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Article Title: Impairment-Based Rehabilitation Increases Lower Leg Muscle Volumes and Strength in Chronic Ankle Instability Patients: A Preliminary Study

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Title Page

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ABSTRACT

Context: Chronic ankle instability **(**CAI) patients have demonstrated atrophy of foot and ankle musculature and deficits in ankle strength. The effect of rehabilitation on muscle morphology and ankle strength has not previously been investigated in CAI patients. **Objective:** Our objective was to analyze the effect of impairment-based rehabilitation