprains, a cut-off score of ≥28 points on the "Cumberland Ankle Instability Tool" (CAIT) questionnaire and ≥80% on the "Foot and Ankle Ability Measure" (FAAM) questionnaire. Both questionnaires are valid, self-reported questionnaires concerning ankle instability (Carcia, Martin, & Drouin, 2008; Hiller, Refshauge, Bundy, Herbert, & Kilbreath, 2006). Classification of participants into the FI group was based on the model of Hiller et al (2011), in which, among others, a subgroup of individuals with "perceived instability" (equals functional instability) and "recurrent sprain" was defined (Hiller et al., 2011). Inclusion criteria for participants with functional instable ankles (FI) were a frequency of at least 2 sprains at least 4 weeks ago (to ensure not to include participants with acute ankle sprains) and one of two cut-off scores (CAIT score ≤27 points, FAAM sport-subscale score <80%) (Caulfield & Garrett, 2002; Gribble et al., 2013; Hiller et al., 2006; Steib et al., 2013). According to the definition of FI (minimum of 2 ankle sprains), some of the ankles could not be categorised into one group or the other as they were neither healthy nor functionally instable (e.g. only 1x sprain) and thus, were excluded. Participants with acute or chronic infections, acute complaints/injuries of lower limb (e.g. acute ankle instability, tendon or muscular pain), any skeletal diseases or mechanical instability of the ankle were also excluded from the study. The selection criteria for FI within this research were fixed based on different literature. First, the mentioned CAIT questionnaire score was chosen due to Lin et al. (2011) and the guidelines from Hiller and colleagues (Hiller et al., 2006; Lin et al., 2011). The latter study group described a specific threshold score (≤27 points) for the specific population of FI (Hiller et al., 2006). Literature regarding FAAM score cut-off values for participants with FI does not exist, so, the FAAM questionnaire score (<80%) within this study work was determined according to guidelines of the position statement of the International Ankle Consortium (Gribble et al., 2013). Due to the inconsistency in FI terminology and its selection criteria across studies, the position statement provides the best available and endorsed evidence standards/guidelines of selection criteria for chronic ankle instability. These recommendations were reported to produce consistent population characteristics and thus, to improve the consistency/validity and quality of future research conducted in this clinical population.

N=55 individuals were initially assessed for eligibility. N=6 individuals did not attend the initial investigation. Finally, N=49 individuals (23 males, 26 females) were included into the study. They were then randomly allocated (a "simple/complete" kind of randomization) to one of the 3 intervention groups. Anthropometric data of the 49 participants (with questionnaire scores) is presented in Table 3. N=17 participants were allocated to the orthosis group (OG), N=17 participants to the sensorimotor training group (SMTG) and N=15 to the control group (CG). Within the orthosis group, N=16 ankles matched the criteria for healthy ankles and N=2 for functionally instable ankles. Within the sensorimotor training group, N=13 ankles matched the criteria for healthy ankles and N=9 ankles for functionally instable ankles. Within the control group (6 males, 8 females), N=12 ankles matched the criteria for healthy ankles and N=11 ankles for functional instable ankles (see Table 2). The control group was considered for the test-retest reliability study (SQ1a). From N=49 participants, N=9 participants were excluded due to being neither healthy nor having functionally instable ankles. Additionally, data from N=1 participant (frequency of spraining, CAIT- and FAAM score) was missing. Thus, N=39 participants (78 ankles) were considered in the final data analysis (see flow chart Figure 18 [n=11 in orthoses group, n=14 in sensorimotor training group, n=14 in control group], results section).

Table 3: Anthropometric data of the 49 participants (mean±SD), divided into 3 intervention groups, and scoring on CAIT- and FAAM (sport subscale) questionnaires (mean±SD)

Subjects	Age (yrs)	Height (m)	Weight (kg)	Healthy/ functional instable ankles	Frequency of spraining	CAIT score (pts)	FAAM score (pts; %)
OG (N=17)	26±4	1.76±0.84	73±9	**Healthy ankles (n=16)**	N=16: 0x	30±0	31±2; 97±6
				Functional instable ankles (n=2)	N=1: 2x; N=1: 3x	23±5	31±1; 96±2
				Neither H nor FI ankles (N=14)	N=5: 0x; N=5: 1x; N=2: 2x; N=2: 3x N=1: -	27±2	30±2; 95±7
SMTG (N=17)	24±3	1.72±0.80	68±9	**Healthy ankles (n=13)**	N=13: 0x	29±1	31±2; 97±6
				Functional instable ankles (n=9)	N=1: 2x; N=2: 3x; N=6: 3x	24±3	28±4; 87±13
				Neither H nor FI ankles (N=12)	N=7: 1x; N=4: 0x; N=1:2x	26±4	30±4; 95±7
CG (N=15)	25±5	1.77±0.97	76±15	**Healthy ankles (n=12)**	N=12: 0x	30±1	30±2; 95±7
				Functional instable ankles (n=11)	N=5: 2x; N=1: 3x; N=5: 3x	24±5	30±2; 94±5
				Neither H nor FI ankles (N=7)	N=5: 1x; N=2: 2x	27±3	30±2; 95±7

FAAM score calculation: item score total (0-32 points [pts]) were transformed to % scores (division of total sub score of each subscale by highest potential score multiplied by 100); if both ankles were identified as functional instable, the worse value of CAIT was taken; *OG = orthoses intervention group, SMTG = sensorimotor training group, CG = control group*

Group assignment and randomization procedure

A randomization list was generated using the website www.randomization.com and kept in a locked cabinet. To ensure allocation concealment, the allocation sequence (sequentially numbered containers) was concealed from the main investigator until the interventions were assigned to the participants. The main investigator generated the random allocation sequence, enrolled the participants and assigned the participants to the different intervention groups. No procedure of blinding could be performed since the participants were aware of their treatment intervention. However, the randomisation list with individual group assignment of participants was neither seen by the medical doctors nor by the participants before the end of the testing procedure at which group allocation was revealed. Recruitment and randomization procedure is shown in Figure 20 (results section).

2.3. Test Protocol

Initial testing

All participants signed a written informed consent document. Participants underwent an initial screening 1-2 weeks before M1. It consisted of a pedography, a foot scan and an anamnesis of the injury history regarding ankle sprains as well as of the training. Injury history was documented using the following questions (Figure 7):

1. Have you ever had an ankle sprain (acute injury; medical visit)?
Yes ☐
No ☐
(in case of “no“, do not answer questions 2-4)

2. How many times have you sprained your ankle? Which side was affected?
left side
☐ 1x; ☐ 2x; ☐ 3x; ☐ >3x
right side
☐ 1x; ☐ 2x; ☐ 3x; ☐ >3x

3. Which side is/was affected more strongly (if both sides were affected)?
left side ☐
right side ☐

4. How long ago was/were the last ankle sprain event/s?
left side ☐<4 weeks; ☐ <6 months; ☐ >6 months
right side ☐<4 weeks; ☐ <6 months; ☐ >6 months

Figure 7: Injury history anamnesis, including 4 questions

Additionally, the recent training state of participants was queried (last 6 months: training years [n]; type of main sport; training volume per week [units [n]/wk]; training duration per session [min./session]). 2-D-foot scans were taken of those participants, who were randomized to the orthoses intervention group (Figure 8). Thereby, an orthopaedic shoe technology association (IETEC Orthopädische Einlagen GmbH Produktions KG [http://www.ietec.de/]) could be provided with information such as the foot type and individual shoe size. On this basis, the association produced customized foot orthoses for each participant. Furthermore, dynamic plantar pressure distribution (pedography) was recorded separately for left and right (bare-) foot while walking over a pressure platform Emed SF, novel, Munich, Germany) along a walkway (Figure 9).

Figure 8: 2-D-Foot-scanner

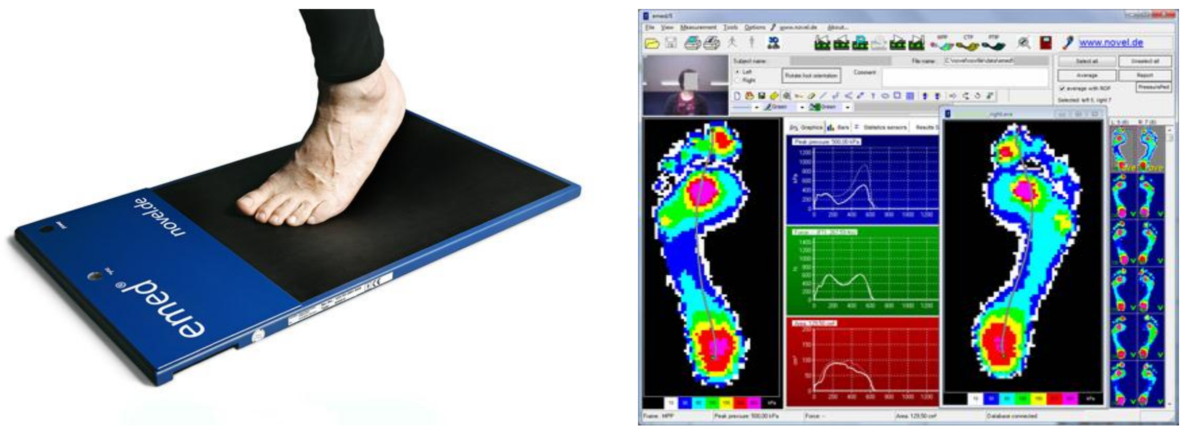

Figure 9: Walking over plantar pressure plate (PEDAR)(left), plantar pressure distribution (parameter: peak pressure, COP) calculated by software Novel, Pedar (right)

Questionnaires

Participants were instructed to complete two valid, self-reported FI questionnaires, the CAIT- and FAAM (Carcia et al., 2008; Hiller et al., 2006; Nauck & Lohrer, 2011). The CAIT questionnaire asks participants about situations in which their ankle joint feels instable (e.g. when running/standing on one leg or jogging on uneven surfaces) and the frequency of the particular event (e.g. always/never/sometimes) (see appendix, Figure 1). By checking boxes, participants choose a statement which best describes the situation of his/her ankle. The CAIT consists of 9 questions with a total of 30 possible points. Lower scores indicate more severe FI. As aforementioned, a score of less than or equal to 27 indicates FI, whereas a score of 28 or higher indicates no FI. The CAIT questionnaire does not require comparison with the contralateral ankle. The FAAM is a 29-item questionnaire divided into two subscales: a 21-item Activities of Daily Living (ADL) subscale and the 8-item Sports subscale (see appendix, Figure 2 a-c). The sports subscale assesses more difficult tasks essential to sport; it is a population-specific subscale designed for athletes. The FAAM inquires on the difficulty a subject has when performing different situations in everyday life and sporting activities (for ADL activities e.g. walking on even ground, walking up hills, going downstairs; for sport activities e.g. running, jumping, cutting). By checking boxes, each question should be answered with a response that most adequately describes the respective condition. At the end of the ADL- as well as the FAAM sports subscale, participants rate their current level of function quantitatively from 0 to 100 (100: level of function before problem, 0: inability to perform any of the ADL activities) and qualitatively (normal/nearly normal/abnormal/severely abnormal). Each item is scored on a 5-point Likert scale (4 to 0) from ”no difficulty at all” to “unable to do”. Scores are then added together to get an item score total. The total number of answered items is multiplied by 4 to calculate the highest potential score. For example, if the subject answers all 21 or 8 items, the highest potential scores are 84 or 32. The item score total then is divided by the highest potential score and multiplied by 100 to compute the percentage. Higher scores represent higher levels of physical function for each subscale, with 100% representing no dysfunction.

Clinical examination

Participants also underwent a clinical examination of their ankle joints. This medical investigation consisted of an anterior and posterior drawer test (ligament laxity) and talar tilt test/inversion stress test ("laterale Aufklappbarkeit")(Parasher, Nagy, Em, Phillips, & Mc Donough, 2012; Phisitkul et al., 2009; Witchalls et al., 2012). If the anterior and posterior drawer test, as well as talar tilt test, was positive, participants' ankles were diagnosed as "mechanically instable". The intention was to examine a portion of the FI population displaying functional limitations due to sensorimotor deficits (Hopkins et al., 2012). Thus, the laxity tests served as differential diagnoses for participants in the study because individuals with mechanical instability were excluded. Additionally, a physician confirmed the suitability of the participants to perform study measures, but not all participants were assessed by the same doctor. In general, two doctors were included in the clinical examination. Before the study, ankle joint laxity tests were standardized in house, therefore avoiding subjectivity.

EMG preparation

The TA, PL and GM muscles of all participants were bilaterally prepared for surface EMG measurements. Localization of EMG electrodes was performed by the same investigator pre- and post-testing according to the recommendations of Winter and Yack, modified by Netter et al. (2006), and SENIAM (Figure 10, Table 4) (Hermens, Freriks, Disselhorst-Klug, & Rau, 2000; Netter, 2006; Winter & Yack, 1987)(www.SENIAM.org). Electrode placement was standardized between sessions. Electrodes were positioned in the center of the muscle belly and the longitudinal axes of the electrodes in line with the presumed direction of the underlying muscle fibres. Relevant skin areas were prepared by shaving, light abrasion, degreasing and disinfecting with alcohol to minimize skin impedance and ensure a proper EMG signal (interelectrode resistance below 5 kΩ) (Horstmann et al., 1988). EMG electrodes (disposable pregelled Al/AgCl bipolar surface electrodes [Ambu, Medicotest, Denmark, type P-00-S, inter-electrode distance 25 mm] were placed on the skin. 6 Channel sEMG (M320 TXB, myon AG, sampling frequency 4000 Hz, Schwarzenberg, Switzerland) was recorded by IMAGO-Software (pfitec, biomedical systems, Endingen, Germany). Cross-talk was minimized with the small size/distance of adjacent electrode pairs and the placement of electrodes on the muscle belly center.

Table 4: Localization of electrodes according to Winter and Yack (1987)

Muscle	Localization
M. tibialis anterior	Over the area of greatest muscle bulk just lateral to the crest of the tibia on the proximal half of the leg.
M. peroneus longus	Midway along the line between the head of the fibula and the lateral malleolus.
M. gastrocnemius	Over the area of greatest muscle bulk on the medial calf.

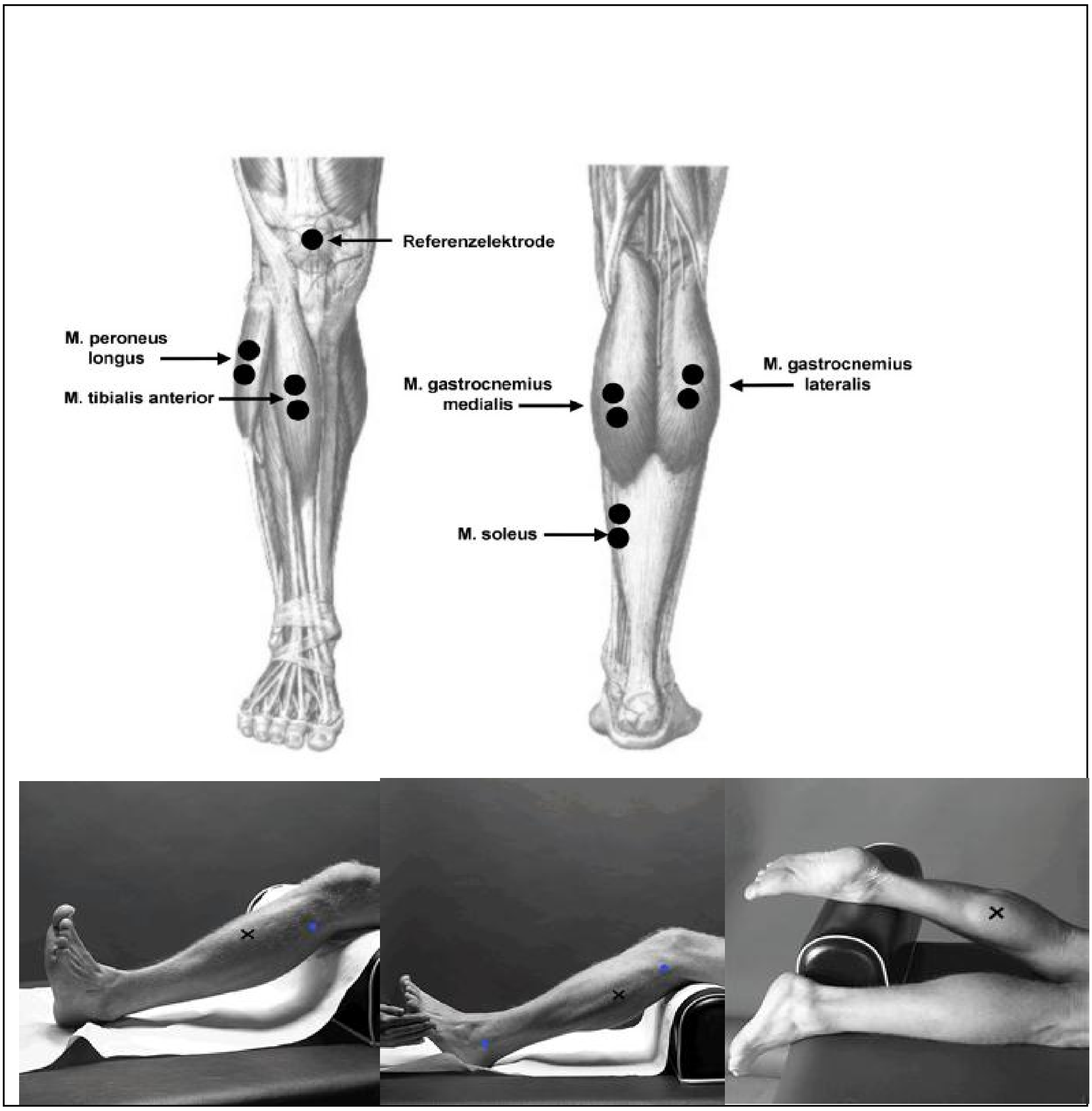

Figure 10: Localization of electrodes according to Winter and Yack (1987)(above), modified by Netter et al. (2006)(Netter, 2006)and based on SENIAM recommendations (below)

After EMG preparation, a measure of maximal voluntary contraction (MVC) of 5 seconds duration was performed (Inglis, Howard, Mcintosh, Gabriel, & Vandenboom, 2011; Palmieri-Smith et al., 2009; Siddiqi, Arjunan, & Kumar, 2015). For testing of PL and GM, a standing calf raise (toe stance) was completed. After a verbal signal, participants moved with one leg forward and lifted up their heel. To maintain balance, they were permitted fingertip contact with a wall in front of them. 3 trials per side were performed. Similar MVC testing protocols during standing have been previously described, although for GM an additionally downward manual force was applied on the shoulders of the participant (Ahn, Kang, Quitt, Davidson, & Nguyen, 2011; Arora, Budden, Byrne, & Behm, 2015; Bellew et al., 2010; Bhaskaran et al., 2015). Measure of TA MVC was conducted in a standing step position (hands fixed to the pelvis). Participants were instructed to push up with the forefoot (without shoe) against the resistance of a taut rope (dorsal extension), below which the dorsum of the foot was firmly strapped. At their ends, the taut rope was fixed on the ground by help of two heavy dumbbells. 3 trials per side were performed. A similar testing setup for TA MVC was performed in other studies, although participants were in a sitting position and the ankle joint was fixed differently (Giesebrecht, Martin, Gandevia, & Taylor, 2010; Inglis et al., 2011; Siddiqi et al., 2015).

Test procedure: Walking and stumbling on split-belt treadmill and side cutting

The participants warmed up for 5 minutes at a baseline velocity of 1 m/s (corresponding to 3.6 km/h) for familiarization on the customized split-belt treadmill (WOODWAY® GmbH, Weil am Rhein, Germany) (see Figure 11). The split-belt treadmill used is a newly designed treadmill with two separately controllable tread-belts by which disrupting stimuli can be initiated separately in desired combinations related to direction, form, duration and distance of time (Berger, Dietz, & Quintern, 1984; Granacher et al., 2010; Horstmann et al., 1988). It is possible to generate disrupting stimuli of powerful acceleration and deceleration within milliseconds. A recent pilot study demonstrated high technical validity and reliability of a split-belt treadmill walking perturbation setup (Engel et al., 2013). For safety reasons, subjects were provided with a waist belt during walking, connected to an emergency stop release from the ceiling. All participants wore a neutral running shoe (Nike, Air Pegasus, 2002) in their individual shoe size (condition 1) or the shoe with the embedded/in-shoe orthosis (condition 2). The order of the test conditions was randomized (Figure 12).

Figure 11: Walking on split-belt treadmill (WOODWAY) with security restraint system connected with the ceiling (red mark 1); in-shoe-sole connected with PEDAR X software at right leg (red mark 3), accelerometer at left leg (red mark 2)

Figure 12: Two different test conditions ("shoe only" [left], in-shoe orthosis [right])

In the subsequent test session (speed was maintained at 1 m/s), a protocol of sudden stumbling stimuli (STIMULI treadmill software [Pfitec® biomedical systems, Endingen, Germany]) was applied with a delay of 200 ms after initial heel contact (IC) related to mid-stance phase of walking (Winter & Yack, 1987)(Figure 14). IC and subsequent perturbation were triggered by a plantar pressure measurement sole (Pedar X® plantar pressure system, 50 Hz sampling rate, threshold value: 40 kPA, Novel GmbH, Muenchen, Germany; Figure 11, 13). The software Pedar X online was used to forward the trigger signal to the STIMULI software of treadmill, which released the perturbations (Figure 13, 14). In-house studies revealed highly reliable trigger delay (TRV 5.7±5.5%, bias ±1.96*SD 3±36)(Engel et al., 2013). However, general measurement delay around 100 ms between IC (external trigger) and the programmed perturbation by treadmill software STIMULI were accepted. The software pre-settings for stimuli characteristic were n=45 perturbations (15 left and 15 right, 15 "dummy perturbations" [no perturbation, but pretending to apply one]; 100 ms duration; change of speed of 2 m/s), randomly assigned over time and by side (Figure 14).

Figure 13: In-shoe based plantar pressure sensor and soles by Pedar Novel (Pedar X)

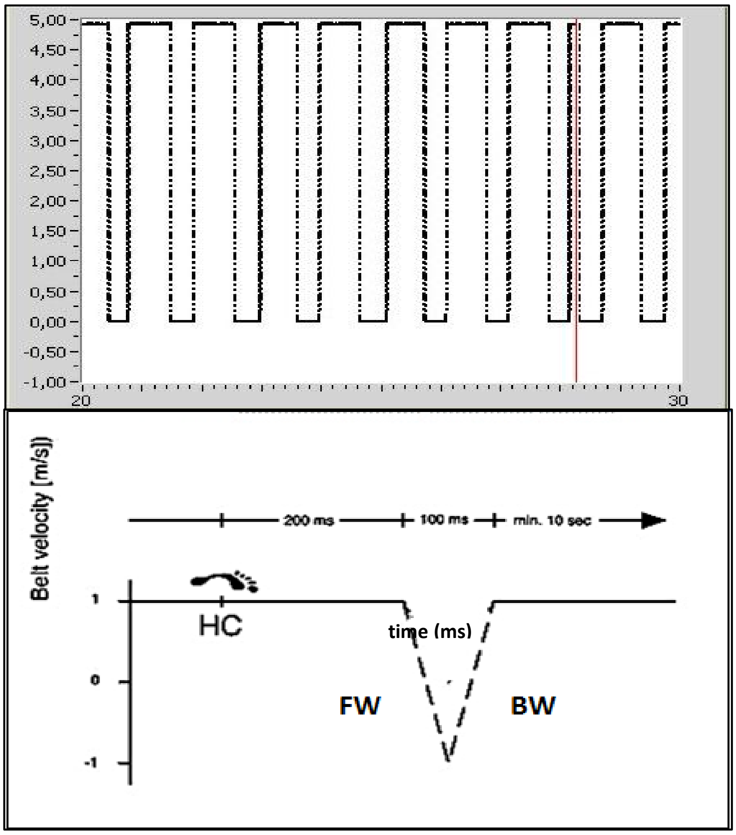

Figure 14: STIMULI software (Pfitec) with external trigger for perturbation (4 point curve, x-axis: time [s]; y-axis: amplitude of trigger signal)(above); Characteristic of perturbation impulse by STIMULI software: baseline belt velocity of 1 m/s; initiation of superimposed perturbation 200 ms after initial heel contact (HC); 100 ms duration of perturbation (50 ms deceleration to -1 m/s [correspond to 40m/s^2, forward motion of belt [FW]]; 50 ms acceleration back to 1 m/s baseline velocity [backward motion [BW] of belt]), minimum of 10 sec. until next perturbation; waveform: 3 point perturbation curve (below)

Additional "dummy" stimuli without perturbation were released to avoid an adaptation of the normal gait pattern in expectation of stumbling. Subjects were informed about the nature of the perturbations prior to testing, however not about exact timing and side of the perturbations since they randomly occurred during the session. Perturbations were adjusted to individual step length, which was recorded by 3-D video motion capture system (VICON MX3, 10-camera setup, frequency of 200 Hz, Oxford; reflective marker at backside of both shoes). Participants underwent 4 perturbed walking sessions (2 times with "shoes only", 2 times with in-shoe orthoses) for approximately 8.5 minutes on the split-belt treadmill at both testing sessions M1 and M2. Both, normal unperturbed walking and perturbed walking trials were collected over 1 treadmill walking session. As the STIMULI software was unable to consider two single analogue trigger signals, one active plantar pressure sole (within left OR right shoe) signal per session was used to trigger the perturbations. According to the randomization protocol, during all perturbed walking sessions (sole in left shoe, sole in right shoe), the sole directly released the belt perturbation (ipsilateral or contralateral perturbation with time delay according to step length). Thereby, it was ensured that both sides could be analyzed accurately (stumbling stimuli without time delay on at least one side). Additionally, acceleration (ACC) sensors (1600 Hz sampling rate), attached bilaterally 10 cm proximal to the Achilles tendon insertion, served to detect IC and beginning of perturbation onset in the EMG signal. The ACC- and EMG signal was synchronously recorded by IMAGO-Software (Record Master, Pfitec® biomedical systems, Endingen, Germany). Bilateral perturbations helped avoid gait adaptations to only unilaterally stumbling incidences. A rest of at least 10 seconds between perturbations guaranteed a normal walking pattern was achieved after the previous and before the subsequent perturbation. Simultaneously, muscular activity (surface EMG) of the TA, PL and GM muscles was recorded by IMAGO software (Process Master, Pfitec® biomedical systems, Endingen, Germany).

After treadmill walking, participants were instructed to perform a side cut movement. The side cut movement was characterized by a quick change of direction (Ford, Myer, Toms, & Hewett, 2005). These movements are key offensive strategies in ball sports, commonly incorporating a sudden deceleration phase on impact, accompanied by a rapid speed and/or directional change to evade an oncoming defensive opponent (Wright et al., 2013). The side cut maneouvre was performed under both conditions, "shoe only" and in-shoe orthosis.

During the trials, subjects wore a standardized “shoe only” (Nike, Air Pegasus) or the orthosis within the shoe. Again, the order of these conditions was randomized. The side cutting maneouvre was performed as follows (see Figure 15). After a verbal signal, participants were instructed to run straight forward in the direction of a plastic skeleton, positioned about 15 cm behind a force platform (AMTI) and in line with the original direction of motion (McLean, Lipfert, & van den Bogert, 2004). The skeleton simulated an opponent player. When participant reached a marker on the ground, he/she initiated the cutting movement by planting/contacting the left/right leg on the force platform and then cutting to the right/left at an angle of 45° from the direction of approach and in the opposite direction of the planted leg (Cowley, Ford, Myer, Kernozek, & Hewett, 2006; Hanson, Padua, Troy Blackburn, Prentice, & Hirth, 2008; Landry, McKean, Hubley-Kozey, Stanish, & Deluzio, 2009)(see Figure 16). Although pivoting angles vary among athletes, 45° from the original movement direction has been used as a standard angle for side cutting in accordance with values typically observed in the game situation (Landry et al., 2009; Wilderman, Ross, & Padua, 2009). To standardize the cutting angle, an alleyway, placed 45° relative to the participant’s forward path of motion, was marked on the ground. The angle was measured from the center of force plate and the corresponding line was marked with athletic tape which was clearly visible for the participants. A trial was deemed successful only when the foot contacting the ground was within and pointing in the direction of prescribed range of the alleyway (Wilderman et al., 2009). A light barrier system (40 cm before the plate; cameras positioned towards each other at edge of runway with 1 m distance to each other) controlled the velocity of the subjects. According to literature, trials with approach speeds between 3.3 to 5.5 m/s were accepted (corresponding to about 11 to 18.5 km/h) (Landry et al., 2009; Wilderman et al., 2009). This velocity was used to ensure movements were fast enough to really simulate a sport-specific situation. Direction of the cut was randomized over 6 trials (3 per side) with a 30 second rest period between trials (Hanson et al., 2008). Simultaneously, muscle activity of the TA, PL and GM muscles was recorded by surface EMG. The same described test situations (stumbling on treadmill, side cut) were performed after 6 weeks at M2.

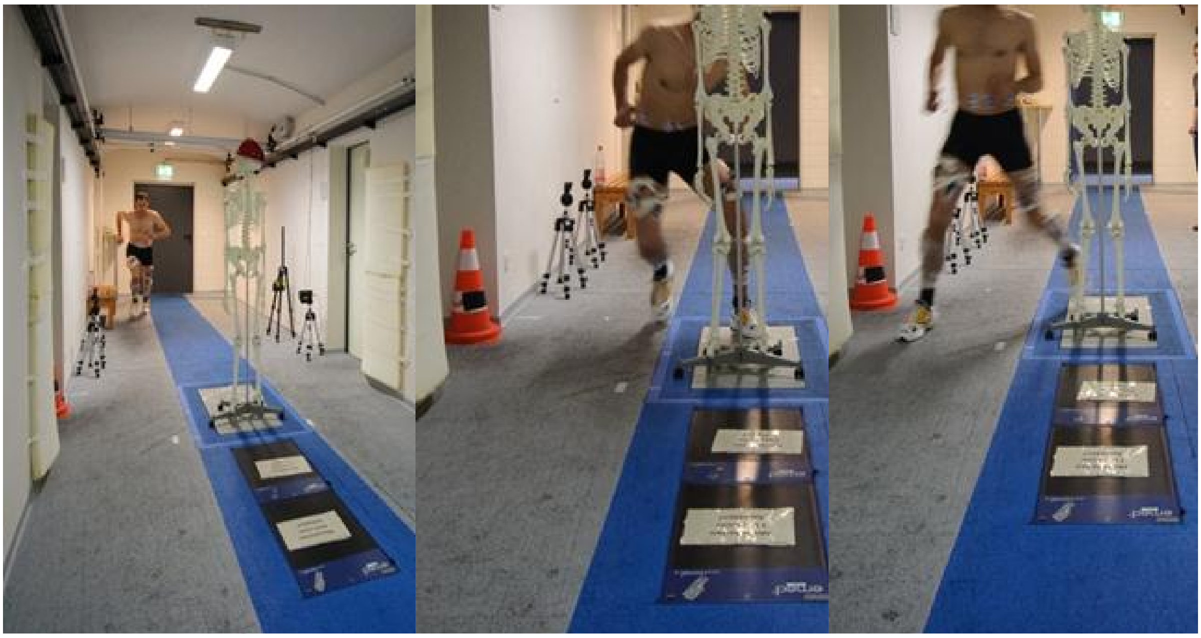

Figure 15: Exemplary performance of the side cut manoeuvre with plastic skeleton simulating a defending player; second picture: planting motion of left leg on force plate; third picture: cutting motion of right leg back to running track

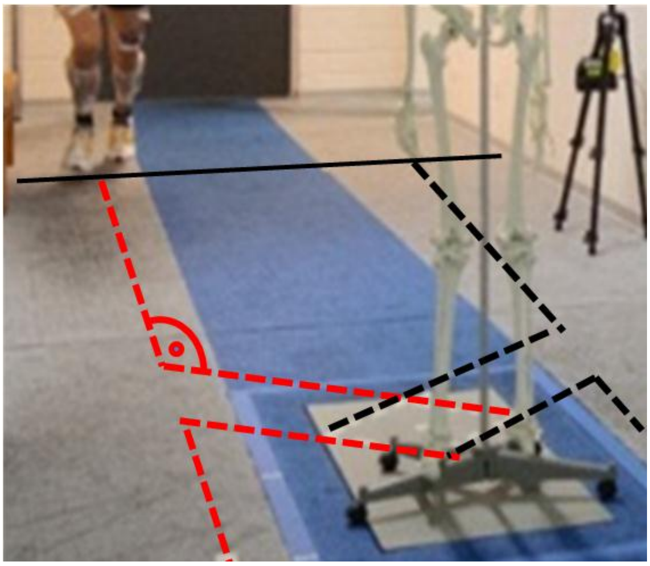

Figure 16: Angle of side cutting, marked by tape on the ground; example of right-sided cut (red lines indicate running direction and the alleyway characterized by an angle of 45° related to running direction [first straight ahead the floor, then plant to the left with left foot on force plate and subsequent cut to the right with the right foot back to initial running track)

2.4 Training Interventions

Foot orthoses intervention

After performing the described tests, participants were informed which of the three intervention groups they were randomly assigned to (orthoses group, sensorimotor training group or control group). Depending on their assignment, they were instructed about their intervention program.

The orthosis group was equipped with a particular in-shoe orthosis. As previously mentioned, the orthosis was individually customized by the orthopaedic shoe technology association (IETEC Orthopädische Einlagen GmbH Produktions KG, Fulda, Germany, type "Move Control") on the basis of 2-D-foot scans and participant's dynamic barefoot plantar pressure distribution using Emed SF pressure platform. The orthosis consisted of the following common functional elements: polyurethane foam material (compression moulded and semi-rigid to ensure possible flexibility of orthoses during walking, a bowl-shaped heel [to guarantee right positioning of foot above functional element], a detorsion wedge and a medial longitudinal arch support. The functional elements of the orthosis were individually adjusted according to the dynamic plantar pressure measurements of each participant. The advantage of the orthosis is the stiffness of the polyurethane material, which is comparable to the midsole material of standard running shoes (Hirschmüller et al., 2011). This relatively stiff material is thought to provide a direct feedback from the running surface and thus enhance proprioception of the foot sole (Hirschmüller et al., 2011). The combination of orthosis and shoe leads to a proper fit and a synergism of their effects (Baur et al., 2003). However, one special characteristic of the foot orthosis was the "peroneus longus stimulation module". This module is characterized by an increased area imbedded in the orthosis at area of the ball of the foot/first metatarsophalangeal bone, designed with the idea to let participants push at this region when wearing the orthosis or performing any kind of sport to increase plantar pressure at the region of the metatarsophalangeal joint of the big toe. This subsequently evokes muscle activity of PL. The customized foot orthosis and its particular feature, the oval-shaped "stimulation module", is shown in Figure 17.

Figure 17: Foot orthosis construction with the particular characteristic "peroneus longus stimulation module" (marked with an arrow) imbedded into the orthosis at area of ball of the foot

For long-term orthotic intervention, participants were informed about the features of the orthosis. The individual orthosis was handed out to participants and a correct fitting to their personal sport shoes was verified. Additionally, two practice sessions were completed, describing to participants how the orthosis should properly be worn. For the first exercise (at least 3 practice trials), participants were instructed to lift up the big toe and to then build up pressure below the ball of the big toe at the area of first metatarsophalangeal bone**.** Activation of peroneal musculature was initiated by a small foam sheet simulating the stimulation module, which was placed below the ball of the foot at the metatarsophalangeal joint of the big toe (see Figure 18). For orthotic familiarization, the same exercise was performed with individual orthoses below their foot (without a shoe). The second exercise (at least 3 practice trials) consisted of similar instructions and was executed with the foot orthosis inserted inside the shoe in standing position. During briefing, emphasis was put on actively building up increased pressure medially, below the ball of the big toe at region of the stimulation module when wearing the orthosis during roll motion of foot (push off phase), while performing active exercises during the next 6 weeks of intervention phase.

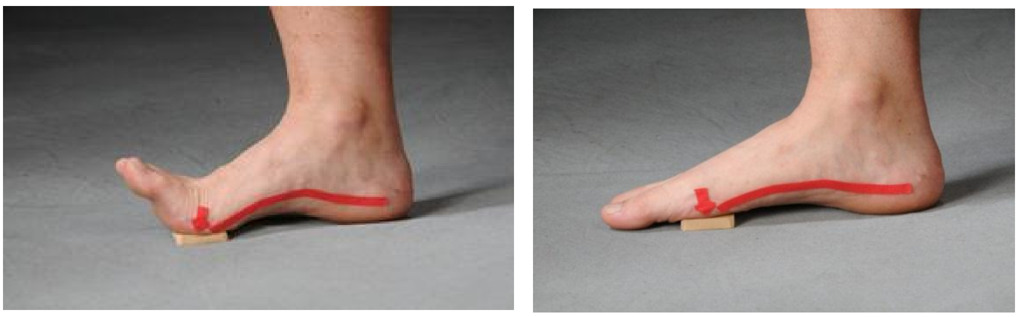

Figure 18: Practical exercise for the foot; participants were asked to put pressure medial onto the small foam, which simulated the "stimulation module" (left picture: lifting up first toe, second picture: pushing onto module)

Participants were instructed to contact their study coordinator directly in case of any fitting problems, blisters, bruises or other symptoms. After, participants were briefed on the orthoses protocol and their obligations throughout the intervention period. The requirements during the orthotic wearing period were as follows. The orthoses had to be worn at least during each training session/sport unit throughout the intervention phase (guideline: at least 3x/week [=18 of 42 days intervention], see inclusion criteria). Additionally, participants were asked to wear the orthoses during physical activity, including all everyday life exposures, like walking. The complete 6-week protocol can be found in the appendix (Figure 3).

Sensorimotor training intervention

Training exercises (postural control/balance, strength exercises or a combination of both) were developed as home-based exercises with the aim to stabilize the ankle joint by activating the ankle musculature. The tasks included dynamic weight-bearing on the forefoot and multidirectional exercises targeting the primary biomechanical function of the PL (Bellew et al., 2010). The program contained 5 exercises with increasing levels of difficulty over the 6 weeks (Table 5). Specifically, a one-leg stance on a towel role (folded several times), a one-legged heel raise, a forward lunge on a towel, jumping from a staircase and landing on the ground and side-jumps were used as exercises. In level B and C, the original exercises were complemented with additional tasks (e.g. instable surfaces, back pack with load [additional weight 5% of body weight in level B and 10% of body weight in level C]). During exercises, participants concentrated on actively building up pressure below the ball of the foot. Participants were instructed to perform the training program once per day (minimum 3 times per week, guideline: 18 of 42 days intervention) for 20-25 minutes per unit. If participants were unable to perform the prescribed exercise (level B and C), they were requested to go back one level. The training protocol and any deviations were documented over the 6 weeks of intervention (see appendix, Figure 4).

Table 5: Structure of the home-based training program (with increased levels of the exercises over the 6 weeks)

	Week 1	**Week 2**	**Week 3**	**Week 4**	**Week 5**	**Week 6**
Exercise 1-5 (Level A-C)	A		B		C	

Compliance of the sensorimotor training/orthoses intervention and its documentation was checked by three telephone calls (after 2, 4 and 6 weeks). Both intervention groups were advised to continue their regular training activities without modification of any training habits, which would affect study results. Comparability of study interventions, considering the frequency of training (guideline for sensorimotor training group: at least 3x/week; guideline for orthoses group: each training session/sport unit) was ensured, since both groups performed sensorimotor training program/orthoses intervention for at least 18 of 42 days (43% of intervention phase).

2.5 Data Analysis

Training anamnesis (training years [n]; type of main sport discipline; training volume per week [units [n]/wk]; training duration per session [min./session]), as well as compliance of participant documentation (orthoses protocol: mean duration in wearing the orthoses during every day-day life activities and sport [for each: time [in min.]/day], sensorimotor training protocol: mean duration of days), were analyzed.

The main outcome parameter in this study work was the root mean square (RMS) of EMG signal amplitude for the TA, PL and GM muscles. For EMG signals detected during voluntarily contractions, RMS is the recommended standard and provides the most insight on the amplitude of the EMG signal since it measures the mean power of the signal (DeLuca, 1997; Gitter & Stolov, 1995). After rectification of the EMG signal (by IMAGO-software), the RMS signal was determined during normal unperturbed and perturbed walking (for one stride, respectively) and during side cuts (average of 3 trials/side) within the time epoch of 100-50 ms pre IC and 200 to 400 ms post IC (Figure 16). Ankle stability is mainly required during the initial loading and terminal unloading of stance phase (Stormont, Morrey, An, & Cass, 1985). Thus, time window 100-50 ms pre IC was defined to identify pre-activity of ankles muscles (preparatory activity/feedforward mechanism), whereas the chosen time phase of 200-400 ms post IC detected characteristic (reflex) response activity of ankle musculature (feedback mechanism) after initiation of a stimulus (inversion perturbation) (Gutierrez et al., 2012; Lin et al., 2011; Nakazawa, Kawashima, Akai, & Yano, 2004; Suda et al., 2009). Reflex responses of ankle muscles are typically divided into three distinct responses: short-latency (SLR; 40-70 ms after stimulus), medium-latency (MLR; 70-100 ms after stimulus) and long-latency responses (LLR; >100 ms after stimulus) (Gutierrez et al., 2012; Taube et al., 2006). Only during perturbed treadmill walking, these reflex responses (as a whole reflex response 200 ms time window post perturbation [including SLR, MLR and LLR] without differentiating between each single responses) were taken into account. To enable proper inter-subject comparison of the response amplitudes, RMS of each muscle was normalized to 100% MVC. For calculation of MVC signal, a standardized trigger was set in the middle of the signal (at 2.5 sec) from which the signal was analyzed for a time window of 1 sec. (0.5 sec from trigger to left side, 0.5 sec to right side). In case of an irregular signal, the trigger was set at a point where the signal was constant and the same procedure was completed. ACC sensor signals were used as trigger of IC for subsequent muscle amplitude investigation, indicating the beginning of IC (unperturbed and perturbed walking, side cutting) and beginning of perturbation onset (for unperturbed and perturbed walking; Figure 19). Thus, the ACC signal synchronized the EMG signals (whereas the pedar sole was used to define/trigger IC and perturbation). This approach enabled the most precise event detection, as both ACC and EMG data were recorded synchronously by the same wireless transmission system.

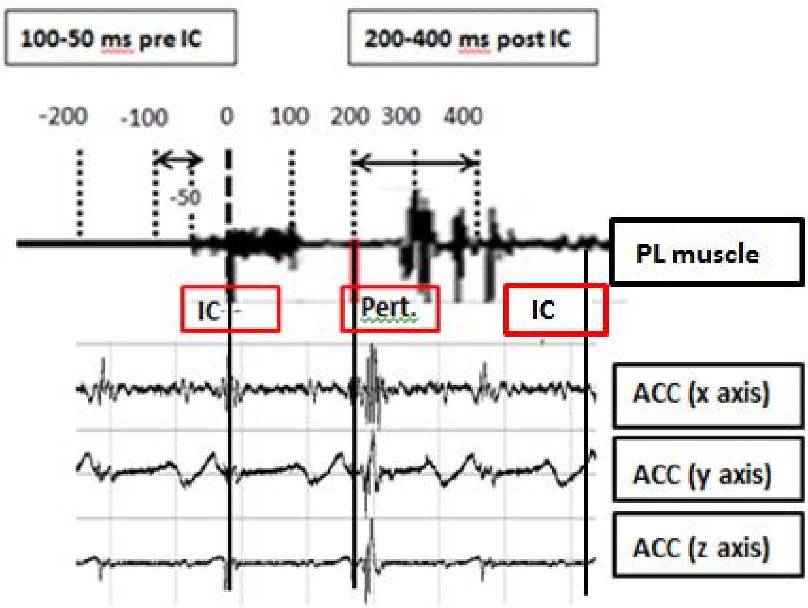

Figure 19: Schematic presentation of IC timing and perturbation (exemplary for unilateral PL muscle):
Pert .= the perturbation occurring 200 ms post IC; *IC* = initial heel contact, defined by accelerometer signal (ACC; x, y, z-axis) with first considerable decrease in signal and two time windows of data analysis (100-50 ms pre IC; 200-400 ms post IC)

EMG amplitude of 15 left and right strides (mean [±SD]) were calculated for unperturbed and perturbed walking. Solely for the side, where a perturbation was initiated, EMG amplitude was assessed and averaged for H and FI group, respectively. Step length was calculated with Vicon Software (Nexus 1.85). Considering the blinding procedure, three independent investigators assessed different packages of the EMG data. None were aware of the assignment of participant group assignment.

2.6 Statistics

Participants were encrypted by IDs. Baseline data from case report forms were manually entered into a database and crosschecked twice. All collected data were analyzed for plausibility and additionally verified with range checks. Implausible values were compared with the raw data and recalculated, if necessary. Furthermore, random samples were recalculated from the original data and manually compared with values in the database (>95% of values were required to be correct). Training anamnesis and compliance parameters were analyzed descriptively (mean±SD). Normalized RMS of EMG amplitudes (EMG-A) for M1 and M2 were also analyzed descriptively (mean±SD, %MVC).

Side Question 1a

Test-retest reproducibility of RMS amplitudes (%) was analyzed between M1 and M2 under both conditions. Verification of reliability served for a reasonable classification of measurement outcomes and the setup (Atkinson & Nevill, 1998). For evaluation of intersession reproducibility, four different criteria were used. The first: test-retest variability (TRV [%] = ($|x_i - y_i| / 0.5 (x_i + y_i) * 100$), where x_i represents the RMS amplitude values of M1 and y_i of M2 for subject i) calculated the group variability mean with each data pair from M1 and M2 and related to absolute differences (Mueller, Baur, Koenig, Hirschmueller, & Mayer, 2007). Individual means are given in %. For estimation of systematic bias and random error, other reliability criteria should also be considered (Mueller et al., 2007). Therefore, as a second criteria, a Bland-Altman analysis with bias and 95% limits of agreement (bias±1.96*SD) was performed (Bland & Altman, 1986, 1999; Hopkins, 2000). The mean and difference of each data pair (M1/M2) and subsequently, mean and SD of the differences was calculated. Graphically, Bland Altman plots illustrated the limits of agreement (LoA) according to the mean of the differences (bias) ± 2 SD (random error). Reliability criteria is fulfilled if 95% of all paired differences lie within the LoA (Bland & Altman, 1986, 1999). The third criteria investigated was intra-class correlation coefficient (ICC [2.1])(Shrout & Fleiss, 1979). This kind of correlation coefficient is used for two-way random single measures and provides absolute agreement/consistency information between two measures (Shrout & Fleiss, 1979). The fourth reliability measure was the coefficient of variation (CV, SD/mean*100 [%]). It expresses intra-subject variation between two measurements, thus describing the amount of variability relative to the mean of the population (dispersion of a probability distribution)(Atkinson & Nevill, 1998). A combined consideration of all four reliability criteria provided adequate information about reproducibility and enabled qualitative validation statements of the measurement setup.

Main Questions 1 and 2

Descriptive statistics were used to analyse normalized RMS of EMG-A (mean±SD, %) of M1 in both groups (healthy participants and those with FI) during both conditions ("shoe only" and in-shoe orthosis) for normal unperturbed and perturbed walking and for side cutting in two different time windows (100-50 ms pre IC and 200-400 ms post IC). Differences (M2-M1) of EMG-A RMS were also presented descriptively. Additionally, outcome variables were compared between both groups depending on condition "shoe only"/in-shoe orthosis and therewith, statistically analyzed by a 2-way between groups analysis of variance (ANOVA) ($p<0.0167$, see below). Independent variables considered were factor *ankle status* (healthy group of participants [H]/ group of participants with functional instable ankles [FI]) and factor *shoe condition* ("shoe only"/ in-shoe orthosis). In addition to main effects of *ankle status* and *shoe condition*, factor of interaction effect was analyzed *(interaction ankle status x shoe condition).* For all tests, EMG-A (RMS) was used as the dependent variable. Normality of the data (Shapiro wilk test for sample sizes n<50) and homogeneity of variances (using levenes test) was checked.

Main Questions 3, 4 and 5

Normalized EMG-A RMS of the intervention groups (MQ3: orthosis intervention group [OG] and control group [CG]; MQ4: orthosis group and sensorimotor training group [SMTG]); MQ5: H and FI in OG, SMTG and CG) during normal unperturbed (NW), perturbed walking (PW) and side cutting (SC) at M1 and M2 is presented descriptively (mean±SD, %). Differences (M2-M1) in EMG-A RMS are also presented descriptively. Mean outcome parameter differences were compared between the three intervention groups over time (MQ5: in dependence on ankle status within each intervention group) and thus, statistically analyzed with a 2-way repeated measures analysis of variance (ANOVA, between and within; $p<0.0167$, see below). The between factor was *intervention group* (OG, SMTG and CG) and the within factor *time* (M1, M2)(MQ5: second within factor was *ankle status* [H or FI]). Factors of interaction effects were also analyzed (interaction of *intervention group x time*)(MQ5: interaction of *intervention group x ankle status x time*). Additionally, baseline values (M1) of EMG-A RMS were compared between the three intervention groups using a Kruskal Wallis one-way-ANOVA to adequately evaluate differences in EMG-A between the groups after intervention (MQ 3, 4). Baseline values (M1) of EMG-A RMS were compared between H and FI in the intervention groups using a Mann-Whitney U-test.

Side Question 3a

Mean differences in EMG-A RMS were compared between "shoe only" condition and in-shoe orthosis condition with dependence on the intervention group (OG and CG) at M2 and therefore, statistically analyzed with a 2-way between groups analysis of variance (ANOVA) ($p<0.0167$, see below). Independent variables were factor *intervention group* (OG, CG) and factor *shoe condition* ("shoe only"/ in-shoe orthosis). Factors of interaction effects were analyzed *(interaction intervention group x shoe condition).* Again, EMG-A RMS was used as the dependent variable.

For all questions (except side question 1a), post-hoc tests with a Bonferroni-adjusted α were used to identify statistically significant differences between variables. Additionally, for all tests, a Bonferroni correction (traditional conservative test, which controls for familywise error rate) was used to correct any set of (pairwise) *p*-values for multiple comparisons (Victor, Elsässer, Hommel, & Blettner, 2010). As three muscles with a desired α-level of 0.05 were tested, significance level was set at $p<0.0167$. All of the data were considered with the approach of "intention to treat", a strategy considering the participants in the way they were randomly assigned at beginning of the trial, regardless of their adherence with the entry criteria, of the treatment they actually received and of subsequent withdrawal from treatment or deviation from the protocol (Fisher, 1999). Additionally, outcomes of "per-protocol" analysis (in which participants were included only if they received the intended intervention in accordance with the protocol) are also given. All statistical analyses were calculated using Statistical Package for Social Sciences (SPSS) version 21.0.

CHAPTER III: RESULTS

3. Results

The age of the N=39 included and randomized participants ranged from 19 to 34 years (25±4 yrs). No significant differences were observed between groups for age, height and weight (p>0.05). None of the participants showed a mechanical laxity of the ankle joint.

The participants trained in their main sport for 12±5 years and performed different kind of sports, mostly ball sports (10x soccer, 6x handball, 5x basketball, 2x volleyball, 1x tennis, 1x beach volleyball). Since approximately 2/3 of the participants were sport students, they also performed/trained other kind of sports (swimming, gymnastics, track and field). Generally, average time phase between pre-and post-testing accounted for 51±14 days. Some of the participants were wearing the orthoses or performing sensorimotor training for a longer time period than others as re-test had to be postponed due to practical reasons (e.g. illness). All of the participants performed 4±2 training units per week with a duration of 90±25 minutes per session. Regarding compliance in fulfilling the orthosis protocol, the participants were wearing the orthoses for a mean duration of 172±143 minutes of 181±143 minutes of all-day life activities and for a mean duration of 101±80 minutes of 103±79 minutes of sport per day (during each sport/training). The participants who were performing the sensorimotor training program, trained with a mean duration of 20-25 minutes per session for 22±8 days of required 18 days of 42 days intervention (at least 3x/week as guideline). Details about recruitment, randomisation, treatment and follow up of the participants are outlined in following flow chart (Figure 20):

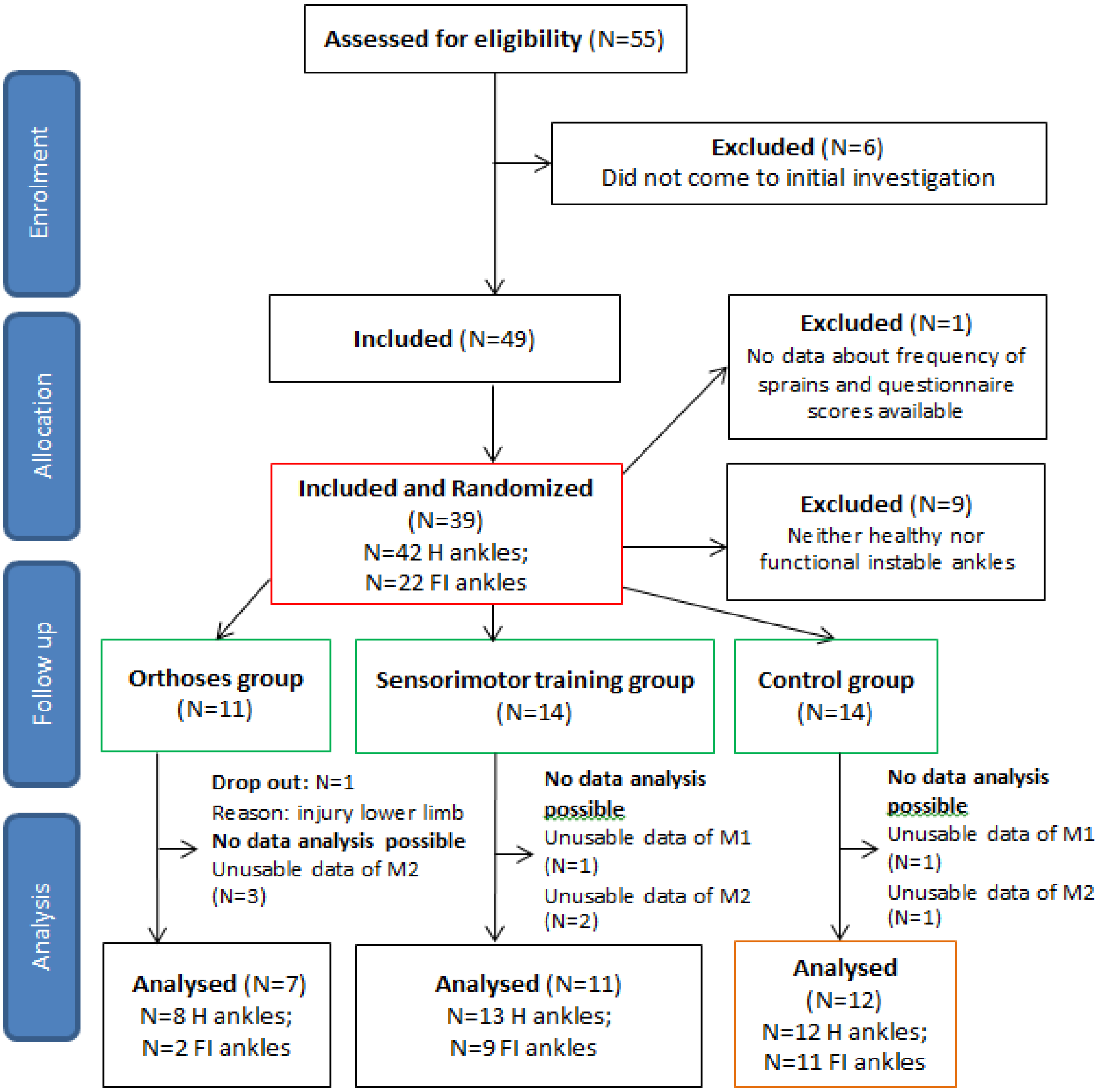

Figure 20: Flowchart of patient recruitment, randomisation, treatment and follow-up; red frame indicates participants used for acute effect orthosis (MQ 2), green frame -"- for long-term effect orthosis (MQ 3-5), orange frame -"- for test-retest reliability of muscle activity (Auxiliary/SQ 1a); *H = healthy ankles, FI = functional instable ankles*

1 participant in OG did not complete the final session (re-test) and was excluded from the analysis. In addition, data of 3 participants in OG could not be analyzed. Thus, in total 7 out of 11 participants in OG entered the final data analysis. Data of 3 participants in SMTG and data of 2 participants in CG were unusable for analysis. Therefore, results of 11 out of 14 participants are presented for SMTG and data of 12 out of 14 participants were used for final data analysis. Furthermore, 4 of 11 participants in OG and 4 of 14 participants in SMTG did not perform the protocol according to the required regulations. Thus, 7 participants in OG and 10 participants in SMTG were considered for per-protocol analysis.

3.1 Test-retest reproducibility of ankle muscle activity individuals with functional ankle instability (SQ 1a)

SQ 1a: Can ankle muscle activity be measured reproducibly in healthy individuals and those with FI between two test sessions (M1, M2)?

The control group of N=12 participants (n=5 H, n=5 FI, n=2 H unilateral and FI ankle contralateral) were tested. In sum, n=10 H ankles and n=9 FI ankles entered the data analysis. It was unable to classify n=5 ankles as either H or FI due to the reason that they only underwent 1 sprain.

MVC values

MVC values for H and FI ranged from 0.21±0.10 mV [retest, PL, H] to 0.43±0.17 mV [test, TA, H] for all muscles with values of TRV from 13.5±12.4% [PL, FI] to 24.6±15.6% [PL, H], Bias±1.96*SD from 0.00±0.01% (PL, H) to 0.04±0.09% (TA, FI) and ICC from 0.54 (TA, FI) to 0.90 (TA, H). RMS amplitudes and reliability criteria are presented in Table 6.

Table 6: RMS amplitudes of MVC measurement (mean±SD, %) of M1 and M2

Group	Muscle	M1 (mV)	M2 (mV)	TRV (%)	Bias (%MVC)	ICC
H	TA	0.43±0.17	0.42±0.22	20.41±15.6	0.01±0.01	0.90
	PL	0.26±0.11	0.21±0.10	24.6±15.6	-0.00±0.01	0.75
	GM	0.30±0.13	0.29±0.15	22.36±16.5	0.01±0.01	0.82
FI	TA	0.40±0.13	0.36±0.08	19.60±11.2	0.04±0.09	0.54
	PL	0.24±0.09	0.23±0.08	13.54±12.4	0.01±0.01	0.82
	GM	0.24±0.14	0.22±0.10	21.13±13.1	0.02±0.04	0.85

H = healthy group, FI = functional ankle instability group; TA = M. tibialis anterior, PL = M. peroneus longus, GM = M. gastrocnemius medialis

Normal unperturbed walking (NW) and perturbed walking (PW) - Pre-activity of ankle musculature

Descriptive Statistics - Differences in EMG amplitude

For H, EMG-A ranged from 7.7±4.0% (GM) to 25.1±8.9% (PL) in H for NW and from 11.8±6.8% (GM) to 32.1±10.0% (PL) for PW. In FI, EMG-A varied from 11.1±4.5% (GM) to 26.0±8.3% (PL) for NW and from 16.3±7.2% (GM) to 34.0±14.0% (PL) for PW. Detailed values of EMG-A (in %MVC) for the different conditions are shown in Table 7.

Table 7: RMS amplitudes (mean±SD, %) during normal and perturbed walking at 100-50 ms pre IC

Group	Muscle	NW/ PW	M1	M2	TRV (%)	Bias (%MVC)	ICC	CV (%)
H	TA	NW	19.0±5.7	20.6±5.8	36.4±25.3	1.4±15.6	0.47	25.7±20.0
		PW	19.5±8.0	26.3±10.0	31.3±36.1	7.0±8.0	0.36	22.1±32.2
	PL	NW	25.1±8.9	23.9±6.8	47.4±25.4	-1.6±27.4	0.56	33.5±15.2
		PW	32.1±10.0	31.4±11.3	53.7±27.2	-2.2±39.2	0.54	38.0±19.4
	GM	NW	12.9±6.5	7.7±4.0	53.7±49.1	-3.9±33.4	0.04	38.0±38.0
		PW	17.8±10.5	11.8±6.8	46.6±35.7	-4.8±34.7	0.36	33.0±28.0
FI	TA	NW	21.9±5.7	22.6±6.6	58.5±49.4	0.7±33.5	-0.12	41.4±37.1
		PW	26.3±11.6	30.0±11.1	57.4±52.8	3.4±33.8	-0.20	37.7±42.1
	PL	NW	26.0±8.3	18.0±5.2	50.0±34.7	-8.0±29.7	0.03	35.3±26.0
		PW	34.0±14.0	23.5±8.0	48.4±35.7	-10.4±42.0	-0.03	31.9±25.6
	GM	NW	16.4±4.1	11.1±4.5	77.3±65.1	-5.3±58.5	-0.23	54.7±48.9
		PW	20.9±9.9	16.3±7.2	89.8±59.0	-3.7±77.6	-0.22	58.0±41.4

H (n=10 ankles) and FI (n=9 ankles) for all muscles (TA, PL, GM) and both walking conditions: normal walking and perturbed walking; test-retest reliability values with TRV (mean±SD, %), Bias± 1.96*SD (%), ICC (2.1) and CV (mean±SD, %); *H = healthy group, FI = functional ankle instability group; TA = M. tibialis anterior, PL = M. peroneus longus, GM = M. gastrocnemius medialis; NW = normal walking, PW = perturbed walking*

Test-retest reliability

For H, TRV varied from 31.3±36.1% (TA, PW) to 53.7±49.1% (GM, NW), Bias±1.96*SD ranged from 1.4±15.6% (TA, NW) to 7.0±8.0% (TA, PW), ICC ranged from 0.56 (PL, NW) to 0.04 (GM, NW) and CV ranged from 22.1±32.2% (TA, PW) to 38.0±38.0% (GM, NW). In H group, NW revealed higher values of reliability for PL, whereas PW showed higher values of reliability for GM. For FI, TRV varied from 48.4±35.7% (PL, PW) to 89.8±59.0% (GM, PW), Bias±1.96*SD ranged from 0.7±33.5% (TA, NW) to 10.4±42.0% (PL, PW), ICC ranged from 0.03 (PL, NW) to -0.23 (GM, NW) and CV ranged from 31.9±25.6% (PL, PW) to 58.0±41.4% (GM, PW). Higher values of reliability were demonstrated in H related to FI for both walking conditions and all three muscles. Summarized values of reliability are displayed in Table 7. Bland & Altman Plots are presented in the attachment (Figure 3a).

Normal unperturbed walking and perturbed walking - Reflex-activity of ankle musculature

Descriptive Statistics - Differences in EMG amplitude

For H, EMG-A ranged from 9.7±5.2% (TA) to 47.1±10.5% (GM) in H for NW and from 46.0±17.6% (GM) to 101.7±20.1% (PL) for PW. In FI, EMG-A varied from 9.2±4.9% (TA) to 41.1±11.0% (GM) for NW and from 42.1±20.1% (GM) to 80.7±20.6% (PL) for PW. Table 8 illustrates detailed values of EMG-A for the different conditions.

Table 8: RMS amplitudes (mean±SD, %) during normal and perturbed walking at 200-400 ms post IC

Group	Muscle	NW/ PW	M1	M2	TRV (%)	Bias (%MVC)	ICC	CV (%)
H	TA	NW	10.5±5.3	9.7±5.2	54.3±44.1	-1.6±21.7	-0.03	38.4±32.9
		PW	70.7±18.1	70.0±22.2	25.8±20.6	-3.6±41.0	0.59	18.3±15.4
	PL	NW	27.0±10.7	24.2±9.4	42.7±27.0	1.0±24.9	0.33	32.4±19.9
		PW	86.3±19.1	101.7±20.1	57.3±45.2	14.8±106.6	-0.24	40.5±33.7
	GM	NW	47.1±10.5	46.7±10.8	42.4±48.2	-4.3±46.4	0.37	30.0±35.9
		PW	53.6±20.3	46.0±17.6	32.9±26.0	-13.2±56.9	0.59	23.3±19.4
FI	TA	NW	9.2±4.9	11.6±8.7	48.5±36.1	2.4±12.2	-0.20	34.3±27.1
		PW	66.7±15.6	77.2±21.0	38.2±33.8	13.5±35.3	0.31	27.0±25.4
	PL	NW	34.3±11.9	24.7±11.4	44.7±39.7	-4.4±27.4	0.35	31.6±29.8
		PW	79.6±18.8	80.7±20.6	53.1±50.0	-1.9±101.4	0.05	37.5±37.4
	GM	NW	33.1±8.7	41.1±11.0	47.5±57.0	6.0±29.1	0.69	33.6±42.8
		PW	42.1±20.1	46.6±17.7	38.2±24.0	5.5±28.1	0.79	27.0±18.0

H (n=10 ankles) and FI (n=9 ankles) for all muscles (TA, PL, GM) and both walking conditions: normal walking and perturbed walking; test- retest reliability values with TRV (mean±SD, %), Bias± 1.96*SD (%), ICC (2.1) and CV (mean±SD, %); *H = healthy group, FI = functional ankle instability group; TA = M. tibialis anterior, PL = M. peroneus longus, GM = M. gastrocnemius medialis; NW = normal walking, PW = perturbed walking*

Test-retest reliability

For H, TRV varied from 25.8±20.6% (TA, PW) to 57.3±45.2% (PL, PW), Bias±1.96*SD ranged from 1.0±24.9% (PL, NW) to 14.8±106.6% (PL, PW), ICC ranged from to -0.24 (PL, PW) to 0.59 (TA and GM, PW) and CV ranged from 18.3±15.4% (TA, PW) to 40.5±33.7% (PL, PW). For FI, TRV varied from 38.2±24.0% (GM, PW) to 53.1±50.0% (PL, PW), Bias±1.96*SD ranged from 1.9±50.8% (PL, PW) to 13.5±24.9% (TA, PW), ICC ranged from -0.20 (TA, NW) to 0.79 (GM, PW) and CV ranged from 27.0±25.4% (TA, PW) to 37.5±37.4% (PL, PW). Only for PL, higher values of reliability were demonstrated during PW in FI related to H. For TA and GM muscle, PW showed higher values of reliability than NW in both groups. Summarized values of reliability are shown in Table 8. Bland & Altman Plots are presented in the attachment (Figure 3b).

Side cutting (SC) - Pre- activity of ankle musculature

Descriptive Statistics - Differences in EMG amplitude

Considering ankle status (H or FI), EMG-A ranged from 31.5±6.1% (TA) to 86.5±32.7% (GM) in H and from 30.8±12.1% (TA) to 83.1±40.9% (GM) in FI. Table 9 depicts detailed values of EMG-A for the different conditions.

Table 9: RMS amplitudes (mean±SD, %) for side cutting during 100-50 ms pre IC

Group	Muscle	M1	M2	TRV (%)	Bias (% MVC)	ICC	CV (%)
H	**TA**	31.5±6.1	40.9±11.9	39.5±31.3	9.4±15.0	0.84	27.9±23.5
	PL	77.3±22.4	82.5±38.0	52.1±32.9	5.1±92.0	0.20	36.9±24.5
	GM	86.5±32.7	74.2±30.6	51.6±28.7	-12.4±108.0	0.14	36.5±28.7
FI	**TA**	30.8±12.1	30.9±8.6	42.5±31.2	0.2±32.1	0.82	30.0±23.2
	PL	33.8±12.1	57.3±18.6	57.3±33.4	23.7±19.9	0.41	40.5±25.3
	GM	83.1±40.9	72.5±36.1	31.1±19.5	-7.5±52.2	0.71	22.0±14.6

H (n=10 ankles) and FI (n=9 ankles) for all muscles (TA, PL, GM) for side cutting; test-retest reliability values with TRV (mean±SD, %), Bias±1.96*SD (%), ICC (2.1) and CV (mean±SD, %); *H = healthy group, FI = functional ankle instability group; TA = M. tibialis anterior, PL = M. peroneus longus, GM = M. gastrocnemius medialis*

Test-retest reliability

For H, TRV varied from 39.5±31.3% (TA) to 52.1±32.9% (PL), Bias±1.96*SD from 5.1±92.0 % (PL) to 12.4±108.0% (GM), ICC from 0.14 (GM) to 0.84 (TA) and CV from 27.9±23.5% (TA) to 36.9±24.5% (PL). For FI, TRV varied from 31.1±19.5% (GM) to 57.3±18.6% (PL), Bias±1.96*SD from 0.2±32.1% (TA) to 23.7±19.9% (PL), ICC from 0.41 (PL) to 0.82 (TA) and CV from 22.0±14.6% (GM) to 40.5±25.3% (PL). Considering ankle status (H or FI), H group demonstrated higher values of reliability for TA and PL muscle. Values of reliability are illustrated in Table 9. Bland & Altman Plots are shown in the attachment (Figure 3c).

Side cutting - Reflex-activity of ankle musculature

Table 10: RMS amplitudes (mean±SD, %) for side cutting during 200-400 ms post IC

Group	Muscle	M1	M2	TRV (%)	Bias (% MVC)	ICC	CV (%)
H	TA	47.8±11.9	48.6±12.0	46.7±15.3	0.8±42.3	0.33	33.0±11.4
	PL	48.9±11.7	59.0±21.2	66.2±36.7	10.0±75.9	-0.24	46.8±27.4
	GM	44.0±10.4	50.7±25.2	86.9±45.2	11.5±90.5	-0.44	86.9±45.2
FI	TA	52.9±10.0	55.5±16.9	25.8±18.5	2.6±45.6	0.56	18.2±13.8
	PL	58.7±12.6	70.0±20.5	32.4±22.9	11.4±31.4	0.39	22.9±17.2
	GM	31.5±15.5	48.3±11.6	50.2±26.0	14.3±49.0	0.55	35.5±19.5

H (n=10 ankles) and FI (n=9 ankles) for all muscles (TA, PL, GM) for side cutting; test-retest reliability values with TRV (mean±SD, %), Bias±1.96*SD (%), ICC (2.1) and CV (mean±SD, %); *H = healthy group, FI = functional ankle instability group; TA = M. tibialis anterior, PL = M. peroneus longus, GM = M. gastrocnemius medialis*

Descriptive Statistics - Differences in EMG amplitude

Considering ankle status (H or FI), EMG-A ranged from 44.0±10.4% (GM) to 59.0±21.2% (PL) in H and from 31.5±15.5% (GM) to 70.0±20.5% (PL) in FI. Detailed values of RMS amplitude for the different conditions are presented in Table 10.

Test-retest reliability

For H, TRV varied from 46.7±15.3% (TA) to 86.9±45.2% (GM), Bias±1.96*SD from 0.8±42.3 % (TA) to 11.5±90.5% (GM), ICC from -0.44 (GM) to 0.33 (TA) and CV from 33.0±11.4% (TA) to 86.9±45.2% (GM). For FI, TRV varied from 25.8±18.5% (TA) to 50.2±26.0% (GM), Bias±1.96*SD from 2.6±45.6 % (TA) to 14.3±49.0% (GM), ICC from 0.39 (PL) to 0.56 (TA) and CV from 18.2±13.8% (TA) to 35.5±19.5% (GM). Considering ankle status (H or FI), FI group demonstrated higher values of reliability for all three muscles. Values of reliability are illustrated in Table 10. Bland & Altman Plots are shown in the attachment (Figure 3d).

Acute effect of foot orthoses on ankle muscle activity in individuals with FI (MQ 1, MQ 2)

MQ 1: Is there a difference in ankle muscle activity between healthy participants and those with FI at M1?

MQ 2: Do participants with FI respond with a different ankle muscle activity to an orthosis condition (related to a "shoe only" condition) compared with healthy participants at M1 (acute effect orthosis)?

Pre-activity of ankle musculature

Table 11: Acute effectiveness of foot orthoses (MQ 1, MQ 2) - 100-50 ms pre IC

	S-O (Δ RMS [%MVC])					
	NW		PW		SC	
	H	FI	H	FI	H	FI
TA	1.7	2.3	1.7	5.0	3.9	0.6
PL	0.6	3.1	0.2	5.1	2.1	3.1
GM	1.2	0.9	0.1	0.2	5.0	12.2

Normalized RMS amplitudes (mean±SD, %MVC); *Δ = difference in RMS (%MVC) S - O; significant main effect of ankle status for PL during NW (p<0.0167) and for PL during* PW (*p*<0.0167)*; S = "shoe only", O = (in-shoe) orthosis; NW = normal walking, PW = perturbed walking, SC = side cutting; H = healthy group, FI = functional ankle instability group; TA = M. tibialis anterior, PL = M. peroneus longus, GM = M.*

Normality of data

Data of all the muscles were not normally distributed, except TA during PW (*p*=0.71) and SC (*p*=0.22). Homogeneity of variances was not shown for all of the data.

Normal unperturbed walking

Statistically significant differences in PL EMG-A were found between H and FI with 10.8% higher PL EMG-A for FI ("shoe only") and 8.3% higher PL EMG-A for FI (in-shoe orthosis) compared to H (significant main effect of *ankle status* for PL [*p=0*.001][Figure 21]. For EMG-A of GM (non-significant; *p*=0.023) differences could be shown between H and FI with 9.4% higher EMG-A for FI ("shoe only") and 9.1% higher EMG-A for FI (in-shoe orthosis) compared to H. TA EMG was 0.6% higher for FI ("shoe only"), whereas it did not differ between H and

FI for in-shoe orthosis condition (p=0.874). For none of the muscles, any statistically significant differences in EMG-A between "shoe only" and in-shoe orthosis could be shown (no significant main effect of *shoe condition* for TA [p=0.26], PL [p=0.51] and GM [p=0.80]). Furthermore, no significant interaction effect of *shoe condition* with *ankle status* was presented (TA p=0.85, PL p=0.64, GM p=0.96). Table 11 illustrates EMG-A for all muscles and groups during 100-50 ms pre IC.

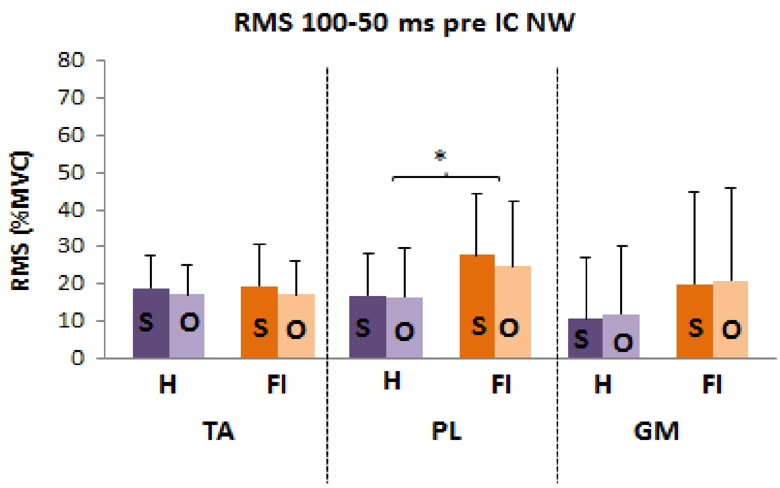

Figure 21: RMS (%MVC) of TA, PL and GM for NW during 100-50 ms pre IC; significant main effect of *ankle status* for PL (*p<0.0167) during NW; *S = "shoe only", O = (in-shoe) orthosis; NW = normal walking; H = healthy group, FI = functional ankle instability group; TA = M. tibialis anterior, PL = M. peroneus longus, GM = M. gastrocnemius medialis*

Perturbed walking

Peroneal EMG-A differed also significantly between H and FI during perturbed walking. For "shoe only", PL EMG-A was 14.9% higher in FI and for the in-shoe orthosis PL EMG-A was 10.0% higher in FI compared to H (significant main effect of *ankle status* for PL [p=0.005] [Figure 22]). For EMG-A of GM (non-significant; p=0.08) differences could be shown between H and FI with 7.6% higher EMG-A for FI ("shoe only") and 7.9% higher EMG-A for FI (in-shoe orthosis) compared to H. TA EMG-A was 1.3% higher for FI ("shoe only") and 2.0% higher for H (in-shoe orthosis)(p=0.88). No statistically significant differences in EMG-A between "shoe only" and in-shoe orthosis were existent (no significant main effect of *shoe* *condition* for TA [*p*=0.10], PL [*p*=0.55] and GM [*p*=0.99]). Additionally, no significant interaction effect of *shoe condition* with *ankle status* could be revealed (TA *p*=0.40, PL *p*=0.56, GM *p*=0.96).

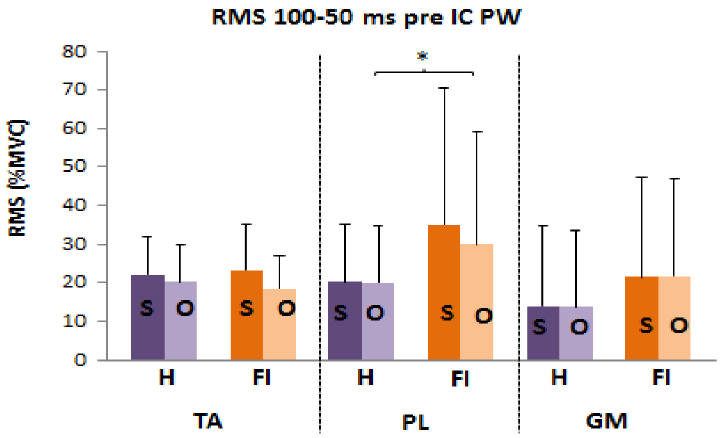

Figure 22: RMS (%MVC) of TA, PL and GM for PW during 100-50 ms pre IC; significant main effect of *ankle status* during PW (**p*<0.0167); *S = "shoe only", O = (in-shoe) orthosis; NW = normal walking; H = healthy group, FI = functional ankle instability group; TA = M. tibialis anterior, PL = M. peroneus longus, GM = M. gastrocnemius medialis*

Side cutting

The outcomes identified significant differences in PL EMG-A between H and FI with 17.2% higher EMG-A for H ("shoe only") and 12.0% higher EMG-A for H (in-shoe orthosis) compared to FI (significant main effect of *ankle status* for PL [*p*=0.02], Figure 23). For EMG-A of GM non-significant differences could be noted between H and FI with 5.5% higher EMG-A for FI ("shoe only") and 12.7% higher EMG-A for FI (in-shoe orthosis) compared to H (*p*=0.29). For EMG-A of TA non-significant differences could be noted between H and FI with 5.1% higher EMG-A for FI ("shoe only") and 8.4% higher EMG-A for FI (in-shoe orthosis) compared to H (*p*=0.20). Additionally, for none of the muscles, any difference in EMG-A between "shoe only" and in-shoe orthosis were statistically significant (no significant main effect of *shoe condition* for TA [*p*<0.66, PL [*p*=0.94] and GM [*p*=0.23]). Furthermore, no significant interaction effect of *shoe condition* with *ankle status* was demonstrated (TA *p*=0.75, PL *p*=0.67, GM *p*=0.61).

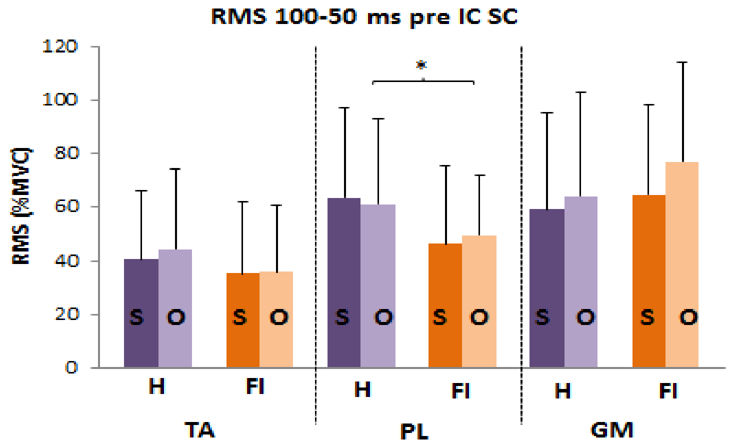

Figure 23: RMS (%MVC) of TA, PL and GM for SC during 100-50 ms pre IC; significant main effect of *ankle status* during SC (**p*<0.0167); *S = "shoe only", O = (in-shoe) orthosis; SC = side cutting; H = healthy group, FI = functional ankle instability group; TA = M. tibialis anterior, PL = M. peroneus longus, GM = M. gastrocnemius medialis*

Reflex-activity of ankle musculature

Table 12: Acute effectiveness of foot orthoses (MQ 1, MQ 2) - 200-400 ms post IC

	S-O (Δ RMS [%MVC])					
	NW		PW		SC	
	H	FI	H	FI	H	FI
TA	0.0	0.1	5.6	2.0	0.0	2.4
PL	2.6	3.4	2.9	1.6	2.2	0.2
GM	2.5	2.8	0.2	8.8	0.9	11.3

Normalized RMS amplitudes (mean±SD, %MVC); *Δ = difference in RMS (%MVC) S - O; S = "shoe only", O - (in-shoe) orthosis; NW = normal walking, PW = perturbed walking, SC = side cutting; H = healthy group, FI = functional ankle instability group; TA = M. tibialis anterior, PL = M. peroneus longus, GM = M. gastrocnemius medialis*

EMG-A of all muscles and groups during 200-400 ms post IC is shown in Table 12. During NW, non-significant differences in EMG-A could be found between H and FI in terms of higher TA EMG-A for FI, independent of *shoe condition,* and higher PL EMG-A for FI ("shoe only") compared to H (*p*=0.83)(Figure 24, attachment). In addition, EMG-A resulted in higher values for PL (in-shoe orthosis) and GM ("shoe only", in-shoe orthosis) in H compared to FI (PL *p*=0.95, GM *p*=0.22). During PW, EMG-A of TA, PL and GM revealed higher values for H, except for GM ("shoe only")(TA *p*=0.31, PL *p*=0.59, GM *p*=0.53)(Figure 25, attachment). Independent of *shoe condition*, higher EMG-A of TA was detected for FI during SC, whereas PL and GM EMG-A was higher for H compared with FI (TA *p*<0.41, PL *p*<0.74, GM *p*<0.16)(Figure 26, attachment).

Furthermore, differences in EMG-A between "shoe only" and in-shoe orthosis were not statistically significant for any of the muscles or test conditions (no significant main effect of *shoe condition* for TA, PL and GM). In addition, no statistically significant interaction effect of *shoe condition x ankle status* was detected for any of the muscles and conditions.

Subsequently, participants with FI respond with a different EMG-A to the acute use of the orthosis compared to healthy participants (higher pre-activity in FI, particularly for NW and PW; higher reflex-activity in H). The acute application of the orthosis had no effect on ankle muscle activity.

3.3. Long-term effect of foot orthoses on ankle muscle activity in individuals with FI (MQ 3, MQ 4, SQ 3a, MQ 5)

MQ 3: Is there a difference in ankle muscle activity between an orthosis intervention group and a control group (no intervention) from M1 to M2 (long-term effect orthosis)?

MQ 4: Is there a difference in ankle muscle activity between an orthosis intervention group and a sensorimotor training group from M1 to M2 (long-term effect orthosis)?

Pre-activity of ankle musculature

Table 13: Long-term effectiveness of foot orthoses (MQ 3 and MQ 4) - 100- 50 ms pre IC

		NW			PW			SC		
		OG	**SMTG**	**CG**	**OG**	**SMTG**	**CG**	**OG**	**SMTG**	**CG**
Δ RMS (%MVC) M2-M1	**TA**	5.0	1.2	1.2	9.0*	2.1	4.9*	0.5	1.3	7.2
	PL	6.2	2.6	4.4	7.3	1.5	5.6	0.6	10.4	13.4
	GM	10.2	1.7	5.2	10.3	4.0	4.9	12.9	28.3	9.2

Normalized RMS amplitudes (mean±SD, %MVC); *Δ = difference in RMS (%MVC) M2 - M1; significant interaction effect of intervention group x time* for TA during PW (*p<0.0167); *NW = normal walking, PW = perturbed walking, SC = side cutting; OG = orthoses intervention group, SMTG = sensorimotor training group, CG = control group; TA = M. tibialis anterior, PL = M. peroneus longus, GM = M. gastrocnemius medialis*

EMG-A of all muscles and groups at 100-50 ms pre IC is presented in Table 13.

Normality of data

Data for all the muscles were not normally distributed, except for TA (p=0.48, M2) during NW and PW (p=0.16 M1; p=0.07 M2). Homogeneity of variances was not shown for all of the data.

Normal unperturbed walking

No significant differences were found between groups over time for all of the muscles (no significant interaction effect of *intervention group* x *time* [TA p=0.31, PL p=0.04, GM p=0.21]). The baseline values (M1) in EMG-A of PL differed significantly between the three intervention groups (p=0.01). Figure 27 (attachment) displays pre- and post EMG-A for NW during 100-50 ms pre IC for all intervention groups.

Orthosis group vs. Control group

6 weeks of training induced a reduction in TA EMG-A (5.0%) and an increase in PL (6.2%) and GM (10.2%) EMG-A in the OG. In the CG the opposite effect was shown after 6 weeks (increase in TA EMG-A, reduction in PL and GM EMG-A).

Orthosis group vs. Sensorimotor training group

TA EMG-A was reduced in the OG as well as in the SMTG, however 3.8% more in the OG. PL EMG-A was increased in the OG as well as in the SMTG, however 3.6% more in the OG. For GM, there was a substantial rise in EMG-A in the OG (see above), whereas EMG-A was slightly reduced in the SMTG.

Perturbed walking

Significant differences between the groups over time could be detected only for the TA muscle (significant interaction effect of *intervention group* x *time* for TA [p=0.007], no significant interaction of *intervention group* x *time* [PL p=0.05, GM p=0.31]). The baseline values (M1) in EMG-A of PL differed significantly between the three intervention groups (p=0.002). Pre- and post EMG-A for PW during 100-50 ms pre IC, for all intervention groups, is presented in Figure 28.

Orthosis group vs. Control group

Post-hoc test revealed that the OG TA EMG-A significantly decreased over time (9%) compared to the CG, in which EMG-A increased (4.9%)(p=0.006). Additionally, PL and GM EMG-A increased in the OG (7.3% PL, 10.3% GM), whereas it decreased in the CG.

Orthosis group vs. Sensorimotor training group

TA EMG-A had a greater decrease within the OG (9.0%) compared to the SMTG (2.1%). Rise in PL EMG-A was more pronounced in the OG (7.3%) compared to the SMTG (1.5%). For GM, the OG had a considerable rise in EMG-A (10.3%), while EMG-A was reduced in the SMTG.

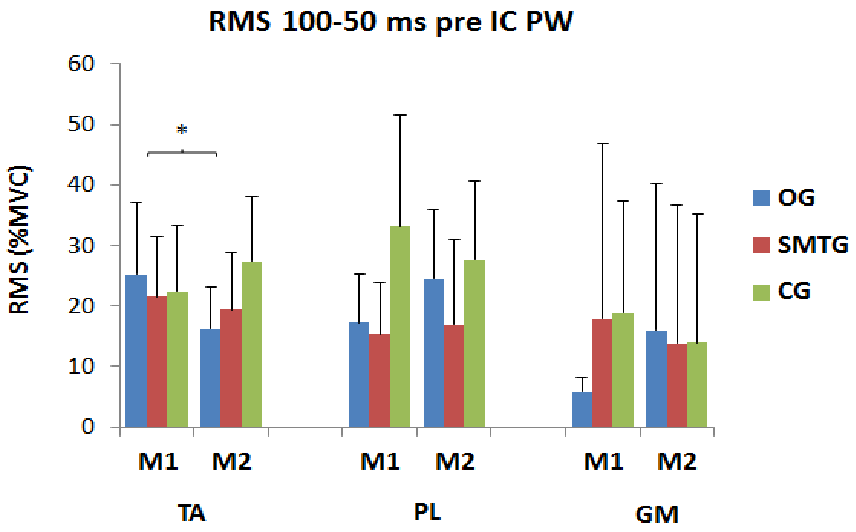

Figure 28: RMS (%MVC) of TA, PL and GM for PW during 100-50 ms pre IC; significant interaction effect of *intervention group x time* between OG and SMTG of TA for PW (*p<0.0167); *PW = perturbed walking; OG = orthoses intervention group, SMTG = sensorimotor training group, CG = control group; TA = M. tibialis anterior, PL = M. peroneus longus, GM = M. gastrocnemius medialis*

Side cutting

The analysis failed to indicate significant differences between the groups over time for any of the muscles (no significant interaction effect of *intervention group* x *time* [TA p=0.50, PL p=0.13, GM p=0.06]). Figure 29 (attachment) shows pre- and post EMG-A for SC during 100-50 ms pre IC for all intervention groups.

Orthosis group vs. Control group

EMG-A decreased 0.5% in the OG (increase in CG) for TA and increased substantially (12.9%) in OG for GM (decrease in the CG). PL EMG-A was increased in both groups, however to a higher extent in the CG (12.8%).

Orthosis group vs. Sensorimotor training group

PL EMG-A was found to be reduced in the SMTG (10.4%) following training intervention, whereas it was marginally increased in the OG. TA EMG-A decreased in both groups (more in the SMTG [0.8%]), whereas GM EMG increased more in the SMTG (15.4%).

Per-protocol analysis

When analysing the outcomes “per-protocol”, significant differences between the SMTG and the CG (*p*=0.001) as well as between the OG and the SMTG (*p*=0.01) over time could be detected for PL during PW (statistically significant interaction effect of *intervention group x time* [*p*=0.01]). Further, changes of GM EMG-A within the SMTG over time (substantial increment by 28.3% [*p*=0.02]) during side cutting was significant (significant interaction of *intervention group x time* [*p*=0.01]). All other differences mentioned earlier remained significant. Figures 30 and 31 depict EMG of PL during PW and GM during SC of all intervention groups at 100-50 ms pre IC.

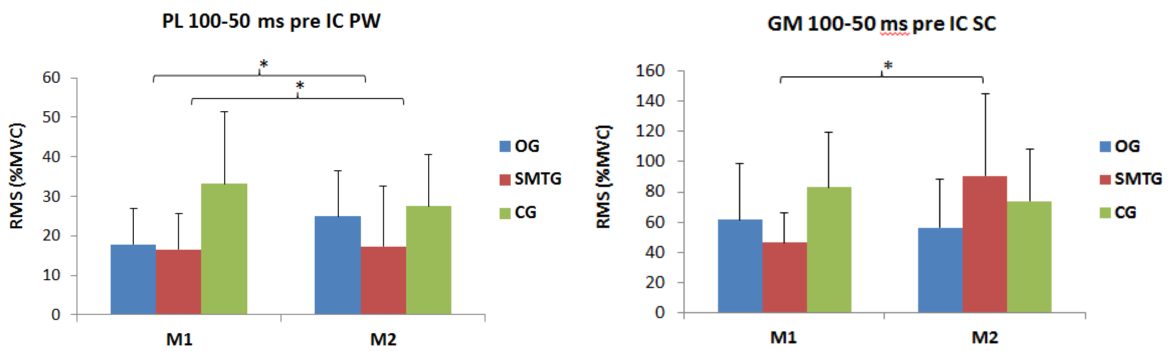

Figure 30 and 31: RMS (%MVC) of PL during PW and GM during SC at 100-50 ms pre IC; significant interaction effect of *intervention group x time* between SMTG and CG and between OG and SMTG for PL during PW and within SMTG for GM during SC (**p*<0.0167); *PW = perturbed walking; SC = side cutting; OG = orthoses intervention group, SMTG = sensorimotor training group, CG = control group; PL = M. peroneus longus, GM = M. gastrocnemius medialis*

Reflex-activity of ankle musculature

Table 14 shows EMG-A of all groups and muscles at 200-400 ms post IC.

Table 14: Long-term effectiveness of foot orthoses (MQ 3 and MQ 4) - 200-400 ms post IC

		NW			**PW**			**SC**		
		OG	**SMTG**	**CG**	**OG**	**SMTG**	**CG**	**OG**	**SMTG**	**CG**
Δ RMS (%MVC) M2-M1	**TA**	1.2	2.3	0.5	27.3*	4.0	4.3*	2.6	4.0	1.8
	PL	1.6	1.2	1.8	4.1	5.9	2.3	12.3	4.0	0.1
	GM	12.3	0.9	8.4	4.6	9.4	4.4	18.0	10.6	14.7

Normalized RMS amplitudes (mean±SD, %MVC); *Δ = difference in RMS (%) M2 - M1;* significant interaction effect of *intervention group x time* for TA during PW (**p*<0.0167); *NW = normal walking, PW = perturbed walking; SC = side cutting; OG = orthoses intervention group, SMTG = sensorimotor training group, CG = control group; TA = M. tibialis anterior, PL = M. peroneus longus, GM = M. gastrocnemius medialis*

Data for all the muscles were not normally distributed, except for PL (p=0.09 M2) and GM (*p*=0.37 M1, *p*=0.15 M2) during NW, for TA (*p*=0.65 M1, *p*=0.15 M2) and PL (*p*=0.40, *p*=0.09 M2) during PW and for TA (*p*=0.21 M1) during SC. Homogeneity of variances was not shown for all of the data.

Normal unperturbed walking

There were no significant differences between the groups over time for any of the muscles (no significant interaction effect of *intervention group* x *time* [TA *p*=0.88, PL *p*=0.72, GM *p*=0.86]). The baseline values (M1) in EMG-A of PL differed significantly between the three intervention groups (*p*=0.01). Pre- and post EMG-A for NW during 200-400 ms post IC for all intervention groups is presented in Figure 32 (attachment).

Orthosis group vs. Control group

Training intervention induced an increase in TA EMG in the OG as well as in the CG (more in OG with 0.7%). PL EMG-A also slightly increased in the OG (1.6%), whereas it was reduced in the CG. EMG-A of GM considerably decreased in the OG (12.3%), while there was a rise in EMG-A in the CG.

Orthosis group vs. Sensorimotor training group

Differences in EMG-A over time were detected in the OG and the SMTG in terms of a rise in EMG-A of TA and PL in both groups (higher pronounced increase in the SMTG with 1.1% for TA and in the OG with 0.4% for PL). GM EMG-A decreased more in the OG in contrast to the SMTG (11.4%).

Perturbed walking

Significant differences between the groups over time could be revealed for TA muscle (significant interaction effect of *intervention group* x *time* [p=0.01]). Pre- and post EMG-A during 200-400 ms post IC for all intervention groups is shown in Figure 33.

Orthosis group vs. Control group

Long-term training period with the orthosis led to statistically significant decline in TA EMG-A for the OG (27.3%) compared with the CG (increase by 4.3%). PL EMG-A was reduced in the OG (4.1%) compared to the CG (increase) and GM EMG-A was increased in the OG (4.6%) in contrast to the CG (decrease).

Orthosis group vs. Sensorimotor training group

After 6 weeks of training, EMG-A of TA was significantly reduced (27.3%) in the OG compared to the SMTG (less pronounced decrease: 4.0%). For PL, EMG-A was decreased in both intervention groups, however slightly more (by 1.8%) in the SMTG. There was a reduction in GM EMG-A for the SMTG (9.4%), whereas EMG-A increased in the OG.

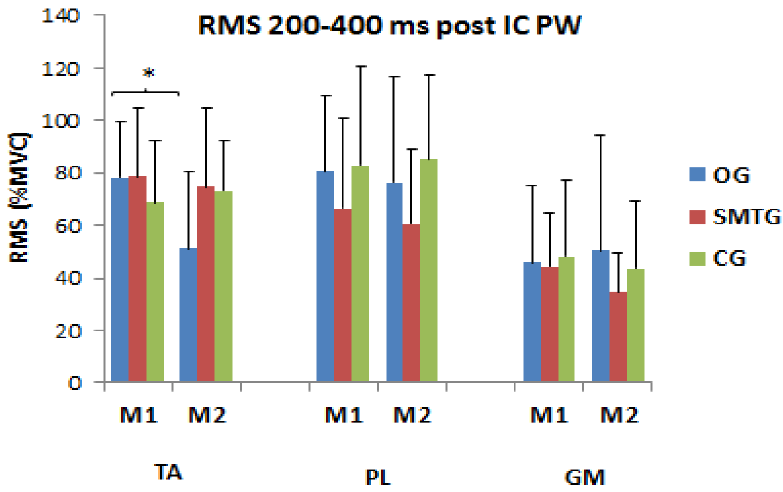

Figure 33: RMS (%MVC) of TA, PL and GM for PW during 200-400 ms post IC; significant interaction effect of *time* between OG and SMTG for TA during PW (*p<0.0167); *PW = perturbed walking; OG = orthoses intervention group, SMTG = sensorimotor training group, CG = control group; TA = M. tibialis anterior, PL = M. peroneus longus, GM = M. gastrocnemius medialis*

Side cutting

No significant differences were observed between the groups over time for any of the muscles from pre- to post-testing (no significant interaction effect of *intervention group* x *time* [TA p=0.65, PL p=0.46, GM p=0.15]). Figure 34 (attachment) illustrates pre- and post EMG-A for SC during 100-50 ms pre IC for all intervention groups.

Orthosis group vs. Control group

EMG-A decreased in the OG for all muscles (most considerably for PL [12.3%] and GM [18.0%]), while EMG-A showed a rise in the CG (most pronounced for GM [14.7%]).

Orthosis group vs. Sensorimotor training group

After 6 weeks of training, EMG-A of TA and PL decreased in the OG (substantially for PL [12.3%]) compared to the SMTG, in which EMG-A of those muscles increased. For GM, EMG-A was found to be reduced in both intervention groups, however, more within the OG in contrast to the SMTG (7.4%)

Per-protocol analysis

By analysing the outcomes "per-protocol", for TA during PW, significant interaction effect of *intervention group x time* (p=0.01) disappeared (p>0.0167). All other differences remained significant. In particular, statistically significant interaction effect of *intervention group x time* was observed for GM during SC (p=0.01). OG was the only group in which the EMG of GM significantly reduced over time (18%)(Figure 35).

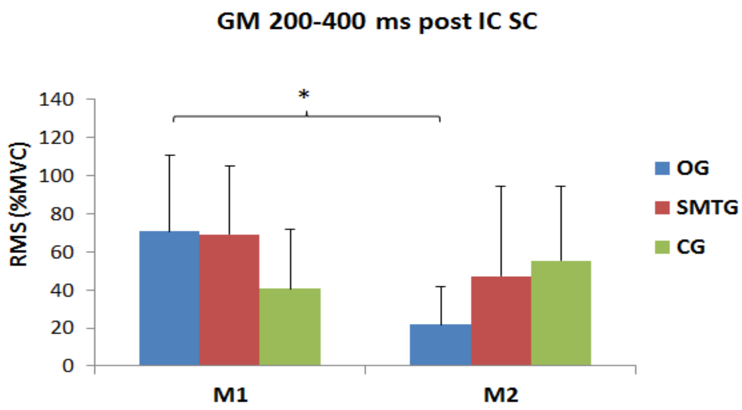

Figure 35: RMS (%MVC) of GM for SC during 200-400 ms post IC; significant interaction effect of *intervention group x time* within OG for GM during SC (*p<0.0167); *SC = side cutting; OG = orthoses intervention group, SMTG = sensorimotor training group, CG = control group; GM = M. gastrocnemius medialis*

Consequently, 6 weeks of wearing the orthosis led to increased pre-activation of ankle muscles in the OG compared to the CG for most conditions. Regarding reflex-activation, EMG-A was mostly shown to be reduced in the OG across all the conditions. When comparing long-term orthoses use with sensorimotor training, ankle muscle activity was increased in both groups (depending on the test condition and muscle) and slightly higher for the orthoses intervention.

SQ 3a: Do the participants in the orthosis intervention group present (even) higher ankle muscle activity by the additional short-term application of a measurement in-shoe orthosis (condition 1) compared to short-term application of "shoe only" (condition 2) after intervention at M2 (="transmission effect")?

Pre-activity of ankle musculature (Per-protocol analysis)

Table 15: Short-term effectiveness of foot orthoses at M2 after intervention (SQ 3a) - 100-50 ms pre IC

		NW		PW		SC	
		OG	**CG**	**OG**	**CG**	**OG**	**CG**
Δ RMS (%MVC) S-O	**TA**	-	-	-	-	12.8	0.0
	PL	1.6	0.4	1.5	4.9	13.4	3.7
	GM	0.1	1.1	0.9	1.5	11.8	13.6

Normalized RMS amplitudes (mean±SD, %MVC); *Δ = difference in RMS (%) S - O at M2; S = "shoe only", O = (in-shoe) orthosis; NW = normal walking, PW = perturbed walking; SC = side cutting; OG = orthoses intervention group, SMTG = sensorimotor training group, CG = control group; TA = M. tibialis anterior, PL = M. peroneus longus, GM = M. gastrocnemius medialis*

Differences in EMG-A between "shoe only" and in-shoe orthosis condition of all muscles of orthoses and control group for normal unperturbed walking during 100-50 ms pre IC, are presented in Table 15. Only these values of EMG-A are shown where the EMG-A increased from pre- to post-test in the orthoses intervention group (values, which are not relevant [see also results of MQ 3, 4] are indicated with -).

Normality of data

Data for all muscles were not normally distributed, except for TA (p=0.19 CG, p=0.83 OG) and PL (p=0.02 CG) during NW, for TA (p=0.54 CG; p=0.56 OG) and PL (p=0.13 CG; p=0.03 OG) during PW and for TA (p=0.04 OG), PL (p=0.02 CG; p=0.05 OG) and GM (p=0.57 OG) during SC. Homogeneity of variances was not given for all of the data.

Normal unperturbed walking

EMG-A differed non-significantly between “shoe only” and in-shoe orthosis in the OG and CG. Higher PL EMG-A during “shoe only” compared to in-shoe orthosis was found in the OG, while higher GM EMG-A during in-shoe orthosis compared with “shoe only” was shown in the OG and CG (Table 15; Figure 36 attachment). Independent of shoe condition, lower GM EMG-A was found in the OG. No significant interaction effect of *shoe condition x intervention group* for EMG-A for any of the muscles in the two intervention groups were detected (no significant interaction effect of *shoe condition x intervention group* [PL p=0.72, GM p=0.89]). EMG-A for the OG and CG during NW at 100-50 ms pre IC is presented in Figure 36 (attachment).

Perturbed walking

EMG-A differed non-significantly between “shoe only” and in-shoe orthosis in the OG and CG. The OG demonstrated higher PL and GM EMG-A during in-shoe orthosis compared to “shoe only” in contrast to the CG (higher EMG-A for “shoe only”; difference between “shoe only” and in-shoe orthosis was higher for CG compared to OG; Table 15, Figure 37 attachment). Independent of shoe condition, again lower GM EMG-A was found in the OG in contrast to CG. The analysis failed to indicate statistically significant interaction effect of *shoe condition x intervention group* for EMG-A for any of the muscles in the two intervention groups (no significant interaction effect of *shoe condition x intervention group* [PL p=0.33, GM p=0.81]). EMG-A for the OG and CG during PW at 100-50 ms pre IC is shown in Figure 37 (attachment).

Side cutting

The analysis resulted in non-significant differences in EMG-A between "shoe only" and in-shoe orthosis with higher TA EMG-A during "shoe only" in the OG and higher PL and GM EMG-A during in-shoe orthosis in the same group in contrast to the CG (lower PL and GM EMG-A for in-shoe orthosis; difference between "shoe only" and in-shoe orthosis was higher for the OG compared to the CG [TA, PL]; Table 15, Figure 38 attachment). Independent of shoe condition, lower TA and PL EMG-A were found in the OG in contrast to the CG. The analysis could not indicate statistically significant interaction of *shoe condition x intervention group* for EMG-A for any of the muscles in the two intervention groups (no significant interaction effect of *shoe condition x intervention group* [TA p=0.47, PL p=0.50, GM p=0.21]). EMG-A for OG and CG during SC at 100-50 ms pre IC is presented in Figure 38 (attachment).

Reflex-activity of ankle musculature (Per-protocol analysis)

Table 16: Short-term effectiveness of foot orthoses at M2 after intervention (SQ 3b) - 200-400 ms post IC

		NW		PW		SC	
		OG	**CG**	**OG**	**CG**	**OG**	**CG**
Δ RMS (%MVC) S-O	**TA**	0.1	1.0	-	-	-	-
	PL	2.5	2.7	-	-	-	-
	GM	-	-	1.2	2.0	-	-

Normalized RMS amplitudes (mean±SD, %MVC); *Δ = difference in RMS (%) S - O at M2; S = "shoe only", O = (in-shoe) orthosis; NW = normal walking, PW = perturbed walking; SC = side cutting; OG = orthoses intervention group, SMTG = sensorimotor training group, CG = control group; TA = M. tibialis anterior, PL = M. peroneus longus, GM = M. gastrocnemius medialis*

Differences in EMG-A between "shoe only" and in-shoe orthosis condition of all muscles of orthoses and control group during all conditions at 200-400 ms post IC are presented in Table 16. Only these values of EMG-A are shown, where the EMG-A increased from pre- to post-test in the orthoses intervention group (values, which are not relevant [see also results of MQ 3, 4], are indicated with -).

Normality of data

Data for all muscles were not normally distributed, except for TA (*p*=0.03 OG) and PL (*p*=0.31 OG) and GM (*p*=0.02 CG) during NW, for TA (*p*=0.04 CG; *p*=0.21 OG) and PL (*p*=0.88 CG; *p*=0.03 OG) during PW and for TA (*p*=0.25 OG) and PL (*p*=0.03 CG; *p*=0.03 OG) during side cutting. Homogeneity of variances was not given for all of the data.

Normal unperturbed walking

Non-significant differences in EMG-A could be identified between "shoe only" and in-shoe orthosis condition in the OG and CG in terms of higher TA and PL EMG-A during in-shoe orthosis in the OG (CG: higher TA EMG-A for "shoe only" condition; Table 16, Figure 39 attachment). Again, lower EMG-A were found in the OG compared to the CG (independent of *shoe* condition). No significant interaction effect of *shoe condition x intervention group* for EMG-A for any of the muscles in the two intervention groups were detected (no significant interaction effect of *shoe condition x intervention group* [TA *p*=0.74, PL *p*=0.97]). Figure 39 (attachment) illustrates EMG-A for the OG and CG for NW during 100-50 ms pre IC.

Perturbed walking

GM EMG-A differed non-significantly between "shoe only" and in-shoe orthosis condition in the OG and CG in terms of higher values during "shoe only" condition in the OG and higher values for in-shoe orthosis condition in the CG (Table 16, Figure 40 attachment). The analysis could not indicate statistically significant interaction of *shoe condition x intervention group* for GM EMG-A in the two intervention groups (no significant interaction effect of *shoe condition x intervention group* [GM *p*=0.95]). EMG-A for the OG and CG during PW at 200-400 ms post IC is shown in Figure 40 (attachment).

In general, a (non-significant) "transmission effect" was present in the OG compared to the CG for pre-activation of most ankle muscles during perturbed walking and side cutting (higher EMG-A for in-shoe orthosis condition in contrast to "shoe only" condition). Considering reflex-activity of ankle muscles, a (non-significant) "transmission effect" in the OG was existent for most ankle muscles during normal unperturbed walking.

MQ 5: Do participants with FI respond with a different ankle muscle activity to an orthosis condition after intervention compared with healthy participants from M1 to M2 (long-term effect orthosis)?(Difference in ankle muscle activity between H and FI in the intervention groups?)

Pre-activity of ankle musculature

Table 17: Long-term effectiveness of foot orthoses (MQ 5) - 100-50 ms pre IC

			Δ RMS (%MVC) M2-M1		
			TA	**PL**	**GM**
NW	**OG**	**H**	5.3	5.4	11.7
		FI	2.1	11.9	27.7
	SMTG	**H**	0.2	1.5	2.2
		FI	4.7	5.1	0.2
	CG	**H**	1.6	1.0	5.2
		FI	0.7	8.1	5.3
PW	**OG**	**H**	8.3	6.0	11.8
		FI	8.4	17.3	4.5
	SMTG	**H**	0.3	0.4	4.7
		FI	6.4	4.3	2.1
	CG	**H**	17.8	0.8	6.0
		FI	3.2	10.9	3.7
SC	**OG**	**H**	9.0*	2.5	7.9
		FI	46.0*	10.0	35.6
	SMTG	**H**	3.9	15.2	7.8
		FI	2.9	15.9	32.9
	CG	**H**	9.3	4.9	9.4
		FI	3.0	30.4	8.9

Normalized RMS amplitudes (mean±SD, %MVC); significant interaction effect of *intervention group x ankle status x time* (*p<0.0167) for TA during SC; *Δ = difference in RMS (%MVC) M2 - M1; H = healthy group, FI = functional ankle instability group; NW = normal walking, PW = perturbed walking; SC = side cutting; OG = orthoses intervention group, SMTG = sensorimotor training group, CG = control group; TA = M. tibialis anterior, PL = M. peroneus longus, GM = M. gastrocnemius medialis*

Differences in EMG-A between H and FI in each intervention group of all muscles during all conditions at 100-50 ms pre IC is presented in Table 17.

Normality of data

Data for all muscles were not normally distributed, except for TA (*p*=0.47 M2) during NW and PW (*p*=0.14 M1) as well as for SC (GM: *p*=0.02 M1). Homogeneity of variances was not given for all of the data.

Normal unperturbed walking

There was no significant difference between H and FI in any of the groups over time for all of the muscles (no significant interaction effect of *intervention group* x *ankle status* x *time* [TA *p*=0.74, PL *p*=0.12, GM *p*=0.23]). The baseline values (M1) in EMG-A of PL differed significantly between H and FI participants in the OG (*p*=0.02) and between H in SMTG and FI in the OG (*p*=0.01). Pre- and post EMG-A for NW at 100-50 ms pre IC for H and FI in all intervention groups is displayed in Figure 41.

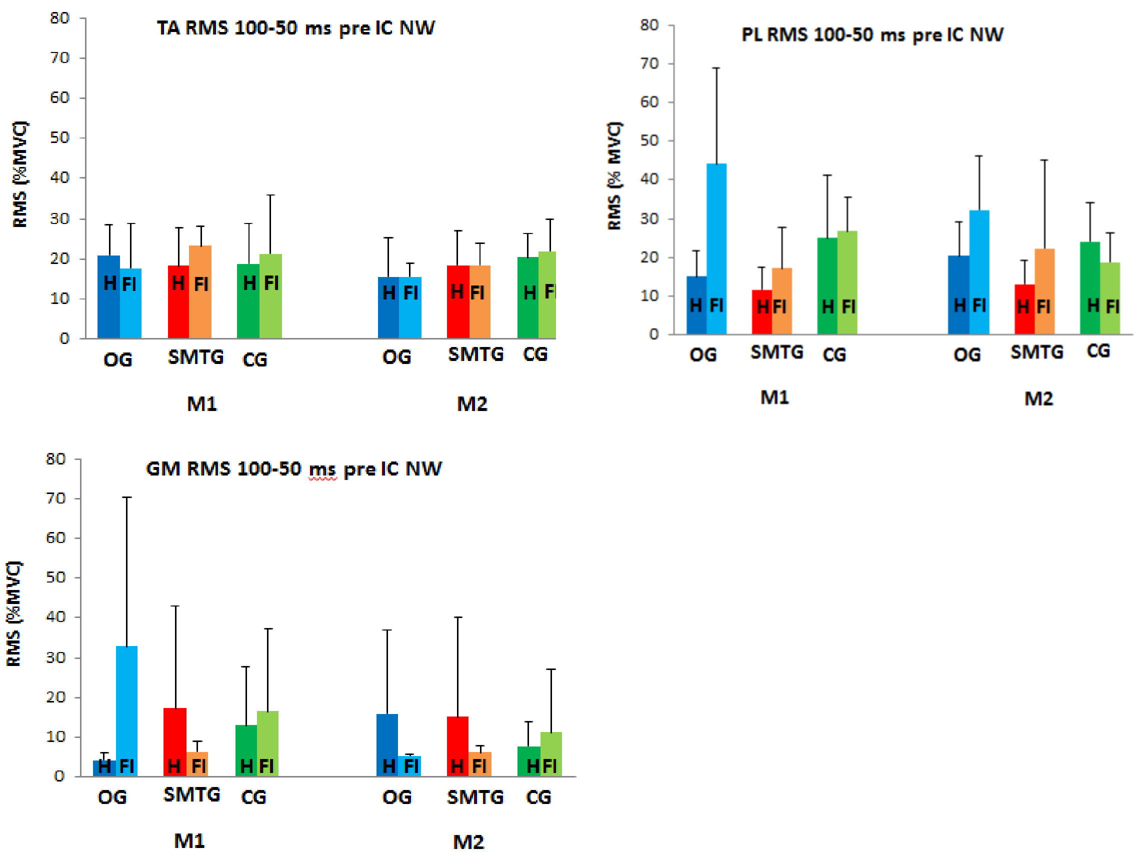

Figure 41: RMS (%MVC) of TA, PL and GM for NW during 100-50 ms pre IC; *H = healthy group, FI = functional ankle instability group; NW = normal walking; OG = orthoses intervention group, SMTG = sensorimotor training group, CG = control group; TA = M. tibialis anterior, PL = M. peroneus longus, GM = M. gastrocnemius medialis*

For TA, EMG-A differed between H and FI in the SMTG in terms of a slight increase in EMG-A in FI (0.2%) compared to H (decrease by 4.7%) after 6 weeks intervention phase. In the OG, EMG-A was reduced for H as well as for FI, while EMG-A increased for both groups in the CG (both more pronounced in H; Table 17). Concerning the PL, differences in EMG-A could be found between H and FI for the OG and CG with increased EMG-A in H and decreased EMG-A in FI (higher pronounced for FI than for H; stronger effect in the OG than in CG). EMG-A was increased for both, H and FI, in the SMTG (again, to a higher extent in FI; Table 17). For GM, EMG-A differed between H and FI in the OG and SMTG with a reduction in EMG-A in FI (substantially for OG with 27.7%) and a rise in EMG-A for H in the OG, whereas EMG-A was reduced in H and increased for FI in the SMTG (effects higher pronounced in the OG than SMTG; Table 17).

Perturbed walking

No significant differences were found between H and FI in any of the groups over time for all of the muscles (no significant interaction effect of *intervention group* x *ankle status* x *time* [TA p=0.74, PL p=0.12, GM p=0.23]). Figure 42 presents EMG-A for PW at 100-50 ms pre IC for H and FI in all intervention groups.

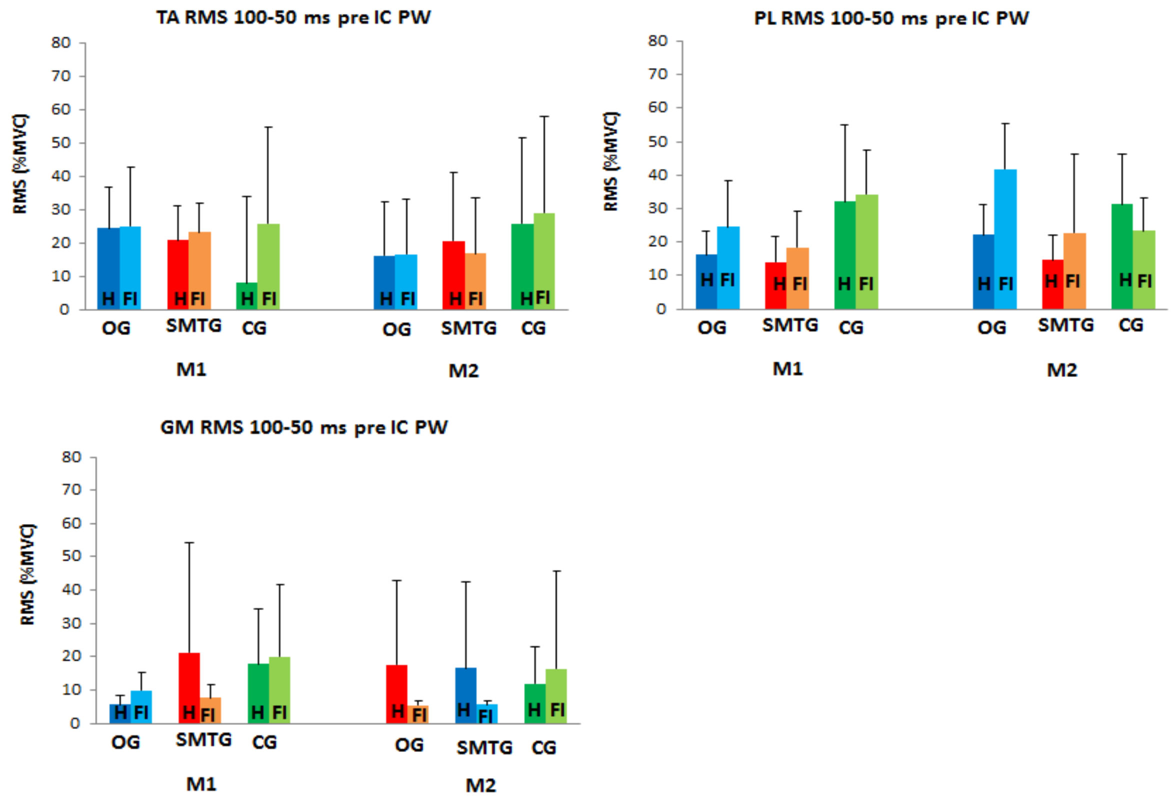

Figure 42: RMS (%MVC) of TA, PL and GM for PW during 100-50 ms pre IC; *H = healthy group, FI = functional ankle instability group; PW = perturbed walking; OG = orthoses intervention group, SMTG = sensorimotor training group, CG = control group; TA = M. tibialis anterior, PL = M. peroneus longus, GM = M. gastrocnemius medialis*

As for NW, EMG-A of TA differed between H and FI in the SMTG, yet also during PW. In contrast to H (slight increase in EMG-A), a reduction in EMG-A was detected in FI from pre- to post-training (Table 17). 6 weeks of intervention also induced a reduction in TA EMG-A in the OG for H and FI, while in the CG an increase in EMG-A occurred for both groups (17.8% in H). For PL, EMG-A differed between H and FI in the OG as well as in the SMTG, in terms of an increase in EMG-A in H and a considerable rise in FI (by 17.3%) in the OG, and a similar effect in the SMTG (rise in EMG-A in H and in FI [more in FI]; Table 17). Regarding GM, EMG-A increased considerably in H (11.8%) and decreased in FI for the OG, while for the SMTG a reduction in EMG-A was reported for both H and FI (more in H).

Side cutting

Significant differences between H and FI in OG could be shown over time for TA muscle (significant interaction effect of *intervention group* x *ankle status* x *time* [p=0.01]). Figure 43 shows EMG-A for SC at 100-50 ms pre IC for H and FI in all intervention groups. Post-hoc test revealed that TA EMG-A increased significantly (by 46.0%) for FI compared to H (reduction by 9.0%) within the OG, while EMG-A for H as well as for FI increased within the other groups, although not statistically significant. PL EMG-A differed between H and FI within the OG and SMTG, such that EMG-A increased for H and was reduced in FI. In contrast, PL EMG-A noted a rise for FI and a decline in H for the SMTG (effect was higher pronounced for FI in all intervention groups; independent of ankle status, higher effect in the SMTG [in the CG rise in EMG for H was even higher pronounced than in the SMTG with 30.4%]; Table 17). 6 weeks of training led to reductions in GM EMG-A for H and a considerable increase in EMG-A for FI within the OG (35.6%), whereas EMG-A decreased substantially (32.9%) for FI and increased for H within the SMTG (Table 17).

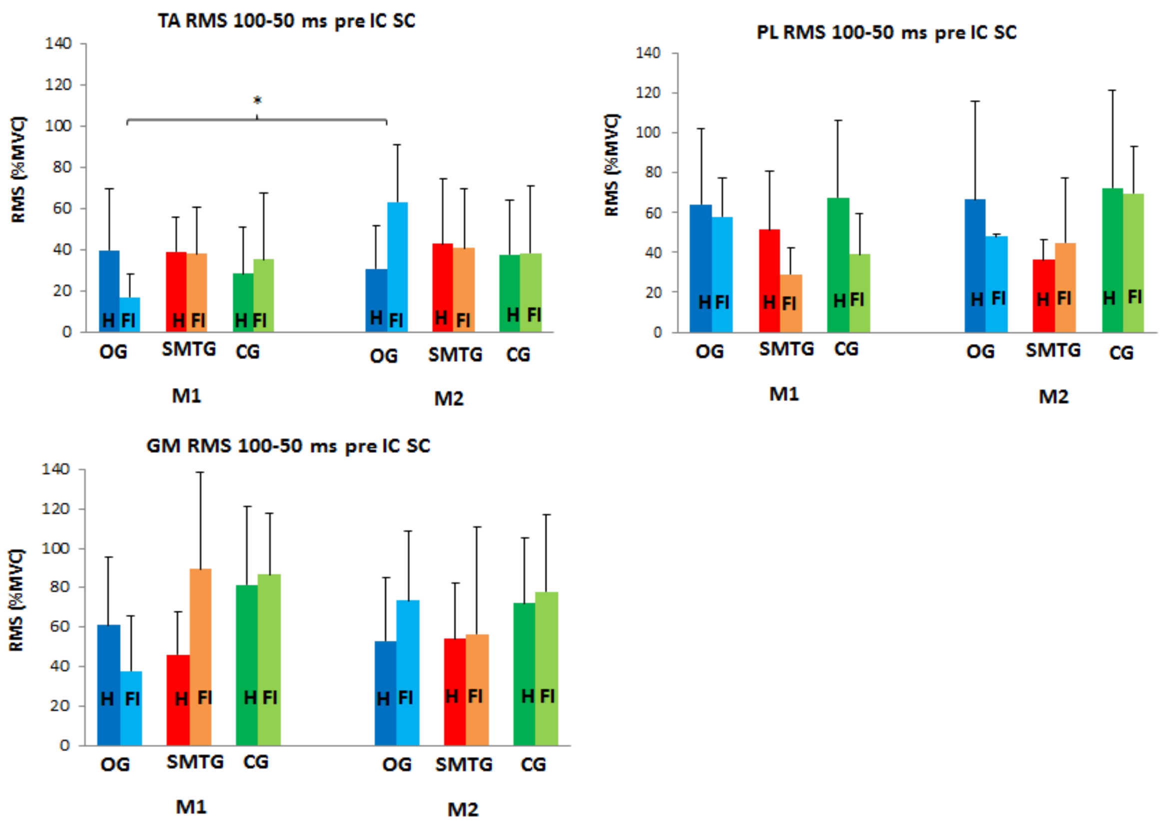

Figure 43: RMS (%MVC) of TA, PL and GM for SC during 100-50 ms pre IC; significant interaction effect of *intervention group x ankle status x time* between H and FI in OG for TA during SC (*p<0.0167); *H = healthy group, FI = functional ankle instability group; SC = side cutting; OG = orthoses intervention group, SMTG = sensorimotor training group, CG = control group; TA = M. tibialis anterior, PL = M. peroneus longus, GM = M. gastrocnemius medialis*

Per-protocol analysis

Analysing the outcomes "per-protocol", significant differences were found between H and FI in the SMTG over time for PL muscle during NW (significant interaction effect of *intervention group* x *ankle status* x *time* [*p*=0.01]; increase for H and FI). However, it was demonstrated that the increase was substantially more for FI, even when compared with the "intention to treat analysis" (see Figure 44). For SC, significant interaction effect of *intervention group x ankle status x time* were not statistically significant anymore. All the other differences remained significant.

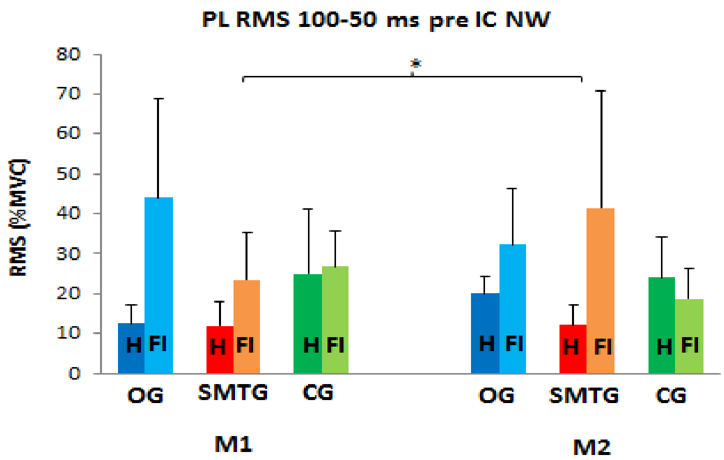

Figure 44: RMS (%MVC) of PL for NW during 100-50 ms pre IC; significant interaction effect of *intervention group x ankle status x time* between H and FI in SMTG for PL during NW (**p*<0.0167); *H = healthy group, FI = functional ankle instability group; NW = normal walking; OG = orthoses intervention group, SMTG = sensorimotor training group, CG = control group; PL = M. peroneus longus*

Reflex-activity of ankle musculature

Table 18: Long-term effectiveness of foot orthoses (MQ 5) - 200-400 ms post IC

			Δ RMS (%MVC) M2-M1		
			TA	**PL**	**GM**
NW	**OG**	**H**	1.3	0.3	4.5
		FI	5.1	13.5	4.2
	SMTG	**H**	2.2	0.4	0.7
		FI	13.3	5.3	1.7
	CG	**H**	1.1	0.1	4.4
		FI	2.3	3.9	5.9
PW	**OG**	**H**	22.2	2.0	5.8
		FI	26.3	20.5	9.3
	SMTG	**H**	4.1	14.9	3.5
		FI	3.7	15.7	27.0
	CG	**H**	3.7	2.3	13.1
		FI	13.1	2.3	5.4
SC	**OG**	**H**	2.1	12.4	13.4
		FI	5.2	10.6	45.9
	SMTG	**H**	3.3	2.1	21.9
		FI	5.4	12.7	11.9
	CG	**H**	0.8	8.5	11.6
		FI	3.1	10.2	18.8

Normalized RMS amplitudes (mean±SD, %MVC); *Δ = difference in RMS (%MVC) M2 - M1; H = healthy group, FI = functional ankle instability group; NW = normal walking, PW = perturbed walking; SC = side cutting; OG = orthoses intervention group, SMTG = sensorimotor training group, CG = control group; TA = M. tibialis anterior, PL = M. peroneus longus, GM = M. gastrocnemius medialis*

Differences in EMG-A between H and FI in each intervention group of all muscles during all conditions at 200-400 ms post IC is shown in Table 18.

Normality of data

During NW, data for all muscles were not normally distributed, except for PL (p=0.09 M2) and GM (p=0.31 M1, p=0.15). During PW, data for all muscles were normally distributed, except for TA (p=0.73 M1, p=0.15 M2) and PL (p=0.31 M1, p=0.09 M2). During SC, data for all muscles were not normally distributed, except for TA (p=0.21 M1) and PL (p=0.05). Homogeneity of variances was not given for all of the data.

Normal unperturbed walking

Significant differences could not be found between H and FI in any of the groups over time for any of the muscles (no significant interaction effect of *intervention group* x *ankle status* x *time* [TA p=0.06, PL p=0.36, GM p=0.85]). Baseline values (M1) in EMG-A of PL differed significantly between H and FI in the SMTG (p=0.003). Pre- and post EMG-A for NW during 200-400 ms post IC for H and F, in all intervention groups, is presented in Figure 45.

6 weeks of training intervention led to differences between H and FI. TA EMG-A increased for H and decreased for FI within the OG. Also, the EMG-A decreased for H and increased for FI in the SMTG (substantially by 13.3%) and among the CG (Table 18). For PL, EMG-A increased for both the H and FI in the OG and SMTG (for FI to a higher extent in OG: 13.5%). Regarding GM EMG-A, values decreased for H within the OG and CG, but increased for FI within the same two groups. Regardless of ankle status, GM EMG-A was reduced from pre- to post-testing in the SMTG (Table 18).

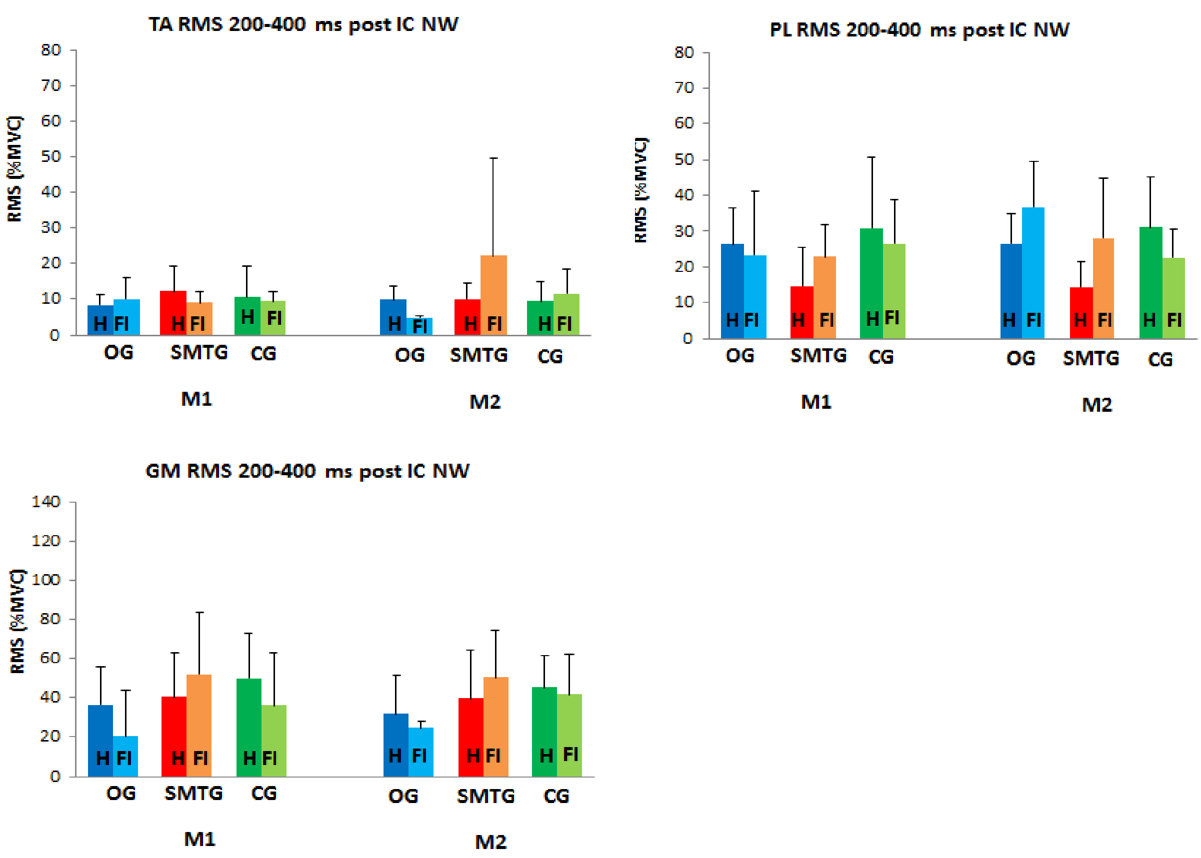

Figure 45: RMS (%MVC) of TA, PL and GM for NW during 200-400 ms post IC; *H = healthy group, FI = functional ankle instability group; NW = normal walking; OG = orthoses intervention group, SMTG = sensorimotor training group, CG = control group; TA = M. tibialis anterior, PL = M. peroneus longus, GM = M. gastrocnemius medialis*

Perturbed walking

No significant differences were demonstrated between H and FI in the intervention groups over time for all muscles (no significant interaction effect of *intervention group* x *ankle status* x *time* [TA *p*=0.63, PL *p*=0.48, GM *p*=0.17]). Figure 46 shows pre- and post EMG-A for PW at 200-400 ms post IC for H and FI in all intervention groups.

TA EMG-A was reduced for H as well as for FI in both groups, the OG and the SMTG. Specifically, in the OG the EMG-A reduced to a higher extent for FI (26.3%) than for H (22.2%). In the SMTG, the H had a larger decrease in TA EMG-A in contrast to the FI. Generally, these effects were higher pronounced in the OG than in the SMTG (Table 18). 6 weeks of training induced an increase in PL EMG-A for H and a considerable decline in EMG-A for FI in the OG (20.5%), while PL EMG-A remarkably decreased for H (14.9%) and increased for FI in the SMTG (15.7%)(Table 18). For GM EMG-A differed between H and FI as EMG-A increased for H, but reduced for FI in the OG in contrast to the CG (decline in EMG-A in H and rise in EMG-A for FI). In the SMTG GM EMG-A was reduced for H as well as for FI (more in FI: 27.0%)(Table 18).

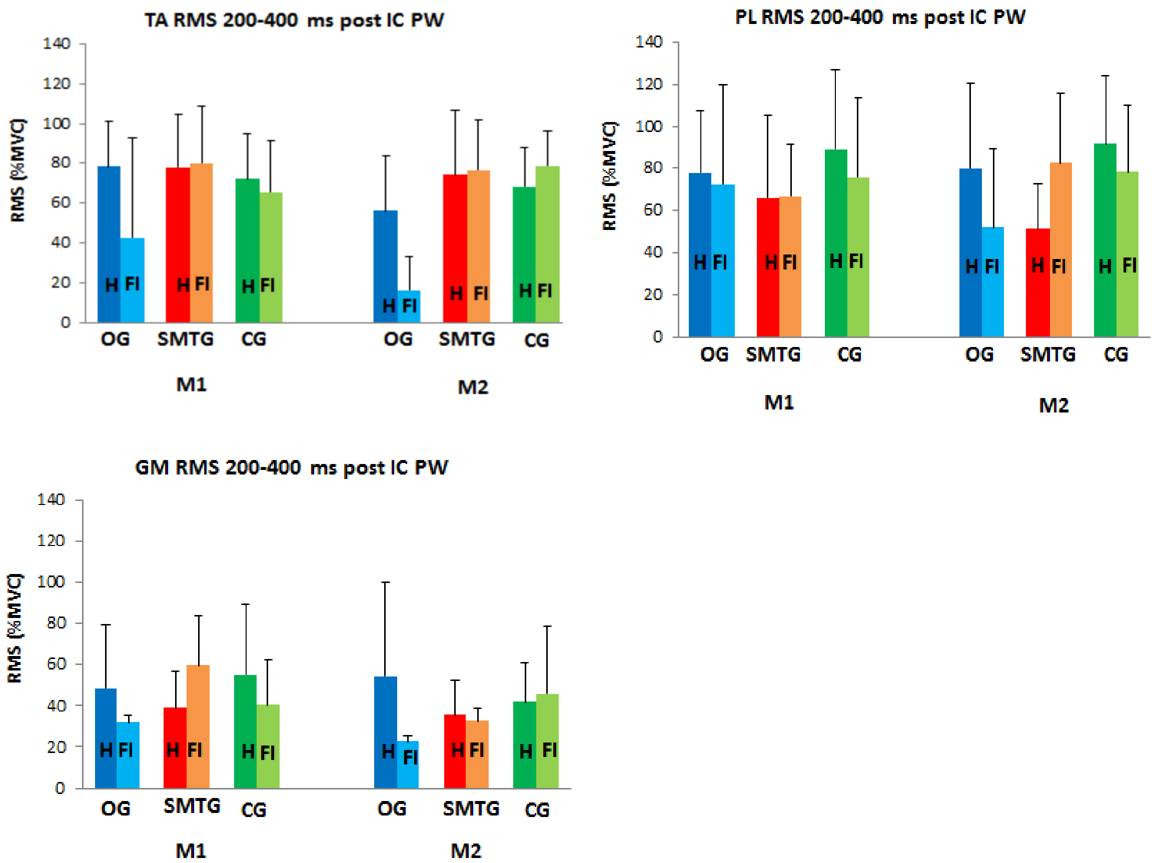

Figure 46: RMS (%MVC) of TA, PL and GM for PW during 200-400 ms post IC; *H = healthy group, FI = functional ankle instability group; PW = perturbed walking; OG = orthoses intervention group, SMTG = sensorimotor training group, CG = control group; TA = M. tibialis anterior, PL = M. peroneus longus, GM = M. gastrocnemius medialis*

Side cutting

No significant differences were revealed between H and FI in any of the groups over time for all of the muscles (no significant interaction effect of *intervention group* x *ankle status* x *time* [TA *p*=0.96, PL *p*=0.88, GM *p*=0.32]). Figure 47 illustrates EMG-A for SC at 200-400 ms post IC for H and FI in all intervention groups.

For TA EMG-A increased for H as well as for FI in the SMTG and CG (higher pronounced rise in EMG-A for FI in both groups; Table 18). In contrast, in OG TA EMG-A decreased for H as well as for FI (again more for FI). Considering peroneal EMG-A, amplitudes demonstrated a reduction in H for the SMTG and CG, but a substantial rise in FI for the same groups (SMTG: 12.7%; CG: 10.2%). In the OG however, PL EMG-A decreased considerably (H: 12.4%, FI: 10.6%), independent of ankle status. The intervention program led to different GM EMG-A with remarkably reduced amplitudes for H (21.9%) and increased amplitudes for FI in the SMTG. In contrast to the CG (increase in EMG-A, regardless of ankle status), GM EMG-A yielded substantially reduced values for H as well as for FI in the OG (FI: 45.9%, H: 13.4%)(Table 18).

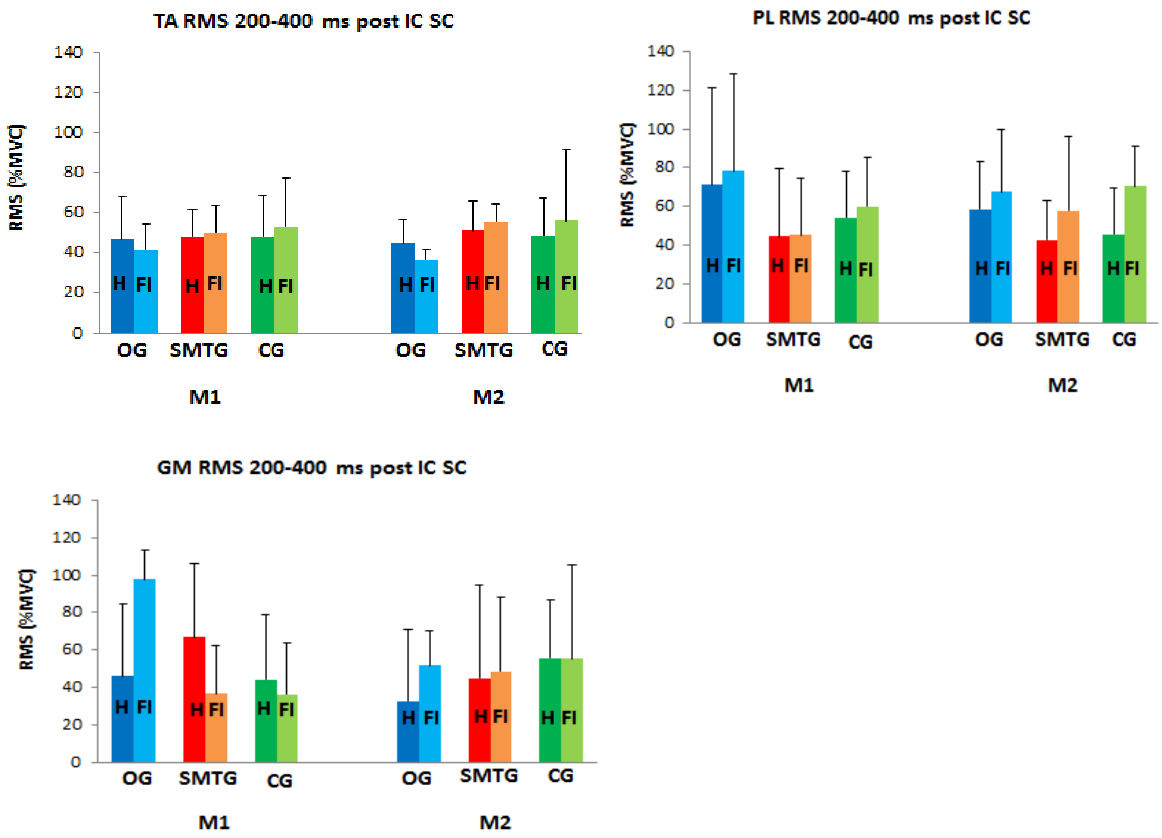

Figure 47: RMS (%MVC) of TA, PL and GM for SC during 200-400 ms post IC; *H = healthy group, FI = functional ankle instability group; SC = side cutting; OG = orthoses intervention group, SMTG = sensorimotor training group, CG = control group; TA = M. tibialis anterior, PL = M. peroneus longus, GM = M. gastrocnemius medialis*

Per-protocol analysis

Analysing the outcomes "per-protocol", significant differences between H and FI in the OG over time for GM muscle during SC (significant interaction effect of *intervention group* x *ankle status* x *time* [p=0.02]) could be revealed (Figure 48). Differences in GM EMG-A between H and FI in the OG (reduction in EMG-A in both groups [however more in FI]; higher reduction in EMG-A in H compared with "intention to treat analysis"; Table 18) were significant.

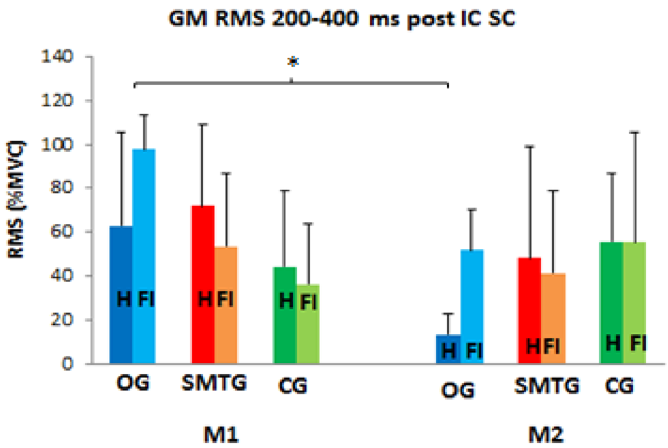

Figure 48: RMS (%MVC) of GM for SC during 200-400 ms post IC; significant interaction effect of *intervention group x ankle status x time* between H and FI in OG for GM during SC (**p*<0.0167); *H = healthy group, FI = functional ankle instability group; SC = side cutting; OG = orthoses intervention group, SMTG = sensorimotor training group, CG = control group; GM = M. gastrocnemius medialis*

Single case analysis - Participants with FI in orthoses intervention group

Concerning main question 5 (MQ5), data of only N=2 participants (see Figure 20) entered the analysis, according to randomisation procedure. Due to that fact, these 2 participants with FI, who conducted the orthoses intervention, will be considered in more detail in the following. A brief anamnesis (anthropometry, training anamnesis, clinical anamnesis) of the 2 participants is described as follows: The first participant (P1; female, 30 yrs, handball since 16 years 3x/week [120 min per unit], 1.70 m, 61.2 kg) had a right instable ankle joint (3 sprains, >6 months ago; CAIT score 19; FAAM sport score 30 [94%]), whereas participant 2 (P2; male, 27 yrs, soccer since 20 years 3x/week [100 min per unit], 1.86 m, 74 kg) suffered from left instable ankle joint [2 sprains, >6 months ago; CAIT score 26; FAAM sport score 31 [97%]). Figure 49 shows only considerable modified EMG-A (>20% difference M2 - M1, see also Table 17 and 18) isolated for the 2 FI participants in the orthosis intervention group (pre-activity: GM for NW, TA and GM for SC; reflex-activity: TA and PL for PW, GM for SC).

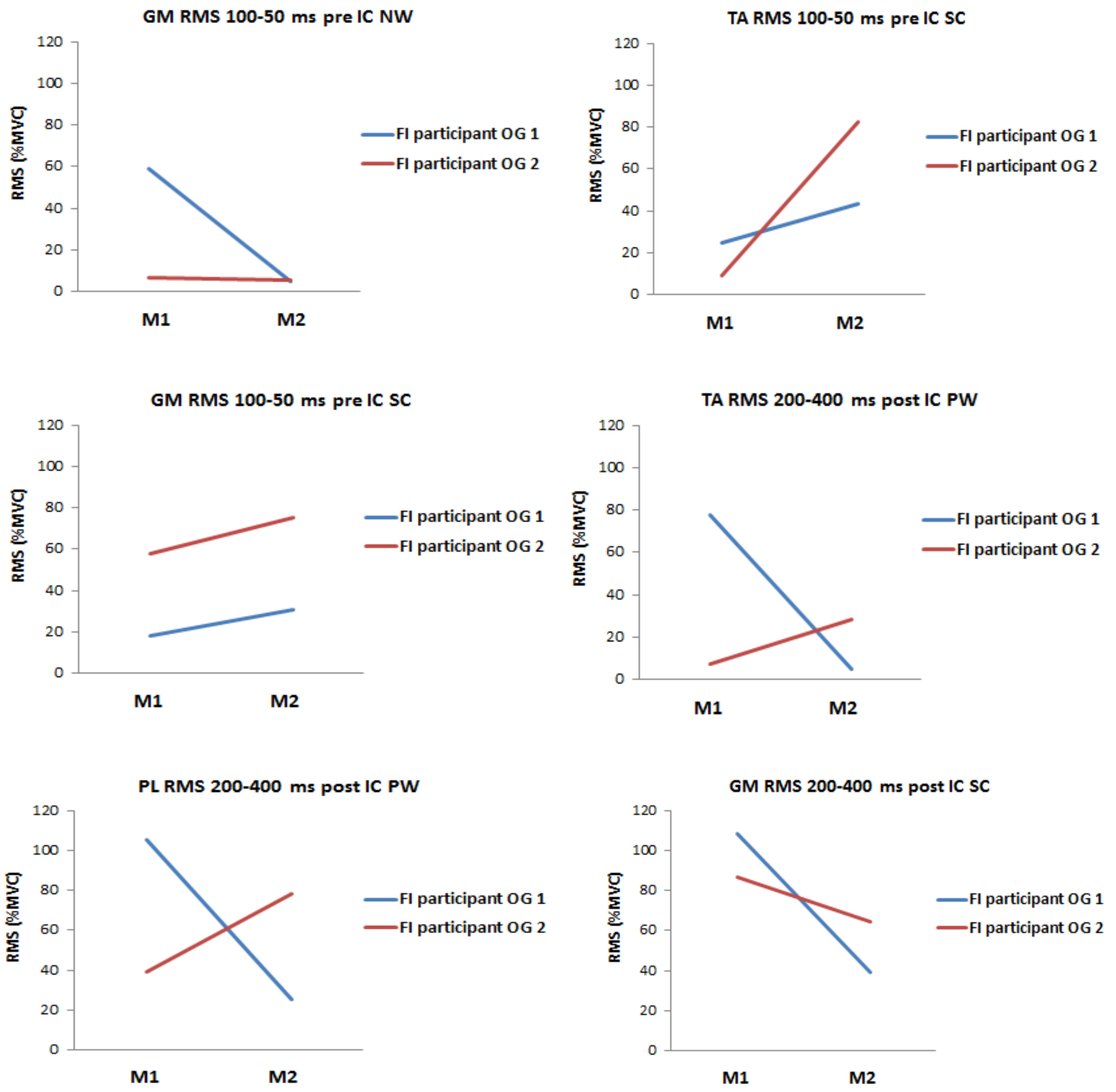

Figure 49: RMS (%MVC) of GM at 100-50 ms pre IC during NW, TA and GM at 100-50 ms pre IC during SC; TA and PL at 200-400 ms post IC during PW and GM at 200-400 ms post IC during SC; *FI = functional ankle instability; NW = normal walking, PW = perturbed walking; SC = side cutting; OG = orthoses intervention group; TA = M. tibialis anterior, PL = M. peroneus longus, GM = M. gastrocnemius medialis*

GM pre-activity substantially decreased from pre- to post-test during NW for P1 and P2, however more for P1 (54.4%) than for P2 (0.8%). Considering TA and GM prior ground contact for SC, EMG-A increased in both participants with FI, however to a higher extent for P2 (TA: 73.5% [P1: 18.6%]; GM: 17.9% [P1: 12.6%]). TA and PL reflex-activity showed a rise during PW in P2 (TA: 20.9%, PL: 39.4%), whereas P1 demonstrated strongly reduced values after intervention (TA: 73.6%, PL: 80.5%). GM EMG-A was reduced from pre- to post-test after ground contact during SC in both participants, however this decline was higher pronounced for P1 (69.7%) than for P2 (22.1%).

Summary of Results

The major findings (key results) are presented in following:

- Test-retest reliability of the assessment of ankle muscle activity was substantially variable in H and FI, depending on time window of analysis, testing situation and ankle muscle tested. Mainly unsystematic outcomes in terms of high TRV (25.8-89.8%), high range of bias (0.2±32.1% to 23.7±19.9%), and poor to good values of ICC (-0.44 to 0.84) across conditions were found.
- Individuals with FI presented a different ankle muscle activity compared to H at M1 (during the acute use of a "shoe only" or an in-shoe orthosis): Individuals with FI showed higher muscle pre-activity than H during normal unperturbed (TA [only for shoe], PL [significantly], GM) and perturbed walking (TA [only for shoe], PL, GM). H showed higher muscle pre-activity than individuals with FI during side cutting (TA, PL, GM). Individuals with FI demonstrated higher muscle reflex-activity than H during normal walking (TA, PL [only for shoe]), however during perturbed walking (TA, PL and GM [only for orthosis]) and side cutting (PL, GM) EMG-A was higher for H.
- Independent of ankle health status, muscle activity did not differ, when wearing a "shoe only" or an in-shoe orthosis at M1 (no acute effect of foot orthosis at M1).
- Ankle muscle activity differed between the orthosis intervention group and 1. the control group (no intervention) and 2. the sensorimotor training group from pre- to post-testing (Figure 50):

		Pre-activity			**Reflex-activity**		
		TA	**PL**	**GM**	**TA**	**PL**	**GM**
NW	**OG**	↓	↑	↑	↑	↑	↓
	SMTG	↓	↑	↓	↑	↑	↓
	CG	↑	↓	↓	↑	↓	↑
PW	**OG**	↓*	↑	↑	↓*	↓	↑
	SMTG	↓	↑	↓	↓	↓	↓
	CG	↑	↓	↓	↑	↑	↓
SC	**OG**	↑	↓	↑	↓	↓	↓
	SMTG	↑	↓	↓	↑	↑	↓
	CG	↓	↑	↑	↑	↑	↑

Figure 50: Increase or decrease in ankle muscle activity of TA, PL and GM for OG, SMTG and CG during NW, PW and SC; significant values (*p<0.0167) for TA in OG during PW; *NW = normal walking, PW = perturbed walking; SC = side cutting; OG = orthoses intervention group, SMTG = sensorimotor training group, CG = control group; TA = M. tibialis anterior, PL = M. peroneus longus, GM = M. gastrocnemius medialis*

- Ankle muscle activity differed between H and FI in the intervention groups (Figure 51): Orthoses intervention was as effective as SMT, increasing PL pre-activity during PW, and TA pre-activity during SC, as well as PL and GM reflex-activity during NW.

			Pre-activity			Reflex-activity		
			TA	**PL**	**GM**	**TA**	**PL**	**GM**
NW	**OG**	**H**	**↓**	↑	↑	↑	↑	↓
		FI	↓	↓	↓	↓	**↑**	↑
	SMTG	**H**	↑	↑	↓	↓	↑	↑
		FI	↓	**↑**	↑	↑	**↑**	**↑**
	CG	**H**	**↑**	↑	↓	↓	↑	↓
		FI	↑	↓	**↓**	↑	↓	↑
PW	**OG**	**H**	↓	↑	↑	↓	↑	↑
		FI	**↓**	**↑**	↓	**↓**	↓	↓
	SMTG	**H**	↑	↑	**↓**	**↓**	↓	↓
		FI	↓	**↑**	↓	↓	↑	**↓**
	CG	**H**	**↑**	↑	**↓**	↓	↑	↓
		FI	↑	↓	↓	↑	↑	↑
SC	**OG**	**H**	↓*	↑	↓	↓	**↓**	↓
		FI	↑*	↓	↑	**↓**	↓	**↓**
	SMTG	**H**	**↑**	↓	↑	↑	↓	↓
		FI	↑	↑	↓	**↑**	↑	↑
	CG	**H**	**↑**	↑	**↓**	↑	↓	↑
		FI	↑	**↑**	↓	**↑**	↑	**↑**

Figure 51: Increase or decrease in ankle muscle activity of TA, PL and GM for H and FI in OG, SMTG and CG during NW, PW and SC; significant values (*p<0.0167) for TA in H/FI in OG during SC; bolded arrows indicate higher effect for the respective ankle status in the respective intervention group; blue (red) frames indicate higher effect in OG (SMTG) in contrast to SMTG (OG) for respective ankle status (H/FI); *NW = normal walking, PW = perturbed walking; SC = side cutting; OG = orthoses intervention group, SMTG = sensorimotor training group, CG = control group; H = healthy ankles, FI = functional instable ankles; TA = M. tibialis anterior, PL = M. peroneus longus, GM = M. gastrocnemius medialis*

- At M2, higher PL pre-activity was shown for “shoe only” in OG and higher GM pre-activity was presented for in-shoe orthosis in OG and CG during NW (=”transmission effect” [TE]). Higher PL and GM pre-activity could be found in OG in contrast to CG for in-shoe orthosis during PW and SC (=TE). In contrast to CG, OG showed higher pre-activity of TA for “shoe only” during SC. For reflex-activity, higher TA and PL activity was identified for in-shoe orthosis in OG during NW (=TE). During PW, higher GM activity was shown for “shoe only” in OG in contrast to CG. None of the “transmission effects” were significant.

CHAPTER IV: DISCUSSION

4. Discussion

4.1 Test-retest reproducibility of ankle muscle activity in individuals with functional ankle instability (SQ 1a)

It was investigated if ankle muscle activity could be measured in a reproducible manner between two test sessions (M1, M2) during perturbed walking (normal unperturbed walking as control condition) on a split-belt treadmill, as well as during side cutting in individuals with FI (in comparison with a healthy cohort as control group).

The hypothesis can be partly confirmed that ankle muscle activity can be measured reproducibly during unperturbed and perturbed treadmill walking, as well as side cutting between two test sessions in individuals with and without FI. Depending on which ankle muscle tested and the time window analyzed, reproducibility measures presented some poor, but also acceptable and good values in healthy individuals and those with FI. As expected, the reproducibility of muscle activation is influenced by substantial variability across the test conditions (unsystematic outcomes, high levels of systematic error for healthy participants and those with FI, high variation within the values). The ankle health status as well as the walking condition did affect the reproducibility of ankle muscle activity between sessions. However, comparable results were achieved in previous studies in healthy individuals, although using different measurement methods (fine-wire EMG), measurement tasks (walking, cycling) and lower leg muscles (tibialis posterior)(Barn et al., 2012; Murley, Menz, et al., 2010). They found that EMG amplitudes varied strongly between two measurement sessions (CV: 7- 88%) (Barn et al., 2012; Jobson et al., 2013; Kadaba et al., 1989; Murley, Menz, et al., 2010). Moreover, the high values of SD for the measurement variables, across the testing conditions, showed that movement variability is a central issue when analysing muscle amplitudes in dynamic test situations (Suda & Sacco, 2011). A better reproducibility of muscle activation (of the TA) could be revealed for trained individuals (cyclists) that have a consistent, training-induced movement pattern/motor control due to specific sport training movements, when compared to the untrained (cyclists)(Jobson et al., 2013). Some of the (non-professionally trained) participants in the present study might have shown variability in walking technique (as stride length variation between steps), which might have affected the values of reproducibility and partly explain the high values of SD. High variability of EMG amplitude values for the mentioned conditions in this study can also be explained by the dynamic nature of measurement. Walking, and particularly perturbed walking on a split-belt treadmill is a complex task involving many degrees of freedom. It places high demands on the neuromuscular system with ankle stabilizing musculature to restore dynamic postural control. Nevertheless, the split-belt treadmill offers the potential to simulate an everyday-like stumbling situation under highly controlled and standardized laboratory conditions. Subsequently, the amount of variability of ankle muscular activity may be kept on a low level.

For walking (both time windows) and side cutting (time window of pre-activity), the EMG-A in the H group revealed more reproducible values, except for the PL during perturbed walking. This observation may indicate a more variable pattern of the ankle muscle neuromuscular activation within the FI group, and is in line with study results of Barn and colleagues (2012)(less reproducible values in lower leg pathologies [pes planovalgus, rheumatoid arthritis] during walking)(Barn et al., 2012). However, a direct comparison of muscle activity to a healthy control group was not performed in that study and the transferability of these findings to patients with FI cannot be made. Nonetheless, it might be suspected that the presence of FI may be associated with a less adaptable sensorimotor system to environmental changes. In contrast, measurements of the PL and GM muscle amplitudes were found to be more reproducible in the FI group during perturbed walking and side cutting (for SC: reflex-activity). This could be due to the fact that individuals with FI have a constantly impaired motor control, thereby leading to a reduced PL muscle firing (Santilli et al., 2005). Furthermore, particularly for reflex-activity, more reproducible values could be identified for perturbed walking, except for the PL in both groups. One possible explanation might be that during stumbling on treadmill reflex-activity of the TA and GM muscles was quite consistent between test sessions, and served to ensure ankle joint stability. Additionally, it could be assumed that due to the anterior-posterior directed motion of the treadmill belt, the TA and GM muscles underwent a stretch reflex arch, which serves to stiffen the ankle joint of the supporting limb in stance phase during perturbed walking (Hopkins et al., 2007; Nakazawa et al., 2004). The TA muscle activity could be consistently facilitated, whereas the GM muscle activity might be consistently inhibited by the spinal cord. Concerning ICC values, the GM muscle revealed highest values of reproducibility, specifically during perturbed walking at 200-400 ms post IC. Large variability in PL muscle activity during stance phase of gait was found in participants with FI, which was also identified by several study groups (Delahunt et al., 2006a; Louwerens et al., 1995; Santilli et al., 2005). Other groups also demonstrated that responses of the GM are much more consistent than those of other lower leg muscles, such as the TA (e.g. highest EMG-A: ICC 0.90 for GM and 0.73 for TA) during running or sudden drop of treadmill surface (Karamanidis et al., 2004; Nakazawa et al., 2004). However, for both time windows, during side cutting, the TA muscle was measured most reliably. This finding can be confirmed by Karamanidis and colleagues (2004)(ICC 0.85 during pre-activation of running in contrast to GM (ICC 0.78)(Karamanidis et al., 2004) as well as by Koshino et al. (2015) (good to excellent values of within-day repeatability of TA EMG during side cutting [coefficient of multiple correlation: 0.71-0.97], in subjects with chronic ankle instability and healthy controls) (Koshino et al., 2015).

Strengths and Limitations

The time period between the two measurements in this study accounted for 51 days. This time phase was chosen since it represents a clinically meaningful time interval, which is valid for the evaluation of a rehabilitation or treatment process (Loudon et al., 2008; O'Driscoll & Delahunt, 2011). According to Jobson et al. (2013), measurement technique is the main source of variability (Jobson et al., 2013). Some authors argue that a re-application of electrodes results in large random error between sessions (Murley, Menz, et al., 2010). Inevitable systematic errors (perspiration, changes in skin impedance etc.) can affect the EMG signal amplitude, however, additionally some inter-session and inter-individual variability of ankle muscle activity could be due to inconsistent electrode placement (Gollhoferl et al., 1990; Horstmann et al., 1988). Nevertheless, in the present research, sensor placement was replicated to a high degree of accuracy as the same investigator conducted the electrode placement at site of anatomical landmarks according to the aforementioned recommended guidelines at both testing sessions. Additionally, it can be argued that the EMG normalisation technique and measurement setup (MVC measure: toe stances for GM and PL; resistance of foot against fixed taut rope for TA) used in the present study may have reduced test-retest reliability (Jobson et al., 2013). Alternative normalisation techniques (e.g. normalising perturbed walking in relation to normal unperturbed walking) and more standardized setups (e.g. resting MVC during quiet standing, MVC against manual resistance) might be preferred, in context of ankle muscle activation measures, since measuring MVC at the ankle might be variable itself (Palmieri-Smith et al., 2009; Suda et al., 2009). It is difficult to control and monitor the participant's effort or output with MVCs, which may be a factor that leads to greater between-participant variability compared to other normalisation protocols (Murley, Menz, et al., 2009). However, the outcomes in the present study work showed that reliability measures of MVC for ankle muscles yielded acceptable values (TRV 13.5% to 24.6%; bias±1.96*SD of 0.00±0.01% to 0.04±0.09% and ICC of 0.54 to 0.90). Moreover, it would be essential to clarify by means of further research whether the detected study findings are generalizable to other studies. Future work should attempt to recruit a larger sample in order to draw more meaningful conclusions.

All in all, there is a lack of experimental studies that have investigated the test-retest reproducibility of EMG-A during normal unperturbed walking, simulated stumbling on treadmill, and side cutting in healthy individuals and those with FI. To the best of our knowledge, this is the first study that demonstrated outcomes for test-re-test reproducibility of ankle musculature activation during unperturbed and perturbed walking on a customized split-belt treadmill, as well as during side cutting in healthy individuals and those with FI. Although reproducibility of the assessment of ankle muscle activity is highly variable in individuals with and without FI, healthy individuals could be tested more reliably than individuals with functional instable ankles during normal unperturbed and perturbed walking (pre- and reflex-activity), as well as during side cutting (pre-activity), depending on which ankle muscle was tested. Other authors supported that subjects with instable ankles present greater individual variance in muscle activation, specifically in the PL muscle (Hopkins et al., 2012; Suda & Sacco, 2011). In addition, ankle muscle reflex-activity was measured more reliably in individuals with FI than in healthy individuals during side cutting. Perturbed walking on treadmill represented higher reproducibility of ankle muscle activation in relation to normal walking, however only for the TA and GM reflex-activation. Hence, walking condition as well as ankle status affected the reliability of ankle muscle activity. Consequently, the used setup can be applied in future studies. In a clinical context, the used measures may be beneficial for the understanding of fundamental characteristics about ankle muscle activity in a population with FI during provoked stumbling on split-belt treadmill. No study is available which presented highly reliable values for ankle muscle activation in healthy individuals or those with FI during dynamic test conditions. A general concern is that walking is affected by gait parameters as individual stride length and frequency (Danion et al., 2003; Hausdorff, 2005). Gait characteristics can be variable between and within subjects, which has to be considered when evaluating the consistency in ankle muscle activity between test sessions. Murley et al. (2010) and other authors stated that researchers planning studies of ankle muscles with a repeated-test design (e.g. to evaluate the effect of an intervention) must consider whether this level of error is reasonable (Barn et al., 2012; Jobson et al., 2013; Karamanidis et al., 2004; Murley, Menz, et al., 2010). Large random errors and high variation for reproducibility, in the present study, may reflect the physiological variability in muscle activation during gait. This must be taken into consideration and accepted with regard to follow-up investigations.

4.2 Acute effect of foot orthoses on ankle muscle activity in individuals with functional ankle instability (MQ 1, MQ 2)

It was evaluated if participants with FI respond with a different ankle muscle activity to an orthosis condition compared with healthy participants at M1 (acute effect orthosis) (difference in ankle muscle activity between healthy participants and those with FI [in dependence on/under consideration of wearing a “shoe only” or an in-shoe orthosis at M1]).

Pre-activity of ankle musculature

Against the hypothesis, for normal unperturbed and perturbed walking, pre-activity of the PL and GM muscles resulted in higher values in individuals with FI compared to healthy individuals, independent of the shoe condition. In addition, unexpectedly no differences between condition “shoe only” and condition in-shoe orthosis in terms of EMG-amplitude could be demonstrated. Other study groups have also shown increased pre-activity of the PL in participants with FI. Although, other test setups (landing from jump on a supinating device, lateral hopping) and EMG measurement parameters (integrated EMG, EMG area and ensemble average, time normalized EMG-A [100% of stance phase]) were partially used (Delahunt et al., 2007; Gutierrez et al., 2012). The finding of a higher PL and GM amplitude in FI group may be the result of a change in pre-programmed feedforward motor control in these individuals, in order to provide anticipatory protection of the ankle joint (Delahunt et al., 2006a; Gutierrez et al., 2012). In this context, the PL muscle works as a primary ankle stabilizer, certainly aiding in the maintenance of lateral joint stability (Donahue et al., 2014). The increased PL activation can be seen as a compensatory strategy in subjects with FI. This leads to a reduced inversion at touchdown during situations at which the ankle joint is vulnerable to potential injury (Gutierrez et al., 2012). Suda and colleagues (2011) supported this explanation. The PL could be active before impact time in a population with FI in order to generate an evertor torque, or to control the magnitude of the invertor torque around the joint (Suda & Sacco, 2011). However, there has been conflicting evidence of whether the PL activity alone is sufficient to prevent joint injury and protect the ankle from injury in case of sudden, unexpected inversion (Delahunt et al., 2006a; Donahue et al., 2014). In context of joint injury protection, the selective facilitation of other lower leg muscles than PL before ground contact also has relevance (Nakazawa et al., 2004). It has been shown that the GM muscle is active before a sudden drop of a supporting surface during walking (Nakazawa et al., 2004). The authors explain this mechanism by the increase in plantar flexion, which served to soften the impact before ground contact (Feger et al., 2015; Nakazawa et al., 2004; Nieuwenhuijzen & Duysens, 2007). As in the present research, a recent study observed that the GM muscle activity 200 ms prior IC was greater for athletes with chronic ankle instability compared to healthy athletes, however during a side cut task (Koshino et al., 2015). According to the authors, those findings can be declared by the crucial role of the GM in absorbing impact load and increasing ankle stiffness to protect the ankle joint immediately after ground contact (Koshino et al., 2015). In the study by Delahunt et al. (2007), it was shown that feedforward motor control of the S and TA muscle aimed at controlling the position of the center of gravity upon IC, which could be altered by a less everted position of the ankle joint in individuals with FI (Delahunt et al., 2007). Muscle activity before or at the onset of perturbations, is more efficient than reactive responses, which may have a sizable delay (Nieuwenhuijzen & Duysens, 2007). This approach is in accordance with other authors (Gutierrez et al., 2009; Holmes & Delahunt, 2009). Open-loop feedforward neuromuscular control may be more important for the maintenance of dynamic joint stability than closed-loop feedback control mechanisms, which rely primarily on proprioception (Gutierrez et al., 2009; Holmes & Delahunt, 2009). Feger and colleagues (2015) however, doubted the effectivity of feedforward anticipatory control in individuals with FI (Feger et al., 2015). Motoneuron-pool excitability might be decreased in individuals with FI, and could be related to a concurrent decrease in sensitivity of the muscle spindles during perturbations. Pre-activity of the PL before IC may decrease the available motor units capable of protecting against inversion moments. The slackened muscle spindles before IC would be incapable of detecting and initiating a response to slight changes in muscle length at ground contact, when ankle sprains occur (Feger et al., 2015). Nevertheless, Akhbari et al. (2007) noted that the role of the feedforward mechanism for ankle joint stability is not clarified yet and requires further investigation (Akhbari et al., 2007).

Furthermore, the hypothesis can be confirmed that the pre-activation of the TA and PL was higher (significant for PL) in healthy individuals compared to individuals with FI for side cutting, independent of shoe condition. Pre-landing muscular activity is considered essential for the preparation of the tendon-muscle complex to be able to support the fast forced elongation that happens after foot impact with the ground, and the subsequent joint rotation during a side cut (Suda & Sacco, 2011). The mentioned outcome was close to those of many studies, which detected diminished ankle muscle pre-activity in subjects with FI during dynamic test situations (Delahunt et al., 2006a; Rosen et al., 2013; Suda & Sacco, 2011). More dynamic tasks such as cutting or jumping, represent the eccentric equivalent to the PL function during walking (Feger et al., 2015). The muscle responses found during cutting or jumping can differ from the responses found during gait, because responses are known to be task dependent (Duysens et al., 1992; Zehr & Stein, 1999). The characteristic muscle activation patterns during perturbed walking and side cutting are modulated by different neural origins. The stumbling situation is more of a reflexive in nature (although partly anticipatory as well), and the cut manoeuvre is characterized more by the involvement of feedforward mechanisms. Thus, the reduced peroneal activity before ground contact might indicate that participants with FI experienced a deficit in feedforward neuromuscular control. This could leave the ankle joint vulnerable to re-injury, especially during unexpected contact with the ground, such as landing on a rutted playing field or an opponent’s foot (Delahunt et al., 2006b). The suppressed PL activation/SLR response at landing will likely lead to decreased intrinsic ankle joint stiffness, which is a critical component in maintaining joint stability (Palmieri-Smith et al., 2009). Another factor that might be responsible for the diminished PL activity in FI subjects might be a weakness or damage to the deep branch of peroneal nerve of PL muscle, which never totally regenerates. The stumbling situation is a horizontal translational displacement, which is more likely processed via spinal proprioceptive, and less via vestibulospinal pathways, which would be the case for e.g. platform rotations (Taube et al., 2006). If patients with FI cannot rely on functioning PL nerve conduction, proprioceptive input to the spinal cord is supressed and thus, protective mechanisms might also be inhibited. Additionally, some authors supported that individuals with FI have a deficit in torque of the PL muscle (Santos & Liu, 2008; Willems, Witvrouw, Verstuyft, Vaes, & De Clercq, 2002). However, dynamic strength testing of ankle muscles or an investigation of nerve conduction velocity was not considered in the current study work. These outcomes would be valuable to gain further knowledge about the causative impairments during pre-activation, which could differentiate individuals with FI from asymptomatic individuals. Moreover, Rosen et al (2013) emphasized the important role of the TA in dynamic stabilization of the ankle during athletic manoeuvres (Rosen et al., 2013). One reason for the fact that healthy subjects demonstrated greater pre-activity of the TA muscle, might be to prepare for a situation where the center of pressure will be moving laterally once the kinetic chain has already closed (Holmes & Delahunt, 2009). This results in a more inverted, but also less plantar flexed position of the ankle at landing. This may be another protective strategy to keep the ankle in a more close-packed, stable position. A recent study could also show increased TA amplitudes in healthy participants during the loading acceptance of the foot while side cutting. This can be explained by modulation of muscle activity, which anticipates potential instability in lower limb joints and assures safety to complete the task (Oliveira et al., 2014). Murley and colleagues (2006) stated that due to its physiological function, the TA muscle has to be most active around heel strike in healthy individuals to contract eccentrically and decelerate the foot pronation as the forefoot approaches the supporting surface (Murley & Bird, 2006). The increased TA and PL activity in healthy subjects could also represent an attempt to enhance co-contraction between ankle muscles in anticipation of the destabilizing moment. Other reasons for the increased TA pre-activity in healthy subjects could be that at the same time a selective inhibition of that muscle might occur in subjects with FI (Holmes & Delahunt, 2009). According to Holmes et al. (2009), selective inhibition is when the decreased stress tolerance of an injured joint triggers a reflexive inhibition that affects muscles that are capable of increasing tensile stress on the damaged ligaments (Holmes & Delahunt, 2009). It follows that the invertors would be inhibited after lateral joint injury as they initiate movement in the same direction as the initial injury. This explanation could be confirmed by Nakazawa et al. (2004)(Nakazawa et al., 2004). Decreasing the activity of TA as an invertor before touchdown would help the evertors to resist the induced inversion (Grüneberg et al., 2003; Nakazawa et al., 2004). Also Hopkins et al. (2012) speculated that decreased activity of the TA in subjects with FI might be a voluntary strategy to position the foot in a safer, more everted position during IC and toe off (Hopkins et al., 2012).

It seems that during normal unperturbed and perturbed walking on treadmill the participants with FI manage to deal with neuromuscular control deficits by providing anticipatory protection of the ankle joint by compensatory pre-activation. However, during side cutting they are not able to counteract deficits in feedforward neuromuscular control. It can be assumed that this finding is due to the nature of the side cut manoeuvre, a more anticipatory and less reflexive movement than treadmill stumbling. The subjects underwent impact absorption, a rapid change of direction and deceleration. Sports-related movements like side cut manoeuvres challenge the neuromuscular system and require more complex joint control for lower limb than movements during activities of daily living as e.g. walking (Koshino et al., 2015).

Reflex-activity of ankle musculature

If the preparatory muscle activity is not efficient to stabilize the joint, then subjects have to rely on reflex mechanisms of lower extremity muscles in order to obtain joint stability (Wikstrom, Tillman, Chmielewski, & Borsa, 2006). As previously mentioned, individuals with FI have the potential to correct a possible inversion and prevent further damage by the help of LLR. Absence of/Inhibited LLR responses after perturbations is/are a strong indicator that the damaged ankle cannot create the necessary stability to protect the injured joint, thereby the role of balance and proprioception during gait might be shifted to other limb muscles. Investigation of the reflex-activity of other adjacent muscles not included in the current study (such as TP [plantarflexion, inversion)], GL [evertor], or more proximal muscles of the upper thigh), would provide valuable information about possible compensation mechanism in post-activation due to stumbling, and would give more insight into their potential role in ankle joint protection (Murley, Menz, et al., 2009; Nieuwenhuijzen & Duysens, 2007; O'Connor & Hamill, 2004).

However, in the current research ankle muscle reflex-activity did not significantly differ between healthy individuals and those with FI in any of the measurement conditions. Another experimental study identified similar findings to our study results (Feger et al., 2015). For amplitudes of the TA, PL and GL muscles, no difference was noted between a healthy group of individuals and a group suffering from FI at post IC during walking. This fact might indicate that the magnitude of ankle muscle response in terminal mid-stance phase is unaffected by the ankle status of the participant, no matter which test condition a participant is measured (gait, stumbling, side cutting). This finding is surprising and must be critically scrutinized since a majority of studies observed lower peroneal muscle activity (e.g. SLR and LLR responses) and H/M-ratio (H-reflex) in patients with FI during perturbed situations (Levin et al., 2015; McVey et al., 2005; Palmieri-Smith et al., 2009). The differences in the outcomes between mentioned studies, and the current study, are unlikely to have been caused by differences in testing situation as they used similar protocols (e.g. standing, inversion perturbation while walking). However, they could be partly due to the fact that those studies differentiated between isolated components of the reflex response (e.g. SLR or LLR), whereas in the present research the reflex responses (SLR, MLR and LLR) were regarded as a whole response. Nevertheless, in the present study the PL muscle reflex-activity was also (non-significantly) lower in participants with FI during perturbed walking. Further, the TA muscle reflex-activation was found to be (non-significantly) higher in healthy participants, which might be attributed to similar explanatory mechanisms as described previously for pre-activation. Furthermore, one recent study reported that the RMS of the PL EMG signal was larger post-landing (200 ms post IC) in a group of participants where FI was compared to healthy controls during a stop jump landing task (running, stopping, both legged vertical jump, bilateral landing)(Lin et al., 2011). The comparability to a side cut task could be criticized, since participants were placing only one leg on the plate, whereas the other was in swing phase. Ankle joint stability has to be provided by one leg, completely without any help of compensation strategies by the other leg. Thus, the discrepancy between the present study results and those of Lin et al. (2011) could be caused by the difference in task position. Physiologically, jumping, which is close to cutting (both presenting a "landing mechanism"), is a self-initiated movement, whereas muscle responses induced by stretch or postural disturbance are not. Jumping, in contrast to perturbed walking, allows supraspinal centres to accurately predetermine timing of ground contact and thus the instance of muscular stretch (Taube et al., 2008). Although it is difficult to separate stretch reflex responses from pre-programmed activation already present during landings. Activation of pre-motoneural pathways may contribute, to a high extent, to muscular activity at time of SLR, MLR and in particular LLR as a voluntary component for launching take off (Gutierrez et al., 2012; Schillings et al., 2000). Taube et al. (2008) found that during LLR responses background EMG (meaning muscle activity before ground contact or perturbation) was high (Taube et al., 2008). Therefore, centrally pre-programmed spinal and supraspinal neural pathways (corticospinal, subcortical and cortical proportions), which are related to the activation of polysynaptic slower conducting afferents, could mediate LLR responses, even after touch down (Nieuwenhuijzen & Duysens, 2007; Taube et al., 2008). Connecting those facts to the outcomes found by Lin et al. (2011), it can be assumed that participants with FI did not have a deficit in the PL and GM feedback motor control during dynamic test conditions (as it was shown in the present study, however non-significantly). They might compensate their impairments by making use of LLR responses in late terminal stance phase after landing. They even suggested that FI individuals recruiting more PL muscle units to minimize the inversion angle and absorbing ground reaction force, and thus maintaining joint stability. In addition, even the TA muscle reflex-activity was found to be (non-significantly) higher in individuals with FI during side cutting in the current research. However, a major concern for side cut testing was that ground contact times accounted for an average of 321 ms (which is in line with other studies (Cowley et al., 2006; Queen et al., 2008). As EMG-amplitude for reflex-activation of ankle muscles was analyzed within a time window of 200-400 ms post IC, muscle activity was also considered for the 79 ms, at which the average of the participants already passed through terminal stance phase and lifted up their foot for swing phase. This fact might partly elucidate the controversy with other studies.

All in all, it could not be detected that patients with FI might suffer from low levels of peroneal AMI (continual altered peripheral afferences from the joint with dampened α motoneuron activation), or have significantly deficient neuromuscular activation (Palmieri-Smith et al., 2009), except for side cutting during pre-activation.

Muscle activity of ankle muscles did not differ between condition “shoe only” and condition in-shoe orthosis, regardless of ankle health status. O’Connor & Hamill et al. (2004) could support these outcomes (O’Connor & Hamill, 2004). They could not find any systematic neuromuscular responses (EMG on-off pattern) of lower limb muscles due to acute foot orthoses application during perturbed treadmill walking in healthy individuals (O’Connor & Hamill, 2004). Similar conclusions were drawn by Sefton et al. (2007) and Kernozek et al. (2008), although they regarded braces instead of orthoses (Kernozek et al., 2008; Sefton et al., 2007). The TA and PL reflex-activity (latency, H_{max}/M_{max}-ratio) was unaffected when applying ankle braces during sudden inversion perturbations in asymptomatic ankles (Kernozek et al., 2008; Sefton et al., 2007). Previously published research however identified increased PL EMG-amplitudes in different phases of gait cycle by the acute use of orthoses compared to shoe conditions (Barlow et al., 2014; Donovan et al., 2015; Ludwig et al., 2013; Murley, Landorf, et al., 2010). However, some of those studies used other ankle support such as lace-up braces or ankle destabilizing devices and measured other populations (healthy individuals with flat arched/pronated-foot type (Barlow et al., 2014; Donovan et al., 2015; Ludwig et al., 2013; Murley & Bird, 2006). Two authors explained the rise in the PL muscle activation was due to the acute application of a particular orthosis that increased the pressure at the foot sole (in the study by Ludwig et al. a lateral stimulation point was used [compared to an in-shoe “dummy insole”]; in the study by Baur et al. a medial longitudinal wedge was used [compared to different insole elements and a barefoot condition)(Baur et al., 2003; Ludwig et al., 2013). This increased pressure might have induced changes in afferent sensory information after landing and reduced inhibiting mechanisms at the spinal level, thus helping in stabilizing the position of the ankle.

One reason for the fact that muscle amplitudes did not differ between condition “shoe only” and in-shoe orthosis might be that responses to orthoses are supposed to be subject-specific (Baur et al., 2003). On one hand, a low magnitude of functional orthotic elements can evoke high maximum pressure, and thus high PL muscle activity. In other cases, a high support of functional elements might only induce moderate rise of pressure with subsequent low PL muscle activity (Baur et al., 2003). Another reason could be that participants in present study were tested more dynamically as in the aforementioned studies. It might have been too challenging for them to build up desired pressure below the ball of the foot during more complex test situations such as side cutting. Although muscle activity was not taken into account, another study observed that walking with orthoses reduced rearfoot kinematic and kinetic parameters when compared to barefoot walking (Williams, McClay Davis, & Baitch, 2003). In the present research, the orthosis condition was not compared to a barefoot condition, although this might have indicated different ankle muscle activity between both conditions. Adequate differentiation between "shoe only" and in-shoe orthosis condition, in terms of muscle activity, might have been aggravated since the neutral running shoe itself partly gave joint stability.

All in all, it can be presumed that the acute application of the specific orthosis in the present study did not sufficiently affect ankle muscle activity. The participants probably were not accustomed enough to the specific orthosis, applying the prescribed pressure during sports. Hence, an orthosis use over long-term could contribute to a relevant modified ankle muscle activity and might give further valuable insight into possible (and different) neuromuscular adaptation processes in (between) healthy individuals and those suffering from FI. Despite the fact that most of the authors stated that the modified activation of ankle musculature is contributing to improved ankle joint protection, it remains unclear whether reducing or enhancing EMG-amplitude during particular gait phases is functionally more beneficial in individuals with FI (Burke et al., 2006; Murley, Landorf, et al., 2010). It might be a matter of debate if a reduced EMG-amplitude of ankle muscles in participants with FI always implies less ankle joint stability. Although some authors associated the decrease in ankle muscle activity due to foot orthoses, with minimized muscle work and improved performance, proposing a possible benefit for patient populations (Mündermann, Nigg, Humble, & Stefanyshyn, 2003b; Nawoczenski & Ludewig, 1999; Nigg et al., 1999). In addition, it is difficult to predict the effect of increasing PL EMG activation on foot function and stability because the muscle may influence movement of hindfoot and midfoot joints simultaneously (Murley & Bird, 2006). The link between facilitated/inhibited ankle muscle activity and potentially more/less stability of the joint should be clarified in further studies to enable a proper interpretation of acute (and long-term) effects of orthotic applications, particularly for patients with FI. In regards to the progress of the present study, increased ankle muscle amplitudes will be interpreted as positive findings in sense of providing stabilization to the ankle joint.

4.3 Long-term effect of foot orthoses on ankle muscle activity in individuals with functional ankle instability (MQ 3, MQ 4, MQ 5, SQ 3a)

It was investigated if the foot orthosis intervention influences ankle muscle activity compared with sensorimotor training, and no intervention (control intervention) from pre-test (M1) to post-test (M2) (long-term effect orthosis). In this context it was assessed if there is a difference in ankle muscle activity between the orthosis intervention group and the control group (MQ 3), and between the orthosis intervention group and the sensorimotor training group (MQ 4). It was further investigated if participants with FI respond with a different ankle muscle activity to an orthosis condition after intervention phase, compared with healthy participants from M1 to M2 (long-term adaptation mechanism). In particular, it was assessed if ankle muscle activity differs between H and FI in the intervention groups from M1 to M2 (MQ 5).

Pre-activity of ankle musculature

During normal unperturbed and perturbed walking, pre-activity of the PL muscle was increased significantly by the orthoses intervention as well as by the sensorimotor training intervention, compared with the control group (reduction in peroneal EMG amplitude). This finding confirmed the expectations. Since there is limited information in literature about the effectiveness of sensorimotor training, particularly in contrast to an orthosis intervention in terms of modifying EMG amplitude of ankle muscles, the outcomes of the present research are essential and a novel finding. Evidence was given that the PL muscle must play a key role in stabilizing the ankle joint by providing neuromuscular control since the muscle has adapted to both training interventions. Studies investigating the effect of sensorimotor training programs evaluated functional outcome parameters, such as self-reported function, joint position sense or postural stability, without considering neuromuscular parameters as muscle amplitudes. Literature is also sparse concerning the neuromuscular adaptations solely due to long-term foot orthoses use. Only one relevant study is available and is in line with the outcomes of the present study work, although a different pathological population (runners with overuse injuries) was examined and no other control intervention group (as a sensorimotor intervention group) was considered. Also, significantly increased pre-activation of the PL muscle could be observed by the long-term use of an orthosis (8 weeks, use >80% of training sessions as requirement) compared to a healthy control group during walking (OG: 1.18±0.43, 95% CI=1.08-1.28; p=.003; CG: 0.97±0.32, 95% CI=0.90-1.05)(Baur et al., 2011). The authors hypothesized that the medial posting of the orthosis might have produced an increase in local pressure at the longitudinal arch and the medial midfoot area. These changes in plantar pressure were detected by cutaneous receptors, peroneal muscle spindles, and/or golgi apparatuses, modulating afferent information/input at the plantar surface of the foot transferred to the interneuron pool. Spinal and supraspinal adaptations may then evoke a change in the underlying motor program. Reductions of inhibition at the presynaptic level might lead to an increase in efferent drive to the peroneal muscle. This possible neuromuscular adaptation mechanism could be confirmed by Taube et al. (2006)(Taube et al., 2006). The authors stated that a reduction in presynaptic inhibition of I a afferences at the spinal level may have caused an increase of the H-reflex at LLR in the S muscle, however during perturbed stance (Taube et al., 2006). Baur et al. (2011) further suggests that the increased PL activation pre IC might be an expression of proper foot placement at touchdown and an improved alignment of the foot, initiated by the prolonged orthoses use. This might help in the control of stiffness regulations of the ankle joint, contributing to an improved dynamic control of ankle stability (mechanical effect). The prolonged orthoses application also led to adjustments in feedforward neuromuscular activation (neuromuscular effects), which also indicates that spinal pathways cannot only be affected by the ankle health status, yet, can also be modulated and adapted due to long-term use of an orthosis. Therewith, the increased pre-activation of the PL muscle was part of a pre-programmed muscle activation strategy, which was adjusted according to the anticipated level of external load (Baur et al., 2011). In the present study, participants trained with a PL stimulation module imbedded in the orthosis next to a medial longitudinal arch post, which should additionally evoke activation of PL musculature. Although in the study by Baur et al. (2011) no particular additional orthosis element was used, the induced sensorimotor adaptation processes could have been similar. Another possible mechanism for facilitated PL activity might be the muscle spindle fibre length, which has not been modified considerably by the prolonged application of the orthoses (Cordova & Ingersoll, 2003). Therefore, the load placed on the muscle spindles, and the threshold setting for muscle spindle activation, could have been diminished over time. As a result, large muscle spindle responses were present with subsequent facilitation in PL stretch reflex amplitude (Cordova & Ingersoll, 2003). Furthermore, the current research presented that in the orthoses group the PL muscle amplitude was increased, although intervention phase was even shorter (6 weeks) as in the study by Baur et al. (2011). Therefore, EMG-amplitude for the PL was specifically influenced by long-term orthoses use. This presented result is essential and might be clinically relevant. Additionally, related to the baseline values (significant lower EMG-A in orthoses group compared to control group (and higher compared to sensorimotor training group during unperturbed and perturbed walking), the rise in the PL muscle activity was even more pronounced in the participants who underwent the orthoses intervention compared to the sensorimotor training. For side cutting, the PL EMG-A was even reduced. It might be suspected that the orthosis group (mean duration of orthoses use: 172 min. during all day life activities and 101 min. during sport/day) underwent more training in the intervention phase than the sensorimotor training group (20-25 min/day; 22 days). However, this finding might be misleading as participants who conducted sensorimotor exercises, additionally performed other activities apart from instructed study exercises, which also could have trained neuromuscular components of the musculoskeletal system. The outcome, rather, might be linked to the fact that the orthosis group were wearing the orthosis during all sport-specific exercises during the whole intervention phase (efficient training stimuli by specific PL module). Therefore, the PL muscle activity could have been addressed to an even higher extent for those participants. Another explanation might be that participants in the sensorimotor training group barely trained medio-lateral exercises (1 exercise out of 5 contained side lunges/hopping), which are essential for training of the PL muscle. They also used a towel role as instable surface, where the ankle joint might have been more stabilized into anterior-posterior direction, which trained more selectively the TA and GM muscles.

Considering the ankle health status (H/FI), muscle pre-activation of the PL was shown to be increased to a higher extent in individuals with FI compared with healthy individuals after long-term sensorimotor training program, when tested during normal unperturbed walking. Therewith, the hypothesis could be confirmed. However, for the participants with FI, the PL and GM activation was reduced (PL: 11.9%, GM: 27.7%) when compared with healthy individuals (increase PL: 5.4%, GM: 11.7%) after 6 weeks of wearing the orthoses (contrast to sensorimotor training). The deficient feedforward pre-activation of the PL and GM might be harmful in this population, since adequate anticipatory PL neuromuscular control is required for providing ankle joint stability, specifically during more dynamic situations. This finding is difficult to interpret due to the fact that only 2 participants with FI were randomly assigned to the orthosis group. The outcomes of this small group of participants cannot be compared adequately to those of healthy participants in the orthosis group. Additionally, no conclusive statement can be made if the sensorimotor training intervention was more effective in relation to the orthosis intervention, in regards to modifying the EMG amplitude of PL in a cohort with FI. When higher number of participants with FI would have been tested, they also might have benefited by long-term orthosis use compared to the sensorimotor training. The present outcomes cannot be compared to similar studies since literature about long-term adaptation mechanisms, in sense of (enhanced) ankle muscle pre-activation by the use of orthoses or sensorimotor training protocols in a population with FI, is sparse. Although in the study by Baur et al. (2011), a different cohort of patients was investigated (runners with overuse injuries) and this population was not compared to a healthy control group, those study results indicate that subjects with FI might have also enhanced their muscular pattern of the PL in pre-activation during walking (Baur et al., 2011).

However, a desired outcome was that, during stumbling, the PL muscle activity increased more in the participants with FI (17.3% vs. 6.0% in healthy), independent of the kind of training intervention (particularly due to prolonged orthosis use). Although Palmieri Smith et al. (2009) stated that any active therapy strategies to overcome persistent AMI and to restore normal muscle function in patients with FI would be unsuccessful, a recent research group came to this controversy conclusion (Mettler et al., 2015; Palmieri-Smith et al., 2009). They argued in sense of a benefit of ankle training programs in individuals with FI which could lead to a repair of some of the damaged sensorimotor system pathways, resulting in a more optimally functioning and less constrained neuromuscular system (Mettler et al., 2015). Due to both training interventions, on the one hand centrally controlled inhibition mechanisms in individuals with FI could have been diminished. On the other hand, they could have (re-) facilitated the activation of the PL motoneurons and of voluntary, corrective LLR responses through supraspinal mechanisms (Donahue et al., 2014). Facilitation of the PL pre-activation emphasizes the relevance of anticipatory ankle muscle activation in individuals with FI before ground contact in a sport-specific situation, which is mainly unexpected and reflexive (as perturbed walking). As supraspinal pathways are presumed to be involved in neuromuscular adaptation processes, there was a change in feedforward

motor control in individuals with FI which could be interpreted as a compensatory mechanism to ensure protective dynamic ankle joint stability. Nonetheless, it can only be speculated, through which neuromuscular mechanism individuals with FI responded differently to prolonged orthosis use. Thus, the present study findings might be promising. However, they are considerably biased by the aforementioned low number of FI participants in the orthosis group.
Against the expectations, muscle activity of the TA was reduced before ground contact after both interventions during normal unperturbed and perturbed walking (considerably in orthoses group for perturbed walking [significant values]). One plausible explanation could be that, from a mechanical point of view, subjects were trained to put pressure at the medial site on the orthosis during the roll motion of the foot. Therewith, increased eversion (and plantar flexion) movement was initiated during push off. As a result, the TA muscle (as antagonistic invertor and dorsiflexor) was constantly less activated. Another reason might be that the TA worked eccentrically before IC, and it was shown in former studies that the EMG-amplitude of ankle muscles is higher during concentric work compared to eccentric work (Hirschmüller, Baur, Müller, & Mayer, 2005).

Unexpectedly, the TA and GM muscle activation decreased to a higher extent in individuals with FI compared with healthy individuals during perturbed walking by the orthosis intervention. It remains questionable for what reason the reduction in the TA and GM muscle activity, before touchdown, was higher pronounced for FI subjects. However, one plausible explanation could be that patients with FI substantially responded more to training of the PL muscle and less to the TA and GM muscle training as an adaptation strategy to avoid a more inverted and instable/insecure position of the ankle prior to landing, assisting the evertors to resist the induced inversion (Hopkins et al., 2012). In addition, higher TA and GM pre-activation for healthy participants, due to prolonged orthotic use (in contrast to sensorimotor training), might give clinical implications in terms of a preventive effect from prolonged orthoses use in asymptomatic populations.

With regard to side cutting, EMG-amplitude of the ankle was not affected significantly by the orthosis intervention program or by sensorimotor training. However, when considering ankle health status, ankle muscle pre-activity of the TA significantly increased for FI (46.0%) compared to healthy individuals (decrease by 9.0%), due to prolonged orthoses use, as well as sensorimotor training. The facilitated eccentric TA muscle activation before ground contact can be interpreted as a pre-programmed strategy to keep the ankle joint in a less plantar flexed, and subsequent more close-packed and stable position (Suda & Sacco, 2011). Hence, individuals with FI might have adopted the protective strategy of healthy individuals during side cutting. Koshino et al. (2015) demonstrated controversial findings for ankle musculature, showing ankle muscle activity did not differ between H and FI. The differences between our study findings and those of Koshino et al. might be explained by the difference in task (side-turning while walking). However, the long-term effect of any intervention on muscular activation was not investigated in that study (Koshino et al., 2015). Muscle pre- and reflex-activity of the PL and GM however was not influenced considerably by any of the intervention programs. Nevertheless, there was a tendency for decreased PL pre-activity in FI (10.0%) due to orthoses use, compared to healthy participants and the other interventions (although this has to be critically discussed because of aforementioned small sample size). Also an increased PL pre-activity in FI was found due to sensorimotor training (15.9%). The latter aspect might be explained by the fact that the healthy participants benefited more by the orthosis intervention, when tested during side cutting. It is difficult to place the present findings in perspective with other literature, due to the lack of comparable experimental studies. The results for side cutting have to be interpreted with caution as they may be associated with the complexity or difficulty of the movement task. The side cut task itself might have been sizably influenced by intra-and inter-subject movement variability, particularly between subjects, although test-retest reproducibility values for side cutting did not result in worse values compared to those for the other testing conditions. The participants tested in this study did not represent a professional athletic population (although they were physically active for at least 3x/week) which may demonstrate less variation in performance of a side cut task than recreationally trained individuals. Since the test situation contains high potential for variable motion patterns, specifically between participants, it may not be able to differentiate ankle muscle activation between an orthosis group and control group/a sensorimotor training group. Although the GM muscle did not reveal any significant values, there was a clear tendency that its pre-activation was specifically facilitated during side cutting in individuals with FI (35.6%) in contrast to healthy individuals (decrease by 7.9%) by long-term orthoses use (contrary outcome for perturbed walking). Hence, it can be assumed that the GM supported PL activity in the time period before ground contact, which was confirmed by previously referred literature. Especially during more complex anticipatory testing tasks, this might serve to increase plantar flexion to soften the impact load before ground contact, which might help to increase protective ankle joint stiffness (Feger et al., 2015; Koshino et al., 2015; Nieuwenhuijzen & Duysens, 2007). Subsequently, the GM muscle might play a crucial role in patients with FI in aligning the position of the center of gravity prior (and upon) IC more medially, which could be altered by a less everted position of the ankle joint in individuals with FI (Delahunt et al., 2007). This mechanism is beneficial for FI as it could serve to stabilize the ankle joint, specifically in case of deficient PL activity. Nevertheless, it remains questionable, for what reason the GM activity was facilitated as a result from prolonged orthosis use, but was substantially inhibited by sensorimotor training program in individuals with FI (by 32.9%).

Per-protocol analysis additionally detected that, independent of ankle status, all the participants who completed the sensorimotor training program, also showed a remarkably increased muscle activation of the GM muscle as a plantar flexor (significant values), while performing the side cutting manoeuvre. This finding might be linked to the efficiency of the calf rise exercise (weight-loaded in progress of the program), which was part of the sensorimotor training program.

Reflex-activity of ankle musculature

When participants were tested during normal unperturbed walking, they did show a significant rise in EMG-amplitude of the TA and PL in both intervention groups. Thereby, the hypothesis was supported. In addition, it has to be questioned if those marginal increases in peroneal amplitude (TA: orthoses group: 1.2%, sensorimotor training group: 2.3%; PL: orthoses group: 1.6%, sensorimotor training group: 1.2%), when related to the baseline values (significantly higher EMG-A for SMTG than for OG and CG for TA; higher EMG-A for CG than for OG and SMTG for PL), were clinically relevant. In a clinical context, the question remains open as how much of a muscular activation pattern is protective enough for the ankle joint. Previous research could demonstrate limited to moderate evidence that balance training programs (Biodex stability program, wobble boards, 4 weeks, 10-12 min. per session) led to significant reductions in the TA and PL onset latencies after sudden inversion perturbations (Akhbari et al., 2007; Clark & Burden, 2005; O'Driscoll & Delahunt, 2011). The observed decrease in latency could signify that the muscles are intrinsically stiffer which enhances muscle spindle activation via feedforward neuromuscular control, resulting in a decreased time to initiation of a reflex response (Clark & Burden, 2005). With regard to orthotic interventions, to the best of our knowledge, only one (previously mentioned) study investigated the long-term effect of an orthosis (Baur et al., 2011). In contrast to the outcomes in the present research (although they were not significant), Baur et al. (2011) found that muscle activity of the PL did not differ between the orthosis and a control group after long-term orthotic intervention, when considering stance phase of running. Both groups showed the same activity level of the PL in weight acceptance (p=.24) and push off (p=.84)(Baur et al., 2011). Baur et al. (2011) additionally stated that the running movement might not elicit selective responses (SLR, MLR, LLR) of PL muscle to be differentiated. There exists other experimental work, which evaluated the effectiveness of the acute application of orthoses. Nonetheless, there is doubt about the transferability of short-term sensorimotor adaptation processes of foot orthoses to the effects that orthoses could have over longer periods of wearing, as different neuromotor adaptation mechanisms may play a role during customization process to orthoses. Ludwig et al. (2013) could confirm an increased activity of the PL muscle during mid-stance phase of walking due to the acute application of sensorimotor foot orthoses with imbedded pressure stimulation points at the lateral edge in healthy subjects (Ludwig et al., 2013). According to the authors, the increased peroneal EMG-amplitude was evoked by areas that imposed pressure on the tendon of the PL, thereby inducing changes in afferent information when body weight is transferred to the foot. The observed muscle response of the PL was interpreted as a stretch reflex, induced by the excitation of peroneal muscle spindle receptors. Additionally, through the reduction of inhibiting mechanisms at the spinal level, the pressure areas contributed to stabilization of the ankle position (Ludwig et al., 2013). A similar pressure stimulus, however in the sense of a PL module at the medial site which more actively should evoke activation of the PL musculature, was used in the present study work. Therefore, the ankle muscle response in the current research was expected to be higher pronounced than it actually was. Another previously mentioned study also argued for an increase in the PL activity due to increased pressure/higher loads in the area of functional elements (medial site) of the orthoses with longitudinal wedges. The pressure was acutely applied during stance phase of walking in healthy runners (Baur et al., 2003). They explained the findings by describing the same sensorimotor mechanism as Ludwig et al. (2013), however they did not find any shifting of pressure load beyond the first metatarsus or big toe (Baur et al., 2003). Nevertheless, the potential sensorimotor processes, described by Ludwig et al. (2013) and Baur et al. (2003) might be partly comparable to those of the present research. An additional study group identified a significant rise in the PL and TA maximum EMG amplitude in healthy subjects after an acute use of inverted orthoses (compared to barefoot condition) (Murley & Bird, 2006). The same researchers also detected that in participants with flat arched feet the PL EMG-amplitude increased during mid-stance/propulsive phase due to the acute wearing of a prefabricated orthosis (Murley, Landorf, et al., 2010). The authors stated that those outcomes were mostly attributed to the contact of the orthoses to the talonavicular arch region of the foot. As the PL muscle has its insertion at the base of the first metatarsus and the medial cuneiform, the contraction during mid-stance may contribute to first ray plantarflexion. Subsequently, dorsiflexion movement at the first metatarsophalangeal joint may help facilitate the windlass mechanism during propulsion and assist sagittal plane motion of the foot during walking (Murley, Landorf, et al., 2010). All the aforementioned studies had one trait in common, that through the contact of the particular orthotic component the PL muscle activity was supported/ facilitated, providing adequate ankle joint stability. Mündermann et al. (2006) however provided a controversial explanatory approach (Mündermann et al., 2006). They stated that orthoses may act as disturbances to the musculoskeletal system. The authors speculated that if an orthotic intervention supports the preferred movement path of a joint, muscle activation will be reduced. On the other hand, if an orthotic intervention (a perceived unstable position) counteracts the preferred movement path, muscle activation will be increased to stabilize the subtalar joint and maintain the preferred movement path (Mündermann et al., 2006). Thus, the increased PL activation can be interpreted as a compensatory pattern to provide ankle joint stability. It can be assumed that in the present study work the PL muscle was rather supported since the specific foot orthosis used did not possess any destabilizing element.

As expected, with regard to ankle health status, individuals suffering from FI benefited to a higher extent from both long-term training interventions compared to healthy individuals in terms of an increased PL reflex-response (orthoses intervention: FI: 13.5%, H: 0.3%) as well as an increased GM activity when tested during unperturbed walking. Individuals with FI benefited even more by 6 weeks of prolonged orthosis use (healthy participants more by sensorimotor training). Individuals with FI also benefited to a higher extent by sensorimotor training, showing an increased GM activation (4.2%) compared to healthy subjects (reduction by 4.5%). The fact that PL activity may have adapted to the prolonged performance of sensorimotor training and particularly by orthoses use, indicates its capability of providing adequate ankle joint stability at ground contact during walking. The facilitated PL muscle response during unperturbed walking in individuals with FI highlights the fact that the PL is also capable of providing essential ankle joint stability and protection during later gait phase (terminal mid-stance phase), a time at which body weight is transferred over the (fore-) foot. This positive adaptation (feedback mechanism) mechanism due to the orthotic long-term use offers the potential that facilitated PL reflex-activity can also be transferred to more harmful and sport-specific test conditions as stumbling or cutting, at which the ankle joint might be more vulnerable to injury. In these situations, the PL reflex responses are crucial to avoid potential ankle joint injury.

Moreover, the TA activation was facilitated more in individuals suffering from FI in contrast to healthy individuals after the sensorimotor training program compared to the orthoses intervention (13.3%; contrary outcomes for orthosis use). This result could be explained by the fact that the FI group benefited to a higher extent due to the positive adaptation from doing the specific exercises, reflecting biomechanical function of the TA muscle (towel role requiring anterior-[posterior] directed neuromuscular control). Literature is rare showing positive effects on ankle muscle activation due to either sensorimotor training or orthoses use in a group of patients with FI compared to asymptomatic individuals. Lee et al. (2013) could not demonstrate any long-term effects due to orthoses, however stated that an orthotic use might lead to an increase in afferent signals delivered to the mechanoreceptors of the ankle in subjects with FI (Lee et al., 2013). Training may have repaired some of the damaged sensorimotor pathways, resulting in an optimal functioning and less constrained neuromuscular system, thereby contributing to improved ankle joint stability (Lee et al., 2013). Although muscle latencies were considered, no effects for muscle amplitude due to a long-term intervention program were evaluated, and no healthy control cohort was analyzed. Concerning the effect of sensorimotor motor training programs, the outcome of the present research is in line with previously mentioned study results (Akhbari et al., 2007; Clark & Burden, 2005; Eils & Rosenbaum, 2001). It could be demonstrated that the PL reaction/onset times improved to sudden ankle inversions in subjects with FI after conduction of proprioceptive and postural control exercise programs (e.g. instable platforms [Biodex, Posturomed], uneven walkway; 20 min. per session, level increased every 2 weeks of 6 weeks in the study by Eils & Rosenbaum et al, 2001) (Akhbari et al., 2007; Clark & Burden, 2005; Eils & Rosenbaum, 2001). Individuals with FI presented facilitated PL activity in contrast to healthy individuals, which might describe one strategy of neuromuscular response to very specific training stimulation (Eils & Rosenbaum, 2001). However, more detailed explanatory approaches were not given by the authors. As it was supported by Clark & Burden et al. (2005) for healthy individuals, Lee and colleagues (2008) stated that enhancements in postural stability due to training of postural control in FI individuals, might signify that their ankle muscles got intrinsically stiffer, which increased muscle spindle activation via neuromuscular control (Lee & Lin, 2008). This might reflect an improved neuromuscular ability along with increased functional joint stability (Lee & Lin, 2008). However, they only considered postural control as one isolated component of sensorimotor training and did not measure ankle muscle activity. Bellew et al. (2010) affirmed that training of the PL may be used to increase the sensitivity of proprioceptive afferent input response, although long-term effects of sensorimotor training in a population with FI were not investigated in that study (Bellew et al., 2010). Subsequently, there is limited knowledge in literature about the specific responsible mechanism for (improved) ankle muscle responses in individuals with FI after ground contact while walking.

Against the hypothesis, reflexive muscle activity of the TA and PL unexpectedly decreased following both interventions, compared to no intervention (specifically in orthosis group for TA EMG-amplitude [significant values]) during perturbed walking. The ankle “stirrups” TA and PL are playing key roles in protecting the ankle joint complex against unexpected destabilization (McVey et al., 2005). Ankle invertor/evertor coupling during movement facilitates a neutral position of the joint, aids in balance and controls loading during the stance phase (Hopkins et al., 2012). The results of the current study are conflicting to those found by other research groups (Cordova, Cardona, Ingersoll, & Sandrey, 2000; Midgley et al., 2007). Midgley et al. (2007) as well as Cordova et al. (2000) demonstrated that the use of an external ankle support (tapes and braces), over an entire season (3-5 months), does not induce neuromuscular changes in the onset timing of the PL (EMD, reaction time) when tested during inversion perturbations (Cordova et al., 2000; Midgley et al., 2007). Ankle supports did not evoke neuromuscular changes within the PL muscles; neither facilitation nor inhibition of PL stretch reflex could be shown. Neuromotor adaptation processes induced by the extended use of external ankle braces (stimulation of cutaneous mechanoreceptors around the ankle) might be similar to those initiated by in-shoe foot orthoses, however the load placed on muscle spindles might have been different over the long-term between those two conditions (Cordova & Ingersoll, 2003; Cordova et al., 2000). Therefore, transferability of the outcomes might be doubted. Concerning the TA activation, it was expected that this muscle was rather facilitated by stretch reflexes due to previously mentioned nature of treadmill belt motion (anterior directed/decelerating). It can be speculated that the TA activity was more diminished by prolonged orthoses use and those of the PL muscle was more inhibited by sensorimotor training, because of aforementioned reasons (higher training stimuli/input for PL muscle in orthosis group; lack of medio-lateral exercises as stimuli for PL in sensorimotor training group).

Concerning side cutting as a test condition, EMG-amplitude was not considerably influenced. This was due to the intervention programs (non-significant reduction of EMG-A in all muscles by orthosis intervention, rise in TA and PL EMG-A by sensorimotor training). As the same result could be observed for ankle muscle pre-activation, the suspicion may have been substantiated that the side cut task itself was affected by movement variability within and particularly between participants. However, the fact that the sensorimotor training intervention induced a slight increase in muscle activity, in contrast to the orthotic intervention, could be due to the complexity of the sensorimotor training exercises which adequately reflected the dynamic characteristics of a side cut task. In addition, there was a tendency for an inhibited GM muscle reflex-activity in individuals with FI due to long-term orthoses use, and for healthy individuals due to sensorimotor training during perturbed walking and cutting. The reason for those findings remains open, however can be understood as a potential negative adaptation mechanism, as the GM activity plays a leading role for time phase of propulsion/push off. Its function might not be important for dynamic ankle joint stabilization following training interventions.

For perturbed walking and side cutting, ankle muscle responses did not differ significantly between individuals with FI and healthy individuals in both interventions. Nevertheless, there was a tendency for higher reduction in muscle response amplitudes of the TA, PL and GM in individuals with FI due to the orthosis intervention, compared to healthy individuals, during side cutting (GM for SC: FI: 45.9% vs. H: 13.4%). In addition, the PL and GM activity was reduced for FI within the orthosis group (PL: 20.5%, GM: 9.3%) during perturbed walking, in contrast to healthy individuals (PL: 2.0%, GM: 5.8%). It remains unknown why in subjects with FI, partaking in long-term use of the particular orthosis, inhibition mechanisms of all studied ankle muscles were evoked. This was found to be true after ground contact during more dynamic test conditions. These facilitated ankle muscle reflex responses might be a protective mechanism during sport-specific situations, such as unexpected foot displacements (e.g. body check). Again, there are objective reasons to doubt if the findings for FI in the orthosis group can be evaluated as clinically relevant due to previously mentioned low number of participants. In addition, there was also a clear tendency for increased PL and GM muscle response in FI participants (PW: 15.7%, SC: 21.9%), compared to healthy individuals (decrease by 14.9% [PW]; 11.9% [SC]) in the sensorimotor training group, when participants were measured during perturbed walking (PL) and side cutting (PL, GM). TA reflex-activation was facilitated in individuals with FI by sensorimotor training in contrast to long-term orthoses use. With those outcomes it could be proven that the use of active exercise to restore normal muscle function will likely prove effective. However, the GM activity was inhibited (by 27.0%) in FI individuals by sensorimotor training intervention during stumbling. There is lack of comparable research, as most of available studies measured/trained ankle muscle responses during more static tasks (e.g. balance exercises on wobble boards).

Per-protocol analysis reported that, independent of ankle status, the participants who underwent the orthoses intervention, showed substantially reduced GM activity in terminal mid-stance phase during side cutting. As mentioned earlier, ground contact times of some of the participants were shorter than the chosen time window of analysis for reflex responses. Thus, the leg might have already been in early swing phase during testing, which could partly explain and have biased the existing outcomes. A promising finding was that, regardless of ankle muscle, test condition, and ankle health status, effects of the orthosis intervention were higher pronounced across most of the conditions (specifically for PL and TA muscle) compared to sensorimotor training program.

It was further investigated if participants in the orthosis intervention group demonstrate (even) higher ankle muscle activity by the additional short-term application of a measurement in-shoe orthosis after intervention phase at M2 (=”transmission effect”, meaning the effect of an increased ankle muscle activity got intensified by short-term orthosis use; the same stimulus is given as in training intervention). Thus, it was assessed if ankle muscle activity differs between a “shoe only” and an in-shoe orthosis condition in the orthosis group (compared to control group) at M2.

Pre-activity of ankle musculature

Positive effects of increased ankle muscle activity after intervention phase in orthosis group were present for the GM activity during normal unperturbed walking. This was also true for the PL and GM activity during perturbed walking and particularly for side cutting (PL [GM]: 13.4% [11.8%] higher EMG-A for orthosis compared with shoe condition) at M2, when wearing an in-shoe orthosis over the short-term. However, those amplitudes were not substantially different between “shoe only” and in-shoe orthosis condition at re-test (non-significant values). Therefore, the increased EMG amplitudes during unperturbed walking (GM: 0.1%) and perturbed walking (PL: 1.5%, GM: 0.9%) for the orthosis group cannot be interpreted as a “transmission effect”, since test-retest variability was high and ICC revealed poor to moderate values for the PL and GM pre-activation. Nevertheless, the increased PL and GM EMG amplitudes during side cutting can be evaluated as a “transmission effect”, which partly confirms the hypothesis. Therewith, positive neuromuscular adaptation mechanisms, due to the long-term orthotic intervention phase, could be transferred into highly dynamic situations where ankle stabilization is required. It also gave evidence for an adequate response of the PL and GM muscle to the stimulation module of the orthosis.

Facilitated PL and GM activity before ground contact, by the short-term in-shoe orthosis use during dynamic and potentially vulnerable test situations for the ankle joint (perturbed walking and side cutting), supports the assumption of protective feedforward mechanisms by the ankle joint stabilizing muscles. As aforementioned, facilitated GM activity by the short-term in-shoe orthotic use also substantiates the fact that the GM serves to increase plantar flexion to soften the impact load before touch down. In contrast, in a less dynamic movement task such as unperturbed walking, neuromuscular adaptations in terms of increased PL activity due to prolonged orthosis use already could be shown with the short-term "shoe only" condition at re-test, and were not enhanced by the short-term in-shoe orthosis use. The question arises, for what reason does the effect of increased PL amplitude in the orthosis group, during unperturbed walking, exists when wearing the "shoe only" at testing, yet disappears when wearing the in-shoe orthosis? This outcome was surprising due to the fact that EMG-amplitude did not differ between short-term use of a "shoe only" or an in-shoe orthosis during testing, and that specifically the PL muscle was trained by the orthosis use. The acute short-term application of an in-shoe orthosis could have evoked inhibiting mechanisms for the PL in pre-activation in orthosis intervention group. It might also be assumed that the orthosis itself had a medio-lateral stabilizing effect during the dynamic test situation, which subsequently put less demands on PL muscle activity, with regard to anticipatory feedforward joint control.

Reflex-activity of ankle musculature

The hypothesis that the effects of increased ankle muscle reflex-activity after orthosis intervention were transferred at M2, when wearing an additional measurement in-shoe orthosis over short-term ("transmission effect"), could not be supported. Muscle reflex-activity was not remarkably different between "shoe only" and in-shoe orthosis condition at re-test (non-significant values). The small differences between "shoe only" and in-shoe orthosis condition for the TA and PL activity during unperturbed walking (TA [PL]: 0.1% [2.5%] higher EMG-A for in-shoe orthoses compared with "shoe only" condition) cannot be interpreted as a "transmission effect", due to the fact that also test-retest variability was high for the TA and PL reflex-activity. Nevertheless, those outcomes proved to be a potential neuromuscular adaptation mechanism in the sense of a facilitated TA and PL activity after ground contact (induced by prolonged orthosis use) and an appropriate peroneal response to the orthotic stimulation module. Facilitated TA and PL reflex-activity by the short-term in-shoe orthosis use during unperturbed walking confirms the assumption of appropriate feedback mechanisms by ankle joint stabilizing muscles. To the contrary, long-term adaptation mechanisms in terms of facilitated GM reflex-activity, due to the prolonged orthosis use, were already presented by the short-term “shoe only” condition during perturbed walking at re-test and were not enhanced by the short-term in-shoe orthosis use. It remains questionable, for what reason the increased GM amplitude in the orthosis group, by wearing “shoe only” at re-test, disappeared when wearing the in-shoe orthosis. This

outcome might be explained by the initiation of inhibitory mechanism in the GM by short-term use of the orthosis during dynamic measurement situations like stumbling on treadmill. Again, it might be supposed that during more dynamic test conditions, the orthosis provided ankle joint stabilization, which required less reflex-activation by the GM muscle.

Strengths and Limitations

Substantial strengths of the present thesis are that it was conducted as a randomized controlled trial (intervention study with longitudinal study design and identical measurement protocols on 2 different days, separated by 6 weeks) and was performed in compliance with the EC-GCP Note for Guidance and the CONSORT guidelines. The fact that a healthy control group was considered, and sport-specific test situations which adequately reflected the injury mechanism of a sprain, were used, also strengthens the thesis. Moreover, data analysis focused on a specific EMG outcome variable (amplitude), which was appropriately evaluated in a gait cycle during relevant time windows. As in a clinical setting, the area of FI has become of great interest in the last years. To date, no other studies have offered evidence-based data on the effectiveness of a specific foot orthosis intervention compared with sensorimotor ankle joint training during perturbed walking on a treadmill and side cutting in healthy individuals and those with FI. The multivariate approach, to treat patients with FI by prolonged orthoses use as a treatment option, was a completely new and innovative scientific concept. Thus, this thesis gives a representative exposition about the benefit of a long-term foot orthoses intervention next to sensorimotor training on dynamic ankle muscle activation in individuals suffering from FI. The presented outcomes offer relevant findings to the literature, essentially contributing to existent evidence, and help guide future decision-making about most optimal treatment strategies in populations suffering from FI. They provide valuable indications for the development and advancement of appropriate future rehabilitation programs in this cohort of patients.

Participants

A key limitation, which considerably affected the outcomes, was the small sample size in some of the subgroups (test retest study: 10 healthy and 9 FI participants; main study: 2 FI participants in orthosis group). However, randomisation determined the assignment of participants to the groups. For the test-retest study, the sample size is within the norm for biomechanical studies of this type (Hopkins et al., 2012; Keles, Sekir, Gur, & Akova, 2014; Levin et al., 2015). The isolated long-term effects of foot orthoses in a population with FI have to be validated in a larger sample size with longer follow-up periods to substantiate the generalizability of the existing outcomes. Another point, that has to be discussed critically, is the determined categorization of the study participants. It might be a matter of debate if the differentiation due to score of the CAIT questionnaire might have been clearly discriminated between healthy individuals and those with FI. Some of the healthy participants were relatively close to the cut-off point for FI (≤27 points) (Hiller et al., 2006). Due to more recent guidelines by Gribble et al. (2013), the classification of participants based on the CAIT score was performed more strict (CAIT <24 points for FI), which subsequently might have led to different study findings (Gribble et al., 2013). Scoring due to FAAM questionnaire can be doubted, as all of the participants with FI showed values above 80% (<80% cut-off value for FI), which categorized them into a healthy group. Although its validity has been proven, it seems as if FAAM questionnaire does not perform as an appropriate discriminative tool (Nauck & Lohrer, 2011). However, it presents a main concern in literature that a universally approved definition of FAI does not exist, and that criteria for classification of participants are varying. Another crucial limiting factor was the grouping criteria of the ankles, since some of the participants were part of both, healthy and FI group. A practical rationale for the categorization was to increase the number of ankle joints for both groups (sample size), as it decrease the variability in the data and therewith also increase the statistical power. Thereby the likelihood of finding differences between groups before and after interventions was increased (Menz, 2004). However, some of the individuals with FI may experience bilateral balance deficits in the presence of unilateral ankle instability (Santos & Liu, 2008). Joint injury often affects contralateral ankle health, which might adapt to compensate for the unstable ankle. A recent study revealed that contralateral ankle muscles increased pre-activity during landing after perturbations in individuals with FI, as a strategy to smoothen the impact on the affected side (Levin et al., 2015). Another current study could demonstrate bilateral improvements in lower extremity function (e.g. Foot and Ankle Disability Index) after unilateral balance training in individuals with FI (Hale, Fergus, Axmacher, & Kiser, 2014). According to the authors, this supports the existence of centrally mediated mechanisms in development of postural-control deficits after injury and improved postural control after rehabilitation. It is likely that some of the significant differences in present research might be affected by type I errors, produced by artificially inflating the sample size (Menz, 2004). The degree of association between left and right foot in the same subject could be greater than the association between different subjects (Menz, 2004). Thus, it is difficult to determine what the results mean for the patient as a whole. For future investigations it may be more appropriate to consider the individual person rather than the feet, independent from each other (e.g. by including patients with bilateral instable ankle joints as one group and those with bilateral stable ankle joints as controls and for each group select one single ankle for the analysis [randomly, dominant or "worst" foot], and excluding patients with a stable ankle joint on one side and an instable ankle joint on the other side). Moreover, the foot posture should be regarded as potential influencing factor of ankle muscle activity when investigating the effect of foot orthoses. It can be assumed that patients with FI are more laterally unstable (e.g. lateral shifted COP) and therefore, requiring more compensatory PL activity. Further, it must be taken into account that neuromuscular responses to orthoses were highly variable within and particular between participants. Subject-specific muscle responses were due to varying compensational mechanisms. Therefore, individual muscle responses to orthoses might have affected the results in a meaningful way. Caution should be taken when generalizing existing results to other clinical populations suffering from FI. Future studies should also consider heterogeneous impairments in individuals with FI (evertor torque, postural control, proprioception) to more adequately target individualized treatment concepts. Further, it is still unknown whether differences in muscle activation (increase/decrease) are beneficial or detrimental in terms of susceptibility to ankle joint injury. It might be indicated that an intervention would be beneficial if it can bring muscle activity closer to that of a non-pathological population. Accordingly, it is difficult to make conclusions about the effect of altered muscle function by the orthosis use on clinical relevant conditions.

Test Situation

A confounding factor that influenced ankle muscle activity, during stumbling on a treadmill, was the presence of anticipation/awareness of perturbations. Although perturbations were randomized throughout the test, participants had to expect one at any time throughout the protocol. Despite the fact that perturbed walking on treadmill is mainly reflexive in nature, awareness of the possibility of perturbations to balance might drastically alter muscle activity firing patterns around foot landing, as an attempt to unconsciously provide a more cautious gait pattern (Gutierrez et al., 2012; Nieuwenhuijzen & Duysens, 2007). This anticipation on its own might also increase the movement variability between each stride.

Ankle injuries typically happen unexpectedly, thus monitoring participants during artificial stumbling, when they know a perturbation may happen, might not truly represent their neuromuscular control patterns before or during an actual incident of injury (Gutierrez et al., 2012). However, due to ethical reasons, the stumbling stimuli within the present study work had to be applied within a safe range (3.6 km/h velocity of walking, security harness). The reflexive muscle activity following the first perturbation stimulus is always the most meaningful, since it is a more unexpected one, compared to those of subsequent perturbations. This event is called the “first trial-(response)-effect” (Grüneberg et al., 2003). In this context, the “startle like response” represents the reduction of amplitude responses with repetition of further perturbations as habituation or learning effect (Jackson, Gutierrez, & Kaminski, 2009). To avoid anticipation and habituation effects, the amplitude response to the first applied perturbation should be exclusively evaluated. Future studies should incorporate 2 isolated protocols one after the other, where the first protocol serves to let subjects walk a designated time without any perturbation, so they would not be anticipating the future stumble. In a second protocol, the future perturbations would then be randomly applied. Another adequate way of dealing with/eliminating anticipation could be to subtract expected trials of “dummy” inversion perturbations (randomly applied perturbations/”dummy” perturbations) from control trials (non-expected “dummy” inversion perturbations; “dummy perturbations” applied only)(Grüneberg et al., 2003). Any difference between the two sets of data had the possibility of being influenced by the anticipation of the potential inversion.

Another critical point might be the question if the bilateral perturbation stimulus appropriately represented a fall outside of the laboratory environment. A general concern with lab-based assessments of movements in sport has been the extent to which they accurately reflect the sport environment (McLean et al., 2004). Perturbed walking represents a dynamic situation that is more close to a sport-specific task when compared to e.g. stumbling while standing (Nieuwenhuijzen & Duysens, 2007). Although perturbations were artificially arranged, they closely approximated the natural disturbances occurring in everyday life or during a sport event, when compared to conventional electrical stimuli used to elicit reflex responses during walking (Nieuwenhuijzen et al., 2002). The perturbation stimuli in the present study were unexpected and reflexive in nature, although affected by anticipatory mechanisms. Therefore, applied perturbations might have reflected the sudden injury mechanism of a real sprain event adequately, since they placed stress on lateral ligaments (Docherty et al., 2005). The used perturbation stimulus did not optimally target the medio-lateral sprain direction, as no specific inversion moment was evoked due to anterior-posterior directed belt motion. However, split-belt treadmills have the advantage of transferring an everyday situation into a laboratory setting, where movement execution can be effectively controlled. It offers the potential of simulating unexpected stumbling in highly standardized conditions (Nieuwenhuijzen et al., 2002). The test setup used in the current research was supported by Nishikawa et al. (2002), since the simulation of ankle complex motions associated with inversion injury does not necessarily elicit PL stretch reflexes that are of greater physiological or clinical relevance (Nishikawa et al., 2002). They stated that a dorsiflexion motion stimulus (e.g. lengthening of PL) is adequate to elicit PL stretch reflexes (Nishikawa et al., 2002). Despite those comments, future studies should take test conditions into consideration, which even more appropriately provoke the injury mechanism of a sprain to additionally gain more information about pre-activity of ankle muscles. An appropriate test condition might be a sudden inversion initiated by a trapdoor mechanism while participants are on a walkway or treadmill (Hopkins et al., 2007; Palmieri-Smith et al., 2009). The side cut task in the present study closely reflected an adequate ball-sport-specific situation. As it primarily represents an evasive manoeuvre, future research should also incorporate a defensive opponent or a ball (McLean et al., 2004).

Study Interventions

Another limiting factor in the present study work was the issue of participant compliance, which is a major concern in intervention/longitudinal studies. 4 of 10 (4 of 14) participants in the orthosis group (sensorimotor training group) did not correctly follow the prescribed guidelines, and thus were considered for per-protocol analysis. A factor which might have decreased compliance is the “home-based”/unsupervised nature of intervention programs. Although participants were called/mailed every 2 weeks to remind them of the training exercises/orthotic use, it would have been more efficient if participants were guided more extensively by sport-therapists in a controlled environment. In further studies the participants should be monitored continuously during exercising/wearing the orthosis, however obviously it is difficult to supervise participants in all day life when wearing the orthosis. Separate practice sessions for the orthotic use (learn to deal with PL stimulation

module) would help to habituate individuals to the orthotic use. Therewith, a desired adaptation process to the specific orthosis and also the adherence to the intervention phase could have been supported in a more efficient way. A further critical point could be that it is unknown which of the functional elements of the specific foot orthosis used induced the existing results in ankle muscle activation. It is hardly possible to identify if the PL stimulation module was the primarily responsible component of the orthosis in initiating the particular muscle responses or whether there were other responsible elements, such as the medial longitudinal wedge. Each kind of orthosis possesses conventional, or more particular elements with predetermined functions, but it was beyond the scope of this research to selectively evaluate effects due to one single orthotic component. Another bias might be that level of subjective comfort was not queried during testing. Comfort is an important and relevant feature of foot orthoses and may be related to subjective perceived fit (Mündermann et al., 2003b). Particularly for those participants who did not undergo the orthoses intervention, any kind of irritation or discomfort felt by acute orthosis use during testing might have caused them to modify the gait pattern (Murley, Landorf, et al., 2010). Subsequently, EMG-response might have been affected (e.g. pain due to discomfort caused inhibition mechanisms). Nonetheless, it is unclear what level of comfort is biomechanically or clinically significant (Murley, Landorf, et al., 2010). However, level of comfort has been rated by participants in the orthosis protocol during the intervention phase (perceived rating scale from 1 to 5 [max. comfortable: 1; max uncomfortable; 5]). It seems that comfort did not substantially influence muscle activity in the orthosis group, as the average rating was 1.9 on the scale throughout the intervention phase. Average rating even improved continuously week by week (1.-6.week: 2.5; 2.05; 1.95; 1.64; 1.6; 1.6). Nevertheless,
subjects needed time to adapt to the orthosis, which was indicated by stated complaints (n=6 of 10) in week 1 (knee pain, pain at ball of big toe, discomfort medial arch), which however disappeared for 4 of those subjects in week 2.

Data Analysis

It is essential that all of the data have to be considered in the high range for test-retest reliability values across all the conditions (high TRV, poor ICCs and systematic errors for some of the variables). It can be estimated that a difference in muscle activity below about 10% between the intervention groups (maximal difference about 30%) is not clinically relevant. Additionally, for some of the data a normal distribution, and (generally) homogeneity of variances, was not given. However, there exists empirical evidence at least for robustness of the ANOVA concerning violation of the normality assumption (Schmider, Ziegler, Danay, Beyer, & Bühner, 2010). Weighting advantages and disadvantages of possible adequate statistical approaches to deal with non-homogeneity of variances did not eventually result in an adequate applicable attempt at a solution for the present data. Further, it can be critically questioned whether Bonferroni is an appropriate post-hoc test when applied for non-parametric data. A major concern of assessing data for side cutting was that ground contact times accounted for an average of 321 ms. As reflex-activity was analyzed within time window of 200-400 ms post IC, muscle activity was also considered for a time phase (79 ms), which was not relevant, since the participants already left the force plate. Given the complexity of muscle activation over the entire stance phase of gait, it may be also important to incorporate the assessment of small components of the stance phase into future studies. Subsequently, a selective observation of single time intervals of reflex responses (SLR, MLR and LLR) might appropriately distinguish between spinal and cortical pathways of the neuromuscular response. Moreover, analysis of muscle activity in a temporal analysis (e.g. latency) was not performed; however this might be worth to gain additional knowledge about sensorimotor deficits in patients with FI. Further studies should take comprehensive approaches into account by including kinetic, kinematic and muscle activity variables to draw more distinct conclusions about changes in neuromuscular control associated with FI.

CHAPTER V: SUMMARY AND CONCLUSION

The pathology “functional ankle instability” (FI) is one of the most common disabilities to the lateral ligament complex of the ankle joint in competitive sports. It is a relevant clinical syndrome that may develop after suffering from recurrent episodes of lateral ankle sprains (recurrence rate: 30-80% of patients; residual symptoms [pain; swelling; subjective feeling of joint instability]: 55-72% of patients). During dynamic activities, ankle joint stability is provided by passive structures and by muscle activations of voluntary and reflexive nature (mainly M. peroneus longus [PL] next to M. tibialis anterior (TA] and M. gastrocnemius medialis [GM]). Proper functioning of both, the open-loop (feedforward/pre-activity) and closed-loop (feedback/reflex-activity) neuromuscular control systems is crucial for maintenance of dynamic ankle joint stability. FI is characterized by a diminished feedback- as well as feedforward motor control which may result in a reduced protection against inversion sprains. A majority of studies presented ankle muscle activity deficits (especially of PL) in individuals with FI before and after initial heel contact (IC) during walking on treadmills, jumping and inversion perturbations. Most often, this could be revealed by reduced amplitude in the electromyographic (EMG) signal. The neuromuscular deficits in patients with FI can be improved by several therapy means, as sensorimotor training (gold standard) or foot orthoses. The application of foot orthoses as passive therapy strategy was shown to be effective in the treatment of lower limb overuse injuries. However, there exists lack of knowledge for the acute- and long-term sensorimotor effectiveness of foot orthoses in terms of affecting ankle muscle activity in individuals with FI. The specific effect mechanism of orthoses with the exact neuromotor control modification and subsequent muscular response is not clarified in detail. Some studies have presented an increase in EMG activity during dynamic test situations after acute- and long-term use of foot orthotics, but other kind of populations than FI was tested (healthy individuals, those with lower limb overuse injuries or flat foot arch). However, the influence of foot orthoses use on sensorimotor adaptation mechanisms of ankle musculature (pre- and reflex-activity) compared to sensorimotor training is not finally investigated; especially not over long-term and in patients with FI. Further, the effects of dynamic constraints in stabilizing the ankle joint are less clear. Functional, sport-specific situations as cutting or simulated stumbling can provoke the ankle sprain mechanism by placing stress on lateral ligaments, requiring adequate neuromuscular control of ankle muscles.

Therefore, the aim of present research was to evaluate 1a) acute- and (1b) long-term effect of a specific foot orthosis intervention, compared with sensorimotor training, on ankle muscle activity in individuals with FI and healthy controls. (2) Further, it was investigated if an orthosis intervention group demonstrate higher ankle muscle activity by additional short-term use of a measurement in-shoe orthosis (compared to short-term use of "shoe only") during re-test after intervention ("transmission-effect"). (3) As prerequisite, it was verified if ankle muscle activity can be tested reliably and (4) if this differs between healthy individuals and those with FI.

N=49 participants (18-35 yrs; 3x/week physically active; 23 males, 26 females) with healthy ankles, functionally instable ankles or both (one side healthy, the other functionally instable) were included. Following, separate ankles, independent from side, were categorized into 2 groups- a healthy ankle group (H) and a group with FI ankles (FI). Inclusion criteria for H were a frequency of no sprains in the past, a cut-off score of ≥28 points on the sport-subscale of the "Cumberland Ankle Instability Tool" (CAIT) questionnaire and ≥80% on the "Foot and Ankle Ability Measure" (FAAM) questionnaire. Criteria for FI were a frequency of at least 2 sprains at least 4 weeks ago and one of two cut-off scores (CAIT score ≤27 points, FAAM sport-subscale score <80%). Healthy participants and those with FI were randomly allocated to one of the three intervention groups (orthosis group [OG]: n=17; n=16 healthy ankles, n=2 FI ankles, sensorimotor training group [SMTG]: n=17; n=13 healthy ankles, n=9 FI ankles, control group [CG]: n=15; n=12 healthy ankles, n=11 FI ankles). The three groups underwent one longitudinal investigation with 6 weeks of intervention phase (randomised controlled trial). After a maximal voluntary contraction measure of TA, PL and GM muscles, the main test protocol was performed. While participants were walking on a customized split-belt treadmill, sudden stumbling stimuli were applied with a delay of 200 ms after IC at mid-stance phase of walking (situation 1). IC and the subsequent perturbations were triggered by a plantar pressure sole. The perturbations (n=45; 15 left and 15 right, 15 "dummy perturbations" [no perturbations]) were randomly assigned over time and by side. Both, normal unperturbed walking (NW) and perturbed walking (PW) trials were collected over 1 treadmill walking session. Afterwards, participants performed a side cut movement

(SC; situation 2). This was characterized by a sudden deceleration phase on impact, accompanied by a rapid directional change (evading an opponent player as in a ball-sport game). The participants were planting one leg on the force platform and then cutting to one side at a standardized angle of 45° from direction of approach and in opposite direction of the planted leg. Both test situations were performed under test condition 1 ("shoe-only") and condition 2 (additional measurement orthosis). The order of these conditions was randomized. Simultaneously, signal of activity (surface EMG) of the TA, PL and GM muscles was recorded. During the intervention phase, OG wore each sport unit (3x/week) a customized in-shoe orthosis with a "PL stimulation module" (=increased area imbedded in the orthosis at area of the ball of the foot/first metatarsophalangeal bone; approach: pushing at this region to increase plantar pressure, subsequently evoking PL muscle activity). At least 3x/week, SMTG conducted 5 home-based exercises (postural control/balance, strength, combination of both) with increasing levels of difficulty over the 6 weeks. Both groups got the instruction to put emphasis on building up pressure below the ball of the big toe. CG did not perform any intervention. They served to measure test-retest reliability of ankle muscle activity. For data analysis, normalized RMS of the EMG amplitude (100% MVC) was calculated during NW and PW (for one stride, respectively) and during SC (average of 3 trials/side). For both test situations, RMS was considered within time phase of 100-50 ms pre IC (pre-activity) and 200 to 400 ms post IC (reflex-activity). The averaged EMG amplitude (for H and FI ankle group, respectively) of 15 left and right strides (mean [±SD]) was calculated for NW and PW. ACC sensor signal (sensors attached at lower leg) served to synchronize the EMG signal by detecting IC for subsequent muscle amplitude investigation and perturbation onset. Reliability was analyzed by Intra-class correlation coefficient (ICC 2.1), Test-Retest-Variability, Bland-Altman (bias, limits of agreement [±1.96*SD]) and Coefficient of variation (3). Descriptive statistics was used to analyse normalized RMS (mean±SD, %)(1a, 1b, 2, 4). Differences (M2-M1) of RMS were also presented descriptively (1b). Outcome variables were analyzed by 2-way between groups ANOVA (1a, 2, 4) and 2-way repeated measures ANOVA (between and within) (1b); both by using post-hoc test with Bonferroni-adjusted α ($p<0.0167$).

(3) Test-retest reliability showed a high range of values (high TRV, poor to good ICCs) in healthy individuals and those with FI. For NW and PW (pre- and reflex-activity) as well as SC

(pre-activity), H group revealed more reproducible values, except for PL during PW (reflex-activity). In both groups (H and FI), PW presented higher values of reliability for TA and GM than NW, particularly for reflex-activity. (4) Independent of condition ("shoe only"/ in-shoe orthosis), patients with FI demonstrated lower PL pre-activity for SC compared to healthy individuals, however they showed higher PL pre-activity for NW and PW. Reflex-activity did not reveal significant different values between the two groups. The foot orthosis intervention presented therapeutic (secondary preventive) effects. (1a) In contrast to acute use of a specific orthosis, (1b) long-term orthosis use was beneficial (and as effective as sensorimotor training) in individuals with FI. This was dependent on the time window of analysis, test situation and ankle muscle tested. Prolonged orthoses use increased PL pre-activity for PW (more than for healthy), TA pre-activity for SC as well as PL and GM reflex-activity for NW (PL: more than for healthy). The foot orthosis intervention also revealed (primary-) preventive effects. In healthy individuals, prolonged orthoses use increased PL and GM pre-activity for NW and PW, PL pre-activity for SC, TA and PL reflex-activity for NW as well as PL and GM reflex-activity for PW. The orthosis intervention was more effective than sensorimotor training in individuals with FI in terms of an increase in GM pre-activity for SC. Sensorimotor training was more beneficial in terms of increasing PL and GM pre-activity and TA reflex-activity for NW, PL pre-activity and TA, PL and GM reflex-activity for SC as well as PL reflex-activity for PW in individuals with FI. (2) Short-term application of an additional measurement in-shoe orthosis after intervention at re-test led to higher GM pre-activity during NW, higher PL and GM pre-activity during PW and SC and higher TA and PL reflex-activity during NW in the orthosis group (=[non-significant] "transmission-effects").

The presented reproducibility measures revealed poor, but also acceptable values for both, healthy individuals and those with FI across all test situations. A high range of muscle amplitudes variability presents a main concern in literature that is investigating the EMG of ankle musculature during walking. It can be party explained by the dynamic nature of measurement. Gait is influenced by intra- and inter-individual gait parameters as stride length and frequency. Large random errors and high variations of reproducibility reflect physiological variability in muscle activity during gait as well as stumbling and therefore deemed acceptable. Compared to healthy individuals, those with FI presented reduced TA and PL pre-activity during side cutting, however increased PL and GM pre-activity during unperturbed and perturbed walking. This finding suggests that FI individuals might compensate neuromuscular deficits during more unexpected, reflexive situations, as stumbling on treadmill. The reduced inversion at touchdown serves adequate ankle joint protection. Acute application of the specific orthosis did not affect ankle muscle activity considerably. This might have been due to subject-specific responses or insufficient adaptation processes to the orthosis (inability to build up prescribed pressure during complex test situations). Considering the long-term effect of orthoses, facilitated PL pre-activity during perturbed walking, as well as facilitated TA and GM pre-activity during side cutting in FI individuals indicate a modified pre-programmed feedforward motor control after intervention. They emphasize relevance of the PL muscle in anticipating potentially vulnerable, destabilizing moments. Stimulated compensatory (GM and) PL response during unperturbed walking can be interpreted as positive (feedback) adaptation strategy in FI individuals. This strategy helps the maintenance of dynamic ankle joint stability during early and terminal mid-stance phase of gait. Although there was a trend toward higher ankle muscle activity due to short-term application of a measurement in-shoe orthosis in the orthosis group after intervention at re-test ("transmission effect"), for most of the conditions increased ankle muscle activity could already be presented by short-term "shoe use only" at re-test. This gives evidence for an adequate response of ankle muscles to the stimulation module of the orthosis after intervention. It also supports the presence of protective feedback- as well as forward adaptation mechanisms due to prolonged orthoses use. These mechanisms could be transferred to highly dynamic situations where ankle stabilization is required. The assumed neuromuscular adaptation mechanism to long-term orthoses use is supported by other literature (increase in plantar pressure at longitudinal arch/medial midfoot area/PL tendon → modulation of afferent input → spinal and supraspinal adaptations [change in underlying motor program] → increase in efferent drive to PL muscle/PL stretch reflex). The main results in this research have clinical implications/practical relevance for the management of FI. For athletic populations with FI, prolonged orthoses use can support PL through GM activity before ground contact as a defending strategy against potential ankle injury during sport-specific situations (e.g. cutting, unexpected foot displacement by body check). Specific foot orthoses can also be used for healthy populations, as they can serve as potential primary prevention against injury. The costs and benefits of each of the training protocols should be weighed against each other. In a clinical setting, the benefit of prolonged foot orthoses use over sensorimotor training may be the time-and-cost-effectiveness (practicability) and the positive subjective feedback of the patients in terms of comfort. A specific advantage is that orthoses can be used during training without the need of separate exercise sessions. Nevertheless, the findings have to be interpreted carefully due to small amount of participants in the main group of interest (FI in orthoses group), and partly high values of test-retest variability. Evidence-based future research is warranted to ascertain and underpin the unique findings of this study work. Further intervention studies should examine if a combined treatment approach (added value of passive orthoses use as adjunctive therapy next to active neuromuscular training) is more effective than isolated training programs in modifying ankle muscle activation. Furthermore, participants should be followed up to give further evidence of neuromuscular adaptation mechanisms, and to quantify the true significance of improvements. Thereby, it can be assessed if changes in neuromuscular control are associated with clinical outcomes (e.g. reduced incidence of future injury). In addition, further investigations are required to determine exact spinal and supraspinal pathways responsible for alteration in ankle muscle activity. Therefore, studies investigating motoneuron pool excitability (e.g. H-reflex, transcranial magnet stimulation) could deliver deeper insight into long-term effect mechanisms of orthoses on a neurophysiological basis.

Concluding, the main findings of this thesis confirm the presence of sensorimotor long-term effects of specific foot orthoses in healthy individuals (primary preventive effect) and those with FI (therapeutic effect). The results indicate that an orthotic prescription with a specific stimulation module adequately addresses PL muscle activity. Long-term orthoses use has the potential to induce compensatory feedback- and anticipatory feedforward neuromuscular adaptation of ankle muscles, specifically of PL. This endorses the key role of PL in providing essential dynamic ankle joint stability. In a clinical context, due to its advantages over sensorimotor training (positive subjective feedback in terms of comfort, time-and-cost-effectiveness), long-term foot orthoses use can be recommended as a promising, applicable and efficient therapy alternative next to conventional sensorimotor training in patients with FI.

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www.SENIAM.org; access on 08/05/2015

www.consort-statement.org; access on 09/05/2015

Appendix

The Cumberland Ankle Instability Tool
Please tick the ONE statement in EACH question that BEST describes your ankles.

	LEFT	RIGHT	SCORE
1. I have pain in my ankle			
Never			5
During sport			4
Running on uneven surfaces			3
Running on level surfaces			2
Walking on uneven surfaces			1
Walking on level surfaces			0
2. My ankle feels UNSTABLE			
Never			4
Sometimes during sport (not every time)			3
Frequently during sport (every time)			2
Sometimes during daily activity			1
Frequently during daily activity			0
3. When I make SHARP turns, my ankle feels UNSTABLE			
Never			3
Sometimes when running			2
Often when running			1
When walking			0
4. When going down the stairs, my ankle feels UNSTABLE			
Never			3
If I go fast			2
Occasionally			1
Always			0
5. My ankle feels UNSTBLE when standing on ONE leg			
Never			2
On the ball of my foot			1
With my foot flat			0
6. My ankle feels UNSTABLE when			
Never			3
I hop from side to side			2
I hop on the spot			1
When I jump			0
7. My ankle feels UNSTABLE when			
Never			4
I run on uneven surfaces			3
I jog on uneven surfaces			2
I walk on uneven surfaces			1
I walk on a flat surface			0
8. TYPICALLY, when I start to roll over (or twist) on my ankle, I can stop			
Immediately			4
Often			3
Sometimes			2
Never			1
I have never rolled over on my ankle			0
9. After a TYPICAL incident of my ankle rolling over, my ankle returns to "normal "			
Almost immediately			4
Less than one day			3
1-2 days			2
More than 2 days			1
I have never rolled over on my ankle			0

Figure 1: "Cumberland Ankle Instability Tool" (CAIT)-questionnaire

Foot and Ankle Ability Measure (FAAM)
Activities of Daily Living Subscale

Please Answer **every question** with **one response** that most closely describes your condition within the past week.
If the activity in question is limited by something other than your foot or ankle mark "Not Applicable" (N/A).

	No Difficulty	Slight Difficulty	Moderate Difficulty	Extreme Difficulty	Unable to do	N/A
Standing	☐	☐	☐	☐	☐	☐
Walking on even Ground	☐	☐	☐	☐	☐	☐
Walking on even ground without shoes	☐	☐	☐	☐	☐	☐
Walking up hills	☐	☐	☐	☐	☐	☐
Walking down hills	☐	☐	☐	☐	☐	☐
Going up stairs	☐	☐	☐	☐	☐	☐
Going down stairs	☐	☐	☐	☐	☐	☐
Walking on uneven ground	☐	☐	☐	☐	☐	☐
Stepping up and down curbs	☐	☐	☐	☐	☐	☐
Squatting	☐	☐	☐	☐	☐	☐
Coming up on your toes	☐	☐	☐	☐	☐	☐
Walking initially	☐	☐	☐	☐	☐	☐
Walking 5 minutes or less	☐	☐	☐	☐	☐	☐
Walking approximately 10 minutes	☐	☐	☐	☐	☐	☐
Walking 15 minutes or greater	☐	☐	☐	☐	☐	☐

Figure 2a: "Foot And Ankle Ability Measure" (FAAM)-questionnaire; ADL subscale page 1

Foot and Ankle Ability Measure (FAAM)
Activities of Daily Living Subscale
Page 2

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

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

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

__ ___ . 0 %

Martin, R; Irrgang, J; Burdett, R; Conti, S; VanSwearingen, J: Evidence of Validity for the Foot and Ankle Ability Measure. Foot and Ankle International. Vol.26, No.11: 968-983, 2005.

Figure 2b: "Foot And Ankle Ability Measure" (FAAM)-questionnaire; ADL subscale page 2

Foot and Ankle Ability Measure (FAAM)
Sports Subscale

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

	No Difficulty at all	Slight Difficulty	Moderate Difficulty	Extreme Difficulty	Unable to do	N/A
Running	☐	☐	☐	☐	☐	☐
Jumping	☐	☐	☐	☐	☐	☐
Landing	☐	☐	☐	☐	☐	☐
Starting and stopping quickly	☐	☐	☐	☐	☐	☐
Cutting/lateral Movements	☐	☐	☐	☐	☐	☐
Ability to perform Activity with your Normal technique	☐	☐	☐	☐	☐	☐
Ability to participate In your desired sport As long as you like	☐	☐	☐	☐	☐	☐

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

___ ___ ___ . 0%

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

☐ Normal ☐ Nearly Normal ☐ Abnormal ☐ Severely Abnormal

Figure 2c: "Foot And Ankle Ability Measure" (FAAM)-questionnaire; sports subscale)

Protocol/Diary Orthosis group; exemplary only week 1 (next 2 pages)

Diary Orthosis Group

Requirements of wearing period and way of wearing the orthosis:

You should wear the orthosis minimum every training/ sport unit. Additionally, it is desirable of wearing the orthosis during every physical activity (all day life exposure as walking)!

During wearing the orthosis you should pay attention on building up pressure under your ball of the big toe downwards during roll motion of foot (push off phase) when walking/running! During jumping and landing you also should build up an increased pressure under your ball of the big toe.

Following, you find the protocol to fill out for each of the 6 weeks.

Contact information:

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Week 1 **Subject – ID:FSI____**

Date	Orthosis „worn“ (√) / „not worn “ (X)	Total time of activity / thereof: Orthosis-period of wearing — Physical activity (All day life)	Sport (Training unit)	Comments (Pain/ Complaints Ankle Joint / Other)	Comfort of the Orthosis (max. comfortable = 1; max. uncomfortable = 5) (mark with a cross)
__.__.__		____min. / ____min.	____min. / ____ min.		☐ ☐ ☐ ☐ ☐ 1 2 3 4 5
__.__.__		____min. / ____min.	____min. / ____ min.		☐ ☐ ☐ ☐ ☐ 1 2 3 4 5
__.__.__		____min. / ____min.	____min. / ____ min.		☐ ☐ ☐ ☐ ☐ 1 2 3 4 5
__.__.__		____min. / ____min.	____min. / ____ min.		☐ ☐ ☐ ☐ ☐ 1 2 3 4 5
__.__.__		____min. / ____min.	____min. / ____ min.		☐ ☐ ☐ ☐ ☐ 1 2 3 4 5
__.__.__		____min. / ____min.	____min. / ____ min.		☐ ☐ ☐ ☐ ☐ 1 2 3 4 5
__.__.__		____min. / ____min.	____min. / ____ min.		☐ ☐ ☐ ☐ ☐ 1 2 3 4 5

Protocol/Diary Sensorimotor training group, exemplary protocol week 1 and 2 (Level A)(next 5 pages)

Training log for stabilization of the ankle joint- Sensorimotor training

<u>Requirements of the home program</u> (Duration: 6 weeks)

The **aim** of the training program is to increase the ankle joint stability to avoid (repeated) trauma of the ankle joint. The program contains **5 exercises** which will be increased over **3 Levels** within the 6 weeks (table 1).

	Week 1	**Week 2**	**Week 3**	**Week 4**	**Week 5**	**Week 6**
Exercise 1-5 (Level A-C)	A		B		C	

Table 1: Increase of the Level of difficulty of the exercises from Level A-C over the 6 weeks

Training should be performed…

- **1x daily (minimum 3x per week)**; **20-25 minutes per unit**; **6 weeks** long

All exercises should be performed **on both sides** and **barefoot**. It is recommended to use a **non-slipping surface** in case of a slipping floor. If you are unable to perform the prescribed **exercises (Level B and C**) as required, you should go **1 Level back**.

Following you find the **training protocol** (with illustrations of an incorrect as well as correct performance of the exercises) **for each Level**. Please **document** in the following **protocol** if you performed the exercises **actually** (as required; with deviations; not performed).

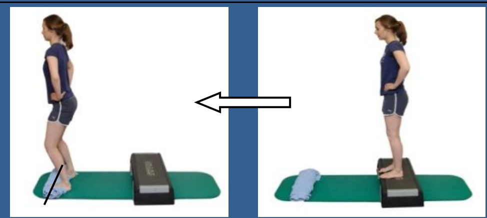
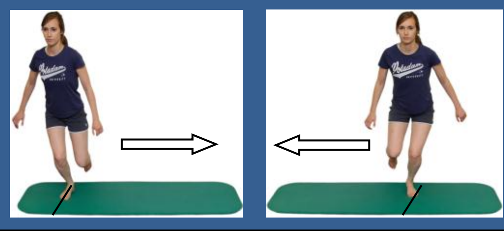
Each training unit begins with a short **warm up** (see following table).

Warm up

Exercise	**Description/ Hints**	**Dosage**
1. Flight of stairs (up and down)	• Step on each single stair • Lifting knees when running up • Swinging arms • Quickly	**Duration:** 2 min.

Contact dates: *Hochschulambulanz der Universität Potsdam; project coord.: Juliane Heydenreich: e-mail: jheydenr@uni-potsdam.de*; Tel.: *0331 – 977 1726*; *Antje Reschke: e-mail: areschke@uni-potsdam.de*; Tel.: *01781801878*

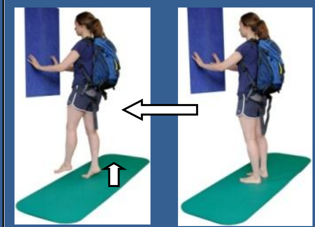
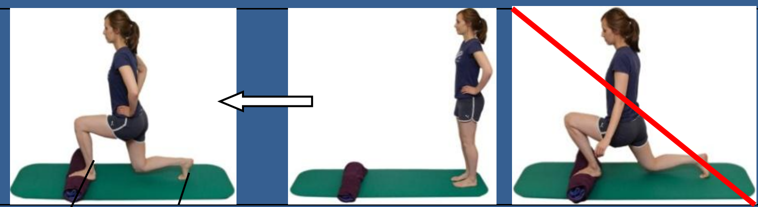
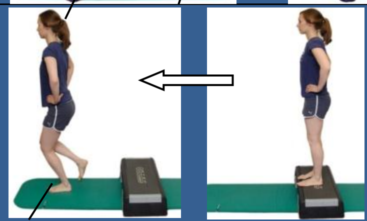
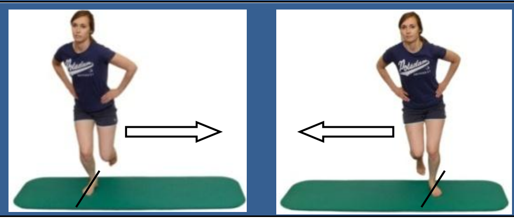
Week 1 and 2 (Level A) Begin with Warm up, [1] 2-3 towels (rolled up; medium size) [2] Balance **Subject-ID:______**

Exercise	Description/ Hints	Execution (Picture)	Dosage DEFAULT
A **1. One-leg stance on towel roll [1] in front of mirror**	• Knees slightly bent • Leg axis ! • NOT rotating to inner/outer side with stable foot • Stabilization of B[2]		**Duration**: 20 s. **Extent:** 3 x per side **Rest**: 20 s
A **2. One-legged heel raise with pressure ball of big toe (BBT)**	• Max. heel raise • Lifting up big toe; BBT into floor! • Stabilization on wall		**Duration:** 3 Serien **Extent:** 10 x per side **Rest:** 20 s
A **3. One sided lunge (Distance 5 foot lengths)**	• Forward step • Post. knee slightly over floor and up • Knee NOT over toes • Leg axis!		**Duration:** 3 Serien **Extent:** 10 x per side **Rest:** 20 s
A **4. Landing on towel roll from staircase (Distance 2 foot lenghts)**	• Jump from first stair to floor • Leg axis ! • Knee slightly bent • Stabilization of Landing		**Duration**: hold approx. 3 sec. **Extent:** 20 x **Rest:** 20 s
A **5. Side jumps (Distance 3 foot lenghts)**	• Jump from one leg to the other • Hands free • Leg axis ! • Knees slightly bent • Stabilization of Landing		**Duration**: Hold approx. 3 sec. **Extent**: 5 Jumps/Side **Rest**: 20 s

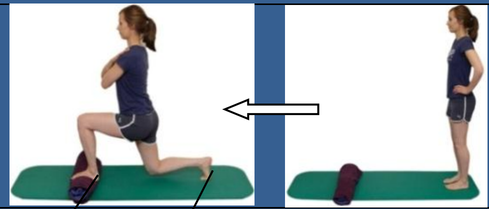
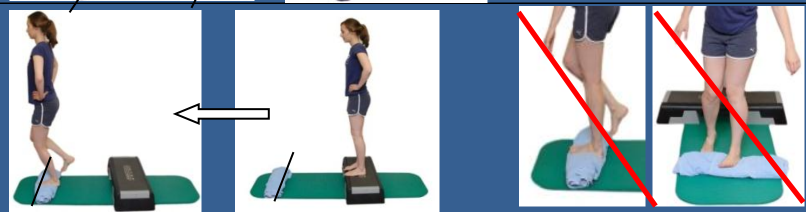
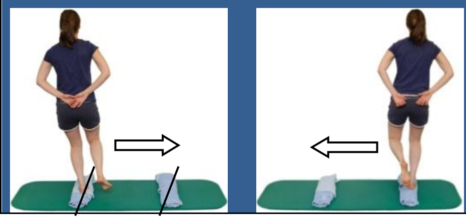
Protocol Week 1 and 2 (Level A): **Subject-ID:______**

Date	Exercises identical performed AS REQUIRED:	Exercises performed, but with DEVIATIONS:	Exercises NOT performed:
Week 1			
__/__/__	❑	❑ Deviations:______	❑
__/__/__	❑	❑ Deviations:______	❑
__/__/__	❑	❑ Deviations:______	❑
__/__/__	❑	❑ Deviations:______	❑
__/__/__	❑	❑ Deviations:______	❑
__/__/__	❑	❑ Deviations:______	❑
__/__/__	❑	❑ Deviations:______	❑
Week 2			
__/__/__	❑	❑ Deviations:______	❑
__/__/__	❑	❑ Deviations:______	❑
__/__/__	❑	❑ Deviations:______	❑
__/__/__	❑	❑ Deviations:______	❑
__/__/__	❑	❑ Deviations:______	❑
__/__/__	❑	❑ Deviations:______	❑
__/__/__	❑	❑ Deviations:______	❑

Week 3 and 4 (Level B) Begin with Warm up, 2-3 towels (rolled up; medium size) [2] Balance **Subject-ID:______**

Exercise	Description/ Hints	Execution (Picture)	Dosage DEFAULT
B 1. **One-leg stance on towel roll [1] in front of mirror with deflection of legs**	• Knees slightly bent • Leg axis ! • **Leg to 1.front, 2. back, 3. left, 4. right besides body (=1x) etc.** • Stabilization of B[2]		**Duration:** 3 Series **Extent:** 5 x per side **Rest:** 20 s
B 2. **One-legged heel raise with pressure ball of big toe (BBT) and additional weight (5% of BW):____**	• Max. heel raise • Lifting up big toe; BBT into floor! • Stabilization on wall • **Backpack filled with water bottles**		**Duration:** 3 Series **Extent:** 10 x per side **Rest:** 20 s
B 3. **One sided lunge on towel roll (Distance 5 foot lengths)**	• Forward step • Post. knee slightly over floor and up • Knee NOT over toes • Leg axis!		**Duration**: 3 Series **Extent**: 10 x per side **Rest**: 20 s
B 4. **Landing on floor from staircase (Distance 2 foot lenghts)**	• Jump from first stair to floor • Leg axis ! • Knee slightly bent • Stabilization of Landing		**Duration**: Hold approx. 3 sec. **Extent:** 10 x per side **Rest:** 20 s
B 5. **Side jumps with hands on back (Distance 3 foot lenghts)**	• Jump from one leg to the other • Hands on hips • Leg axis ! • Knees slightly bent • Stabilization of Landing		**Duration**: Hold approx. 3 sec. **Extent**: 5 Jumps/ Side **Rest**: 20 s

Week 5 and 6 (Level C) Begin with Warm up, 2-3 towels (rolled up; medium size) [2] Balance **Subject-ID:_______**

Exercise	Description/ Hints	Execution (Picture)	Dosage DEFAULT
C **1. One-leg stance on towel roll [1] in front of mirror with changing of viewing direction**	• **Arms lateral stretched** • **Looking mutually into palm of hand (left + right =1x)** • Leg axis ! • Stabilization B[2]		**Duration**: 3 Series **Extent:** 5x per side **Rest**: 20 s
C **2. One-legged heel raise with pressure ball of big toe (BBT) and additional weight (10% of BW):____**	• Max. heel raise • Lifting up big toe; BBT into floor! • WITHOUT Stabilization on wall • **Backpack filled with water bottles**		**Duration:** 3 Series **Extent:** 10 x per side **Rest:** 20 s
C **3. One sided lunge with crossed arms (Distance 5 foot lengths)**	• Forward step • Post. knee slightly over floor and up • Knee NOT over toes • Crossed arms before chest		**Duration**: 3 Series **Extent**: 10 x per side **Rest:** 20 s
C **4. Landing on towel roll from staircase (Distance 2 foot lengths)**	• Jump from first stair to floor • Leg axis ! • Knee slightly bent • Stabilization of Landing		**Duation:** Hold approx. 3 sec. **Extent:** 10 x per side **Rest:** 20 s
C **5. Side jumps on towel roll with hands on back (Distance 3 foot lengths)**	• Jump from one leg to the other • Hands on back • Leg axis ! • Knees slightly bent • Stabilization of Landing		**Duration**: Hold approx. 3 sec. **Extent**: 5 Jumps/ Side **Rest**: 20 s

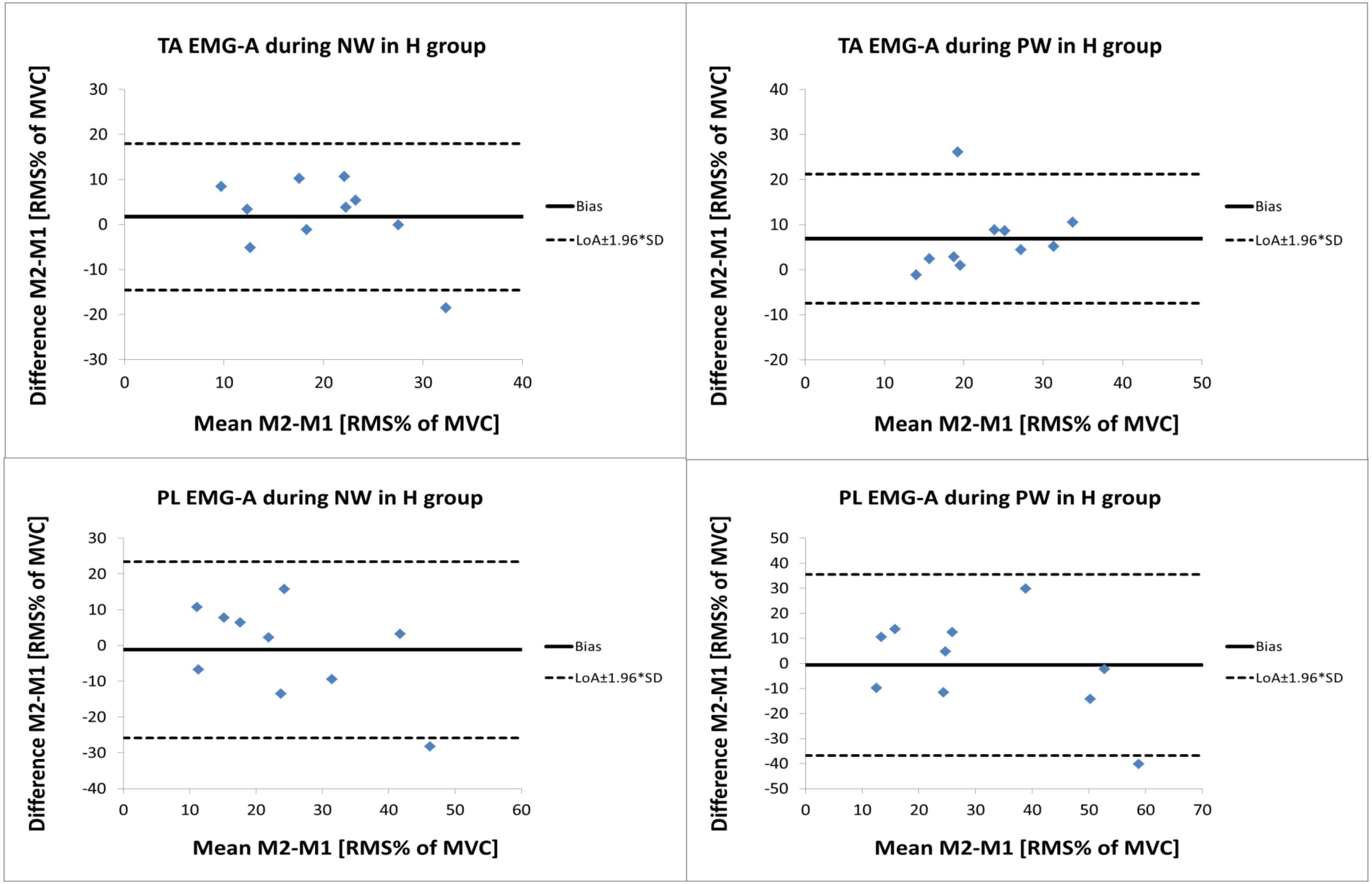


Figure 3a: Bland & Altman Plots (Normal and perturbed walking; 100-50 ms pre IC)

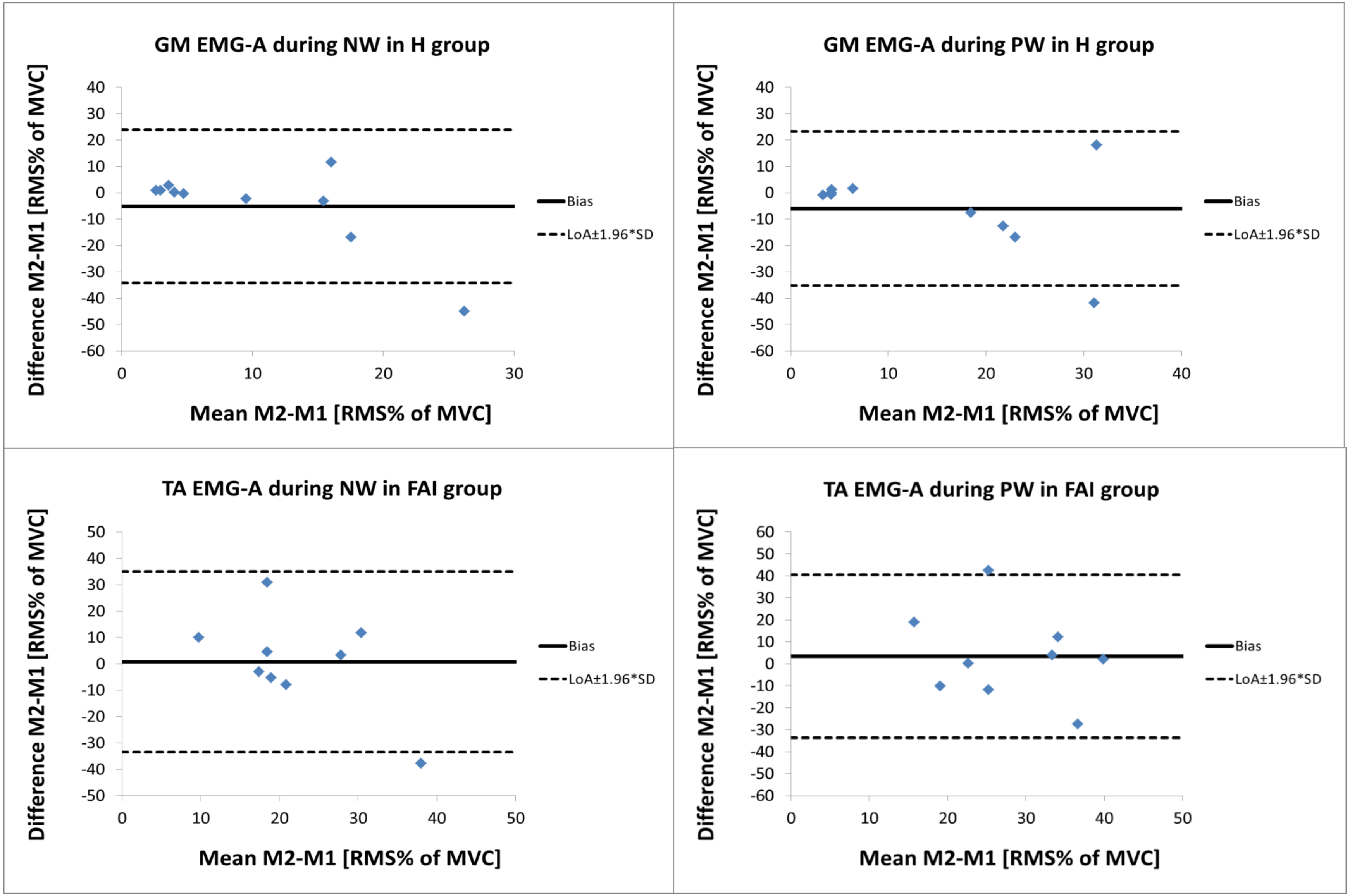


Figure 3a: Bland & Altman Plots (Normal and perturbed walking; 100-50 ms pre IC); FAI means FI

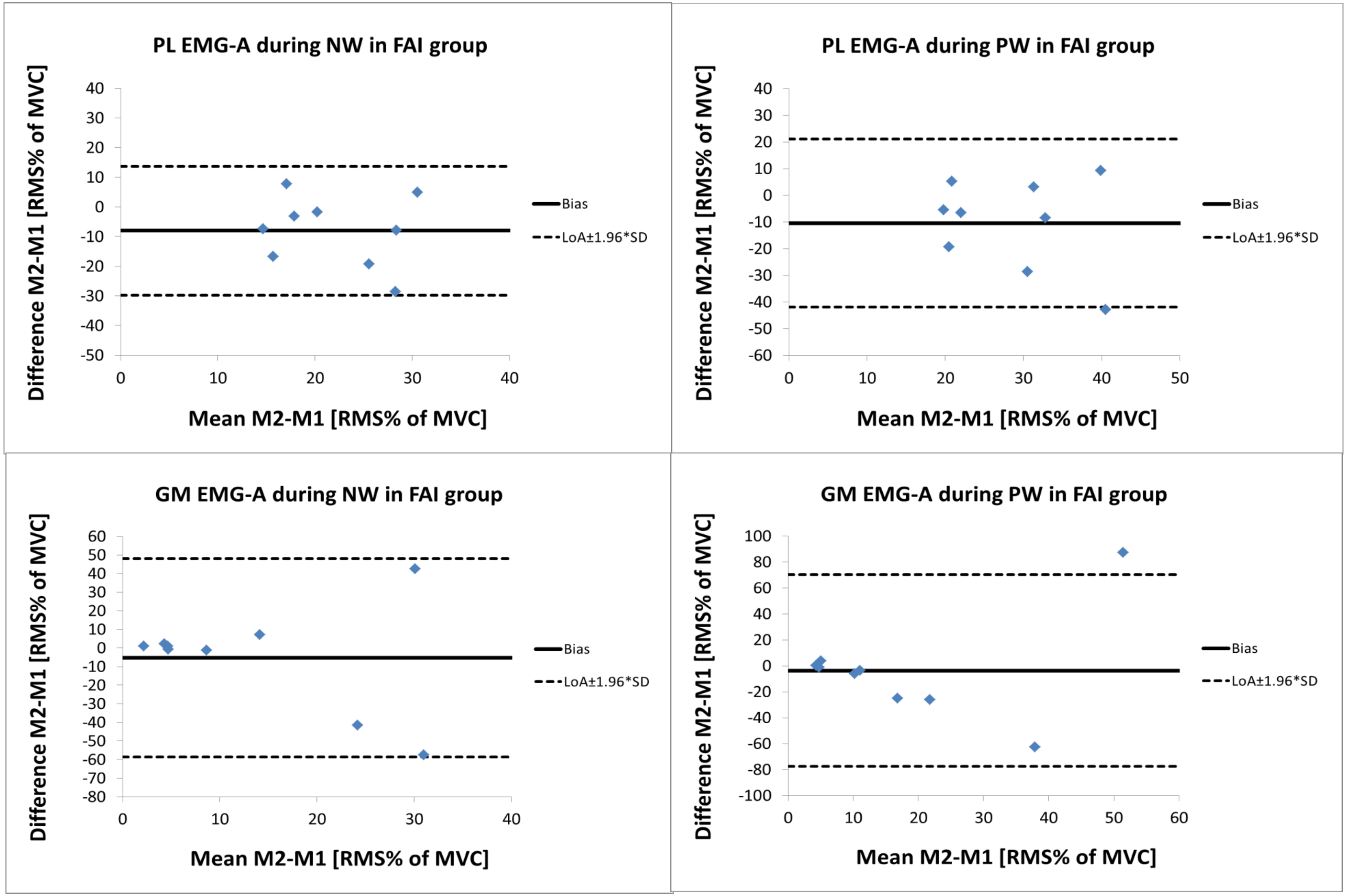


Figure 3a: Bland & Altman Plots (Normal and perturbed walking; 100-50 ms pre IC); FAI means FI

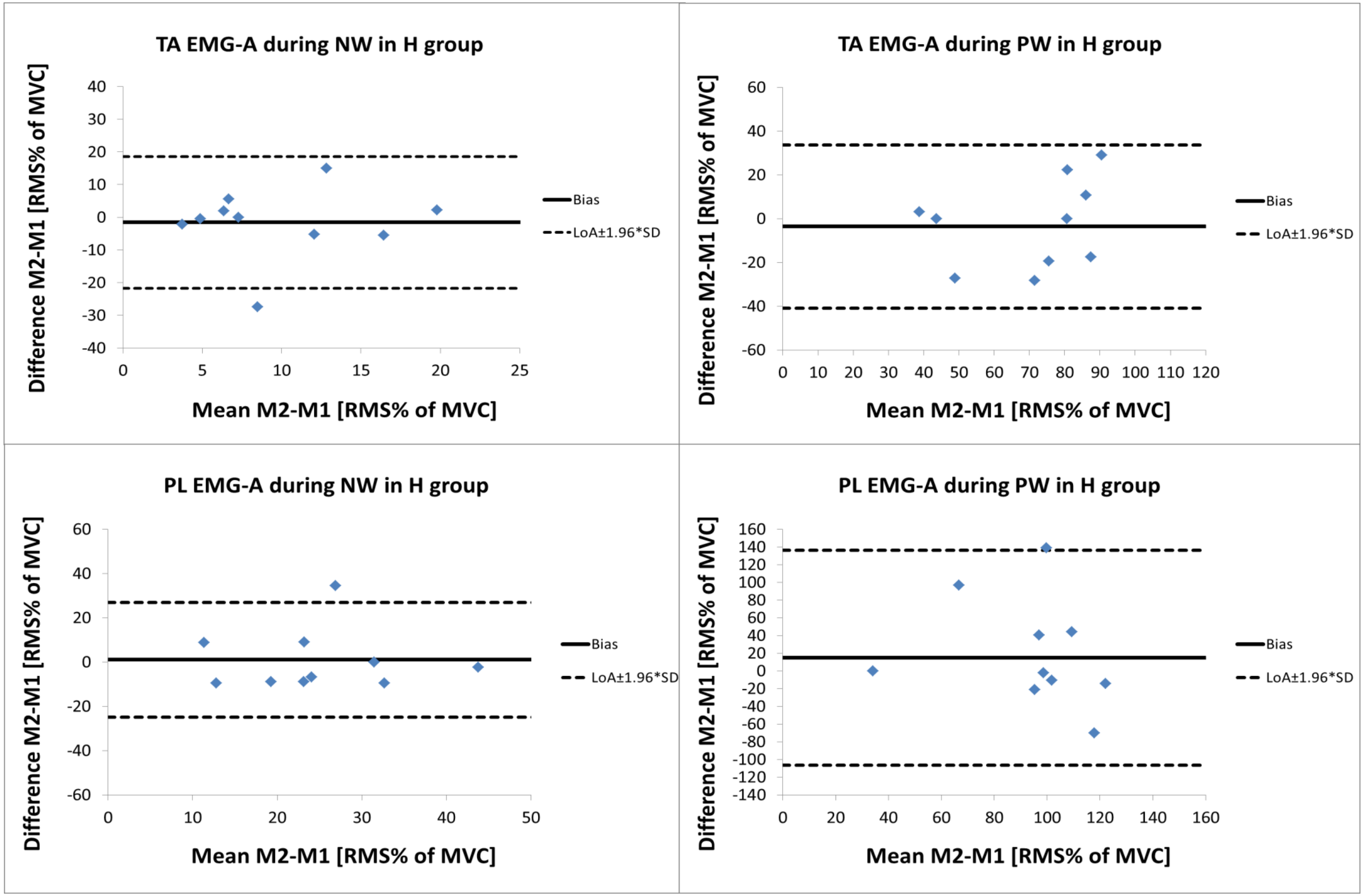


Figure 3b: Bland & Altman Plots (Normal and perturbed walking; 200-400 ms post IC)

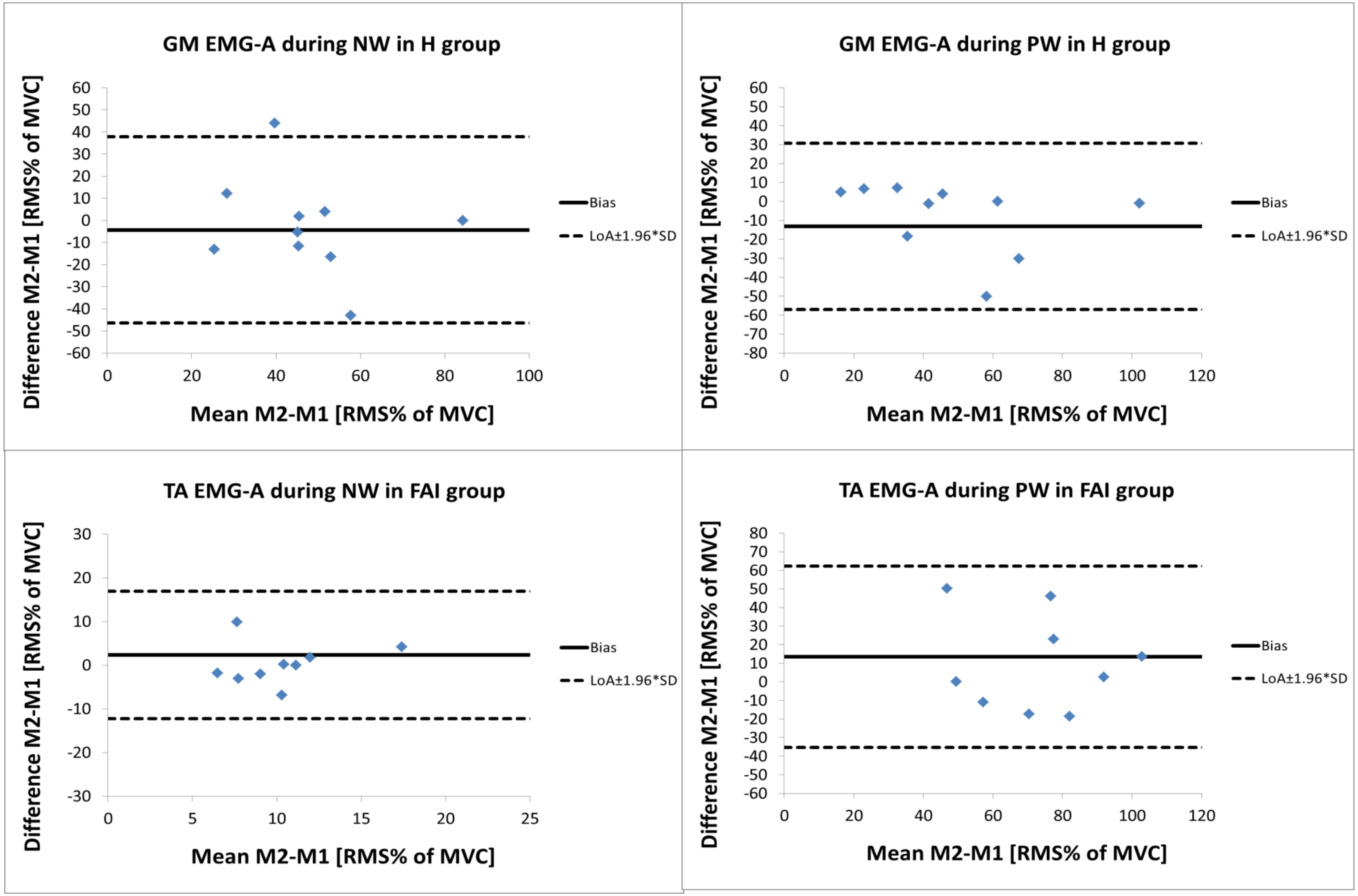


Figure 3b: Bland & Altman Plots (Normal and perturbed walking; 200-400 ms post IC); FAI means FI

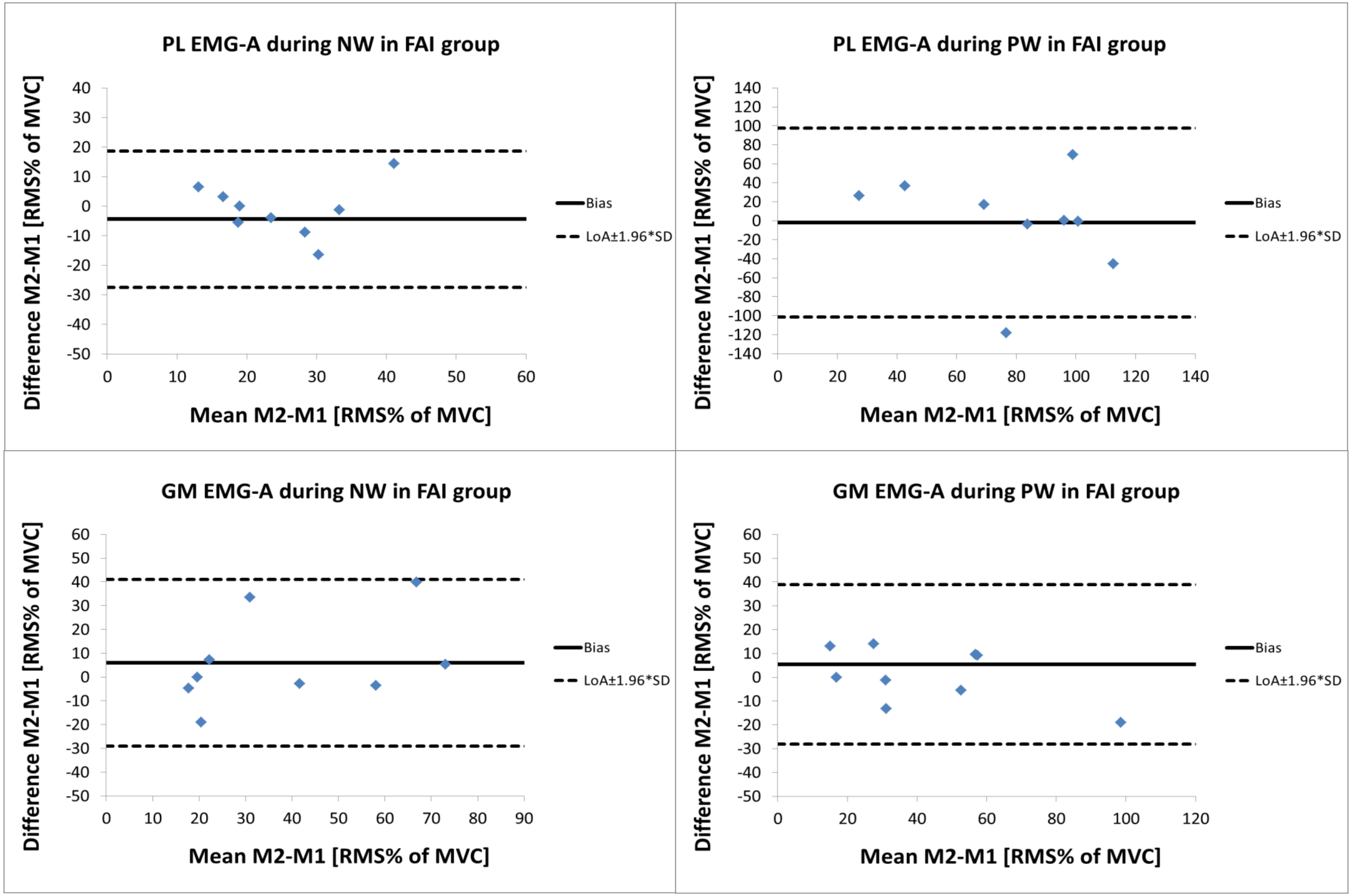


Figure 3b: Bland & Altman Plots (Normal and perturbed walking; 200-400 ms post IC); FAI means FI

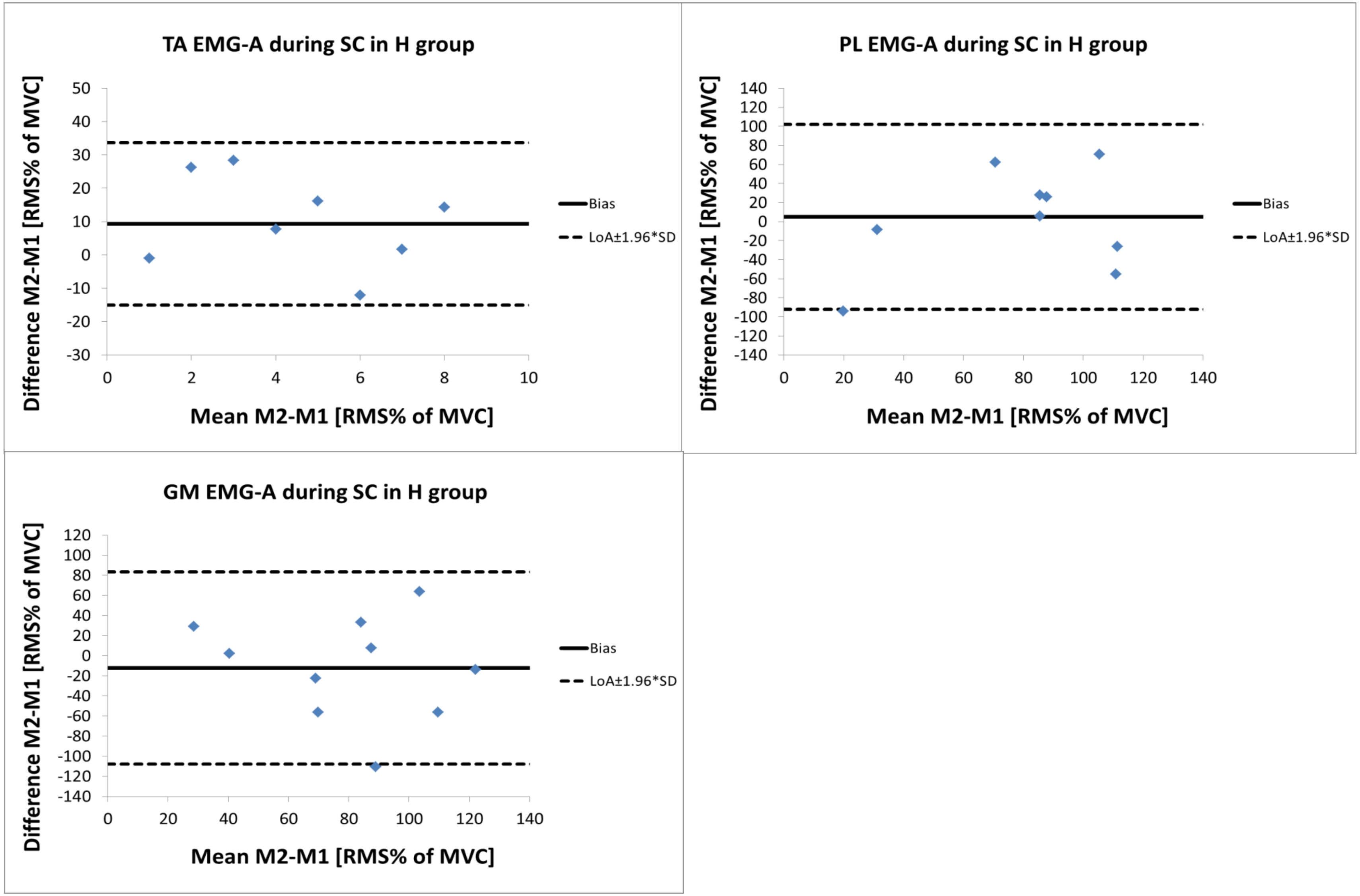


Figure 3c: Bland & Altman Plots (Side cutting; 100-50 ms pre IC)

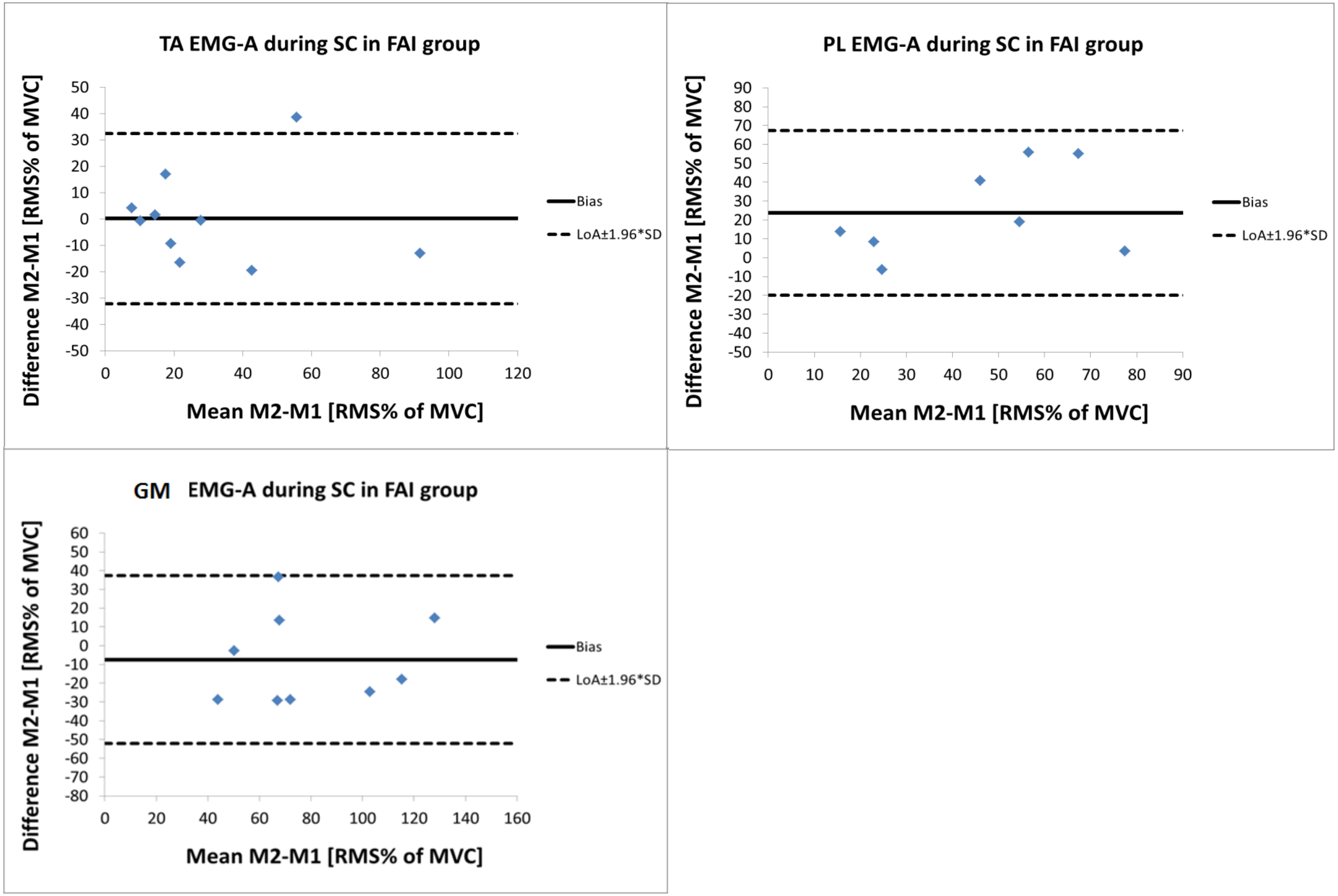


Figure 3c: Bland & Altman Plots (Side cutting; 100-50 ms pre IC); FAI means FI

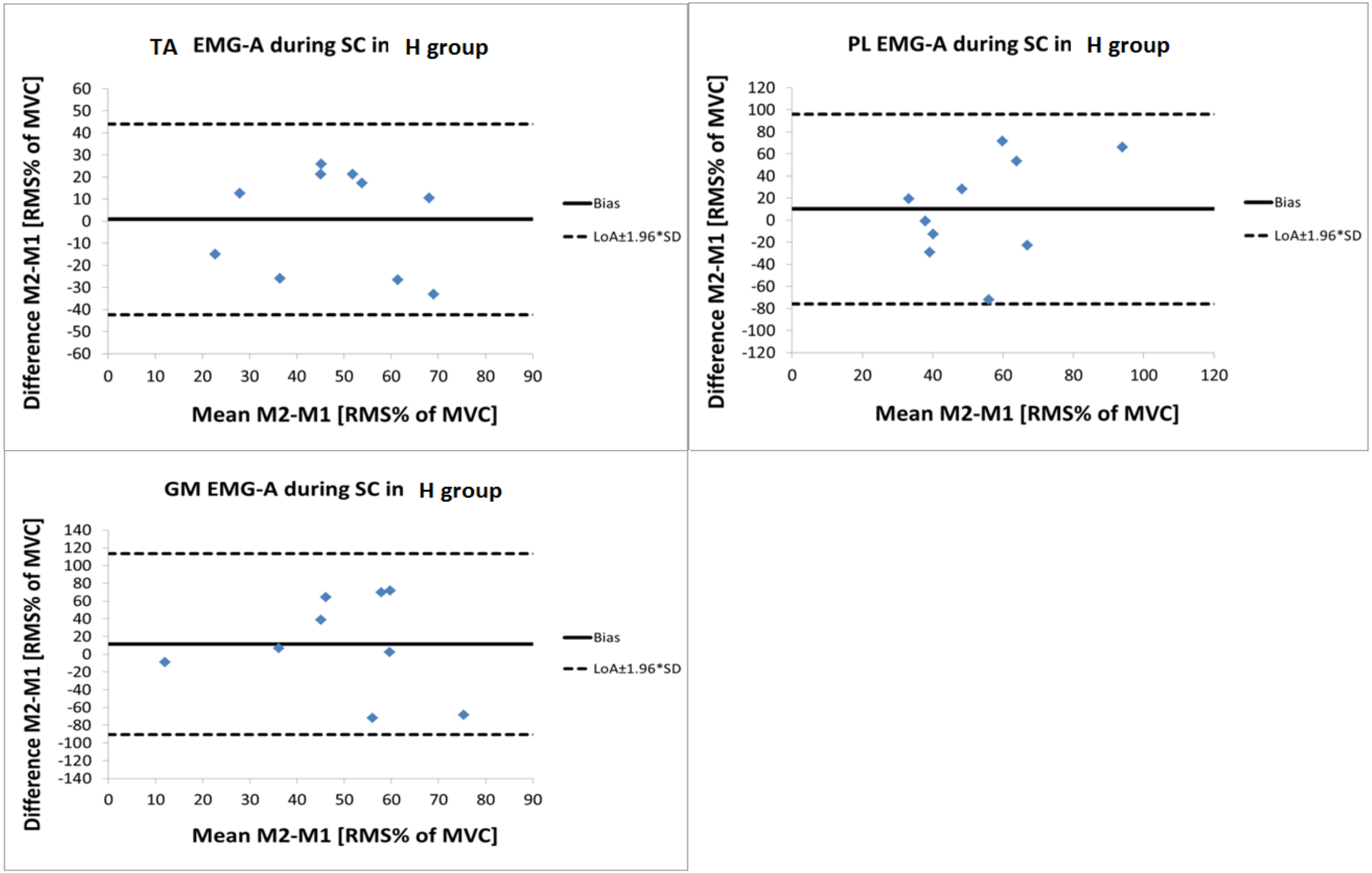


Figure 3d: Bland & Altman Plots (Side cutting; 200-400 ms post IC); FAI means FI

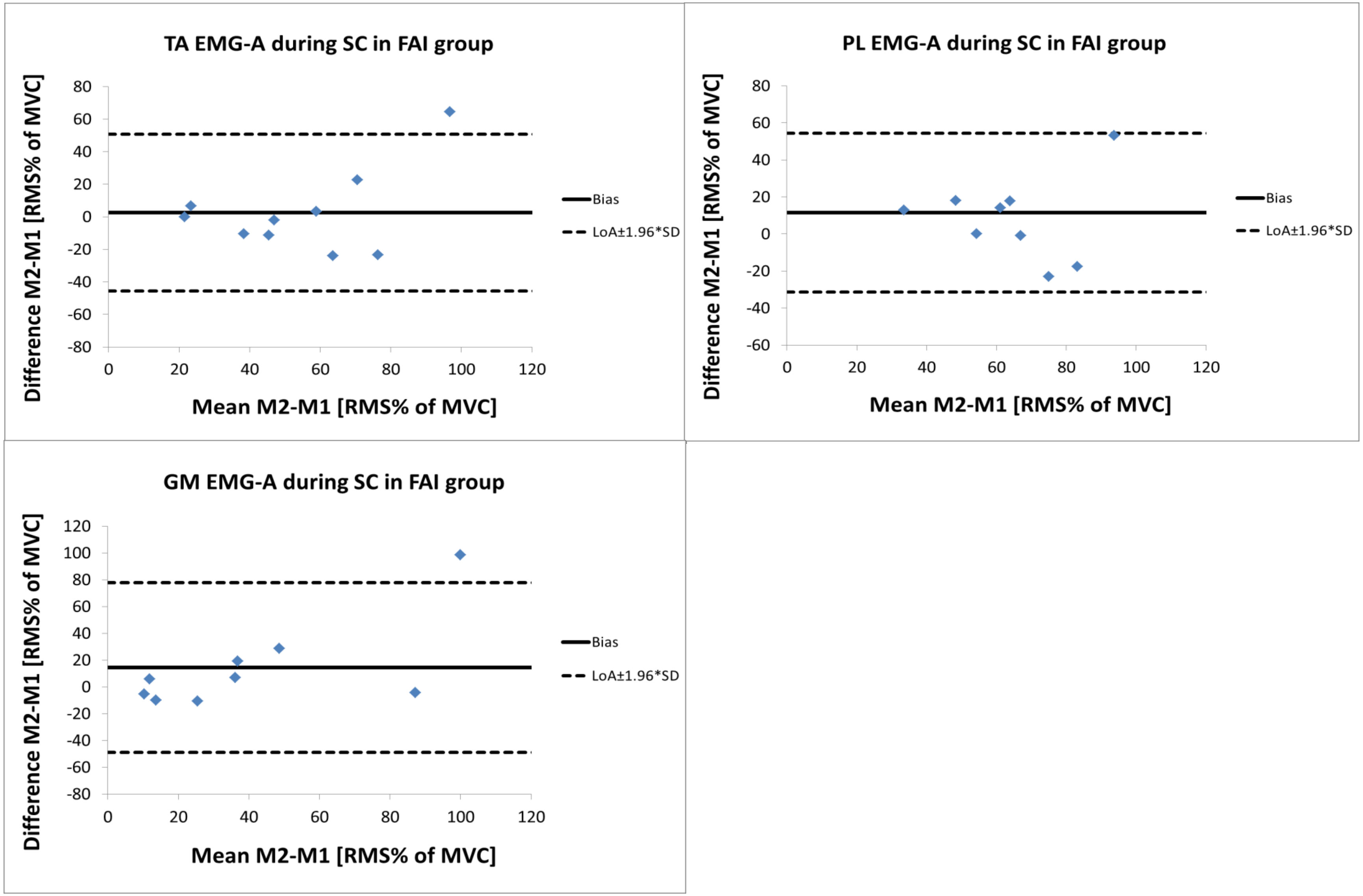
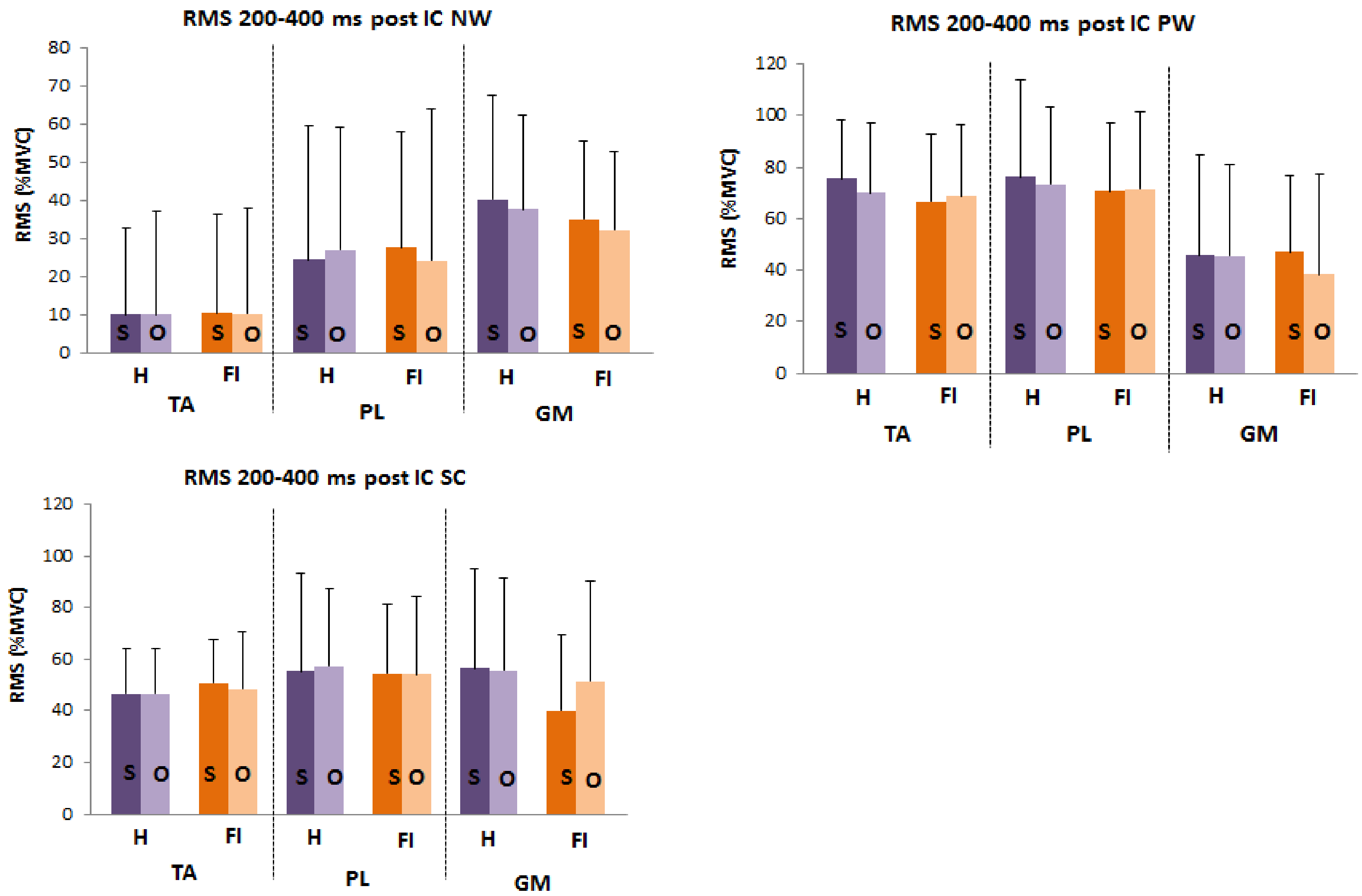
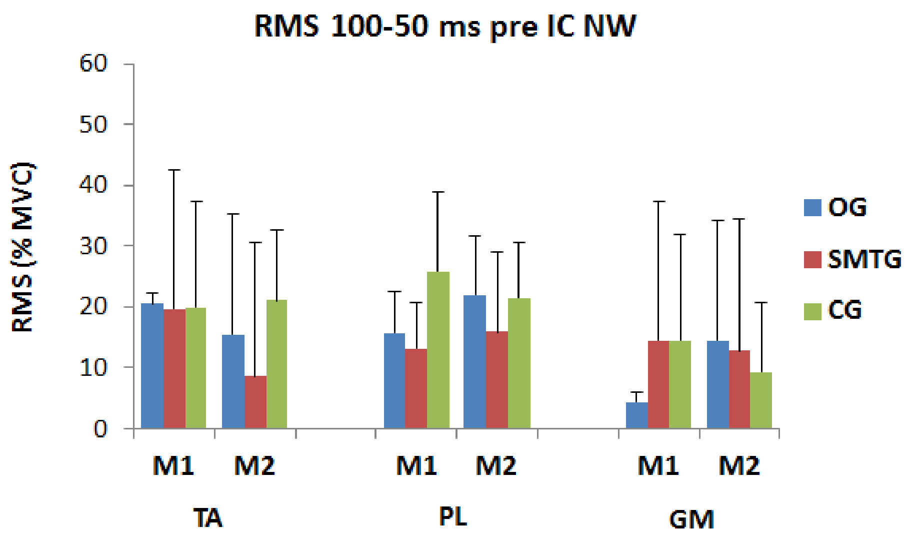
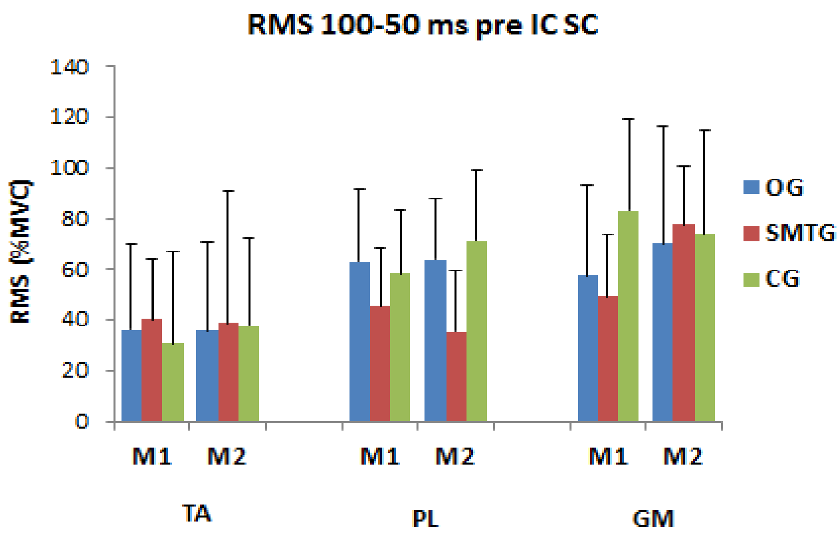


Figure 3d: Bland & Altman Plots (Side cutting; 200-400 ms post IC); FAI means FI

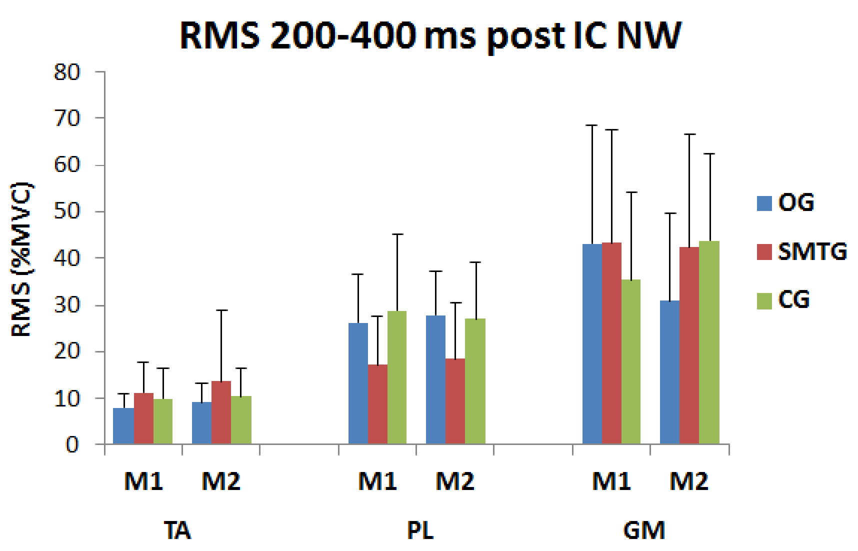


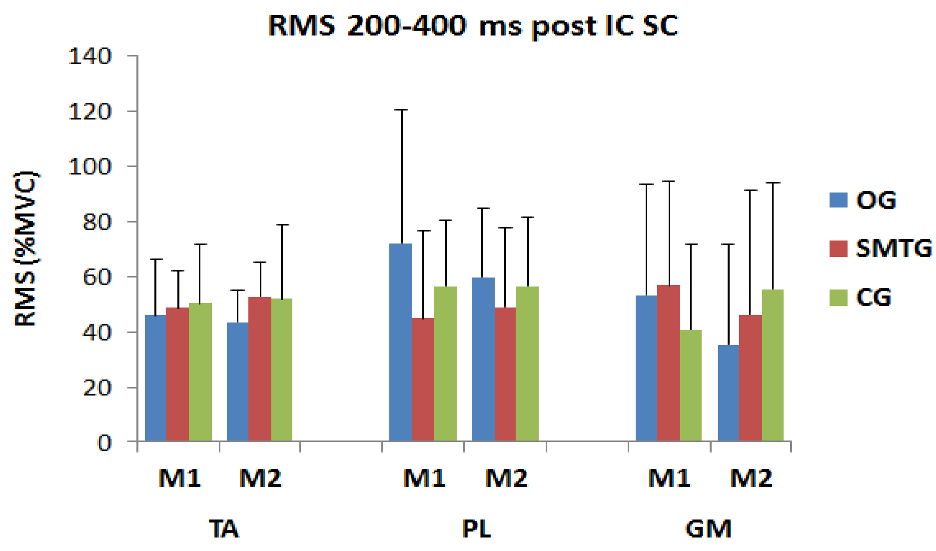
Figures 24-26: RMS (%MVC) of TA, PL and GM for NW, PW and SC during 200-400 ms post IC, *TA- m. tibialis anterior, PL- m.peroneus longus, GM-m. gastrocnemius medialis; S-shoe; O-orthosis; NW-normal walking, H-healthy group, FI-functional ankle instability group*



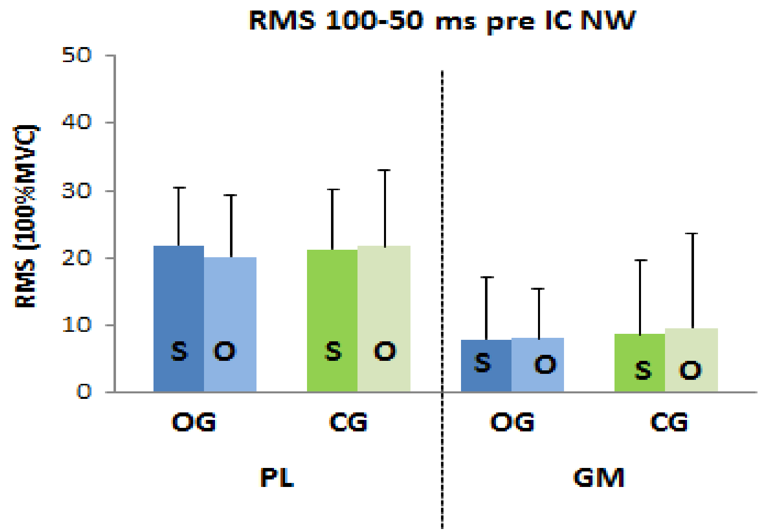


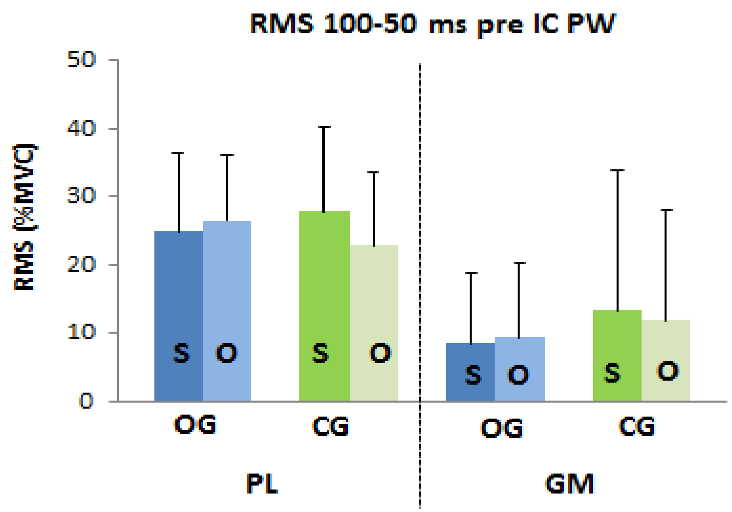
Figures 27, 29: RMS (%MVC) of TA (left) and GM (right) for NW and SC during 100-50 ms pre IC, *TA- m. tibialis anterior, PL- m. peroneus longus, GM-m. gastrocnemius medialis; NW-normal walking, SC- side cutting; OG- orthoses group, SMTG- sensorimotor training group, CG- control group*

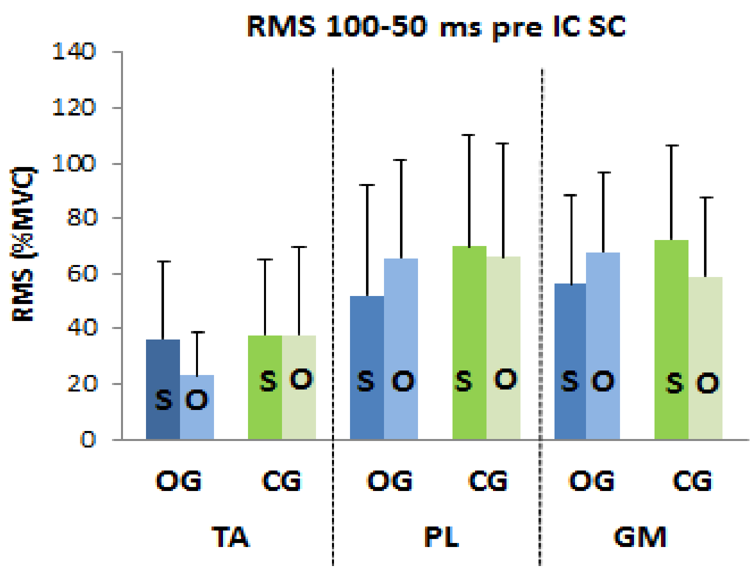




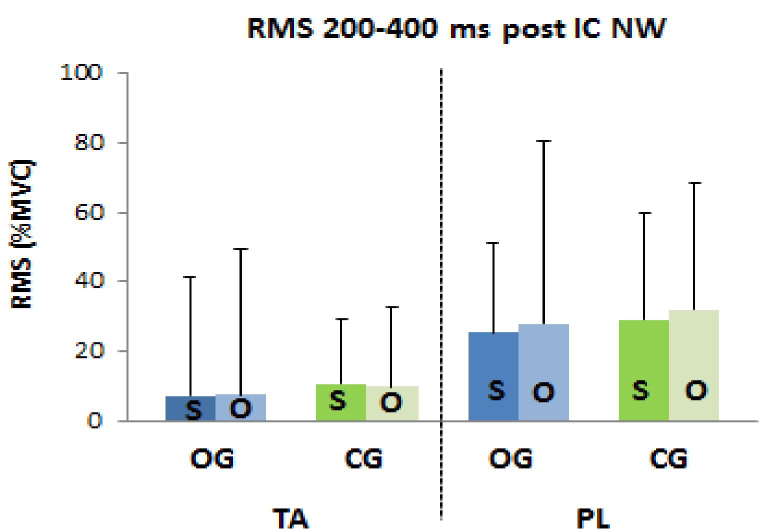
Figures 32, 34: RMS (%MVC) of TA (left) and GM (right) for NW and SC during 200-400 ms post IC, *TA- m. tibialis anterior, PL- m. peroneus longus, GM-m. gastrocnemius medialis; NW-normal walking, SC- side cutting; OG- orthoses group, SMTG- sensorimotor training group, CG- control group*

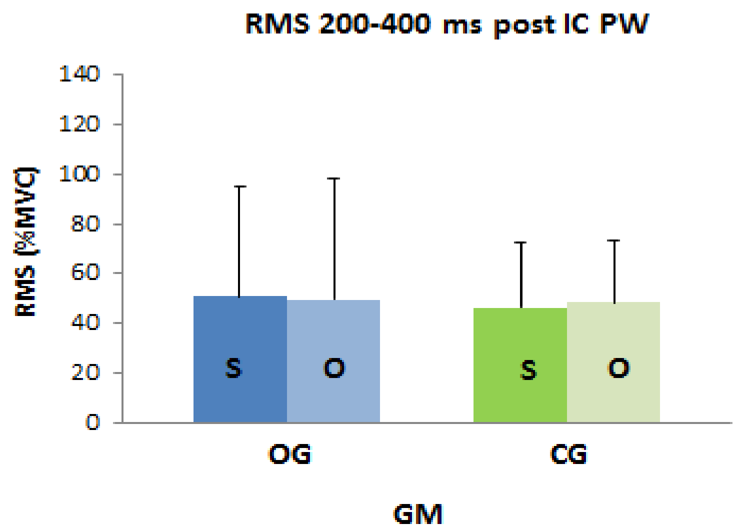






Figures 36-38: RMS (%MVC) of OG and CG for NW (PL, GM), PW (PL, GM) and SC (TA, PL, GM) during 100-50 ms pre IC, *TA- m. tibialis anterior, PL- m. peroneus longus, GM-m. gastrocnemius medialis; NW-normal walking, PW- perturbed walking, SC- side cutting; OG- orthoses group, CG-control group; S-shoe, O-orthoses*





Figures 39, 40: RMS (%MVC) of OG and CG for NW (TA, PL) and PW (GM) during 200-400 ms post IC, *TA- m. tibialis anterior, PL- m. peroneus longus, GM-m. gastrocnemius medialis; NW-normal walking, PW- perturbed walking; OG- orthoses group, CG-control group; S-shoe, O-orthoses*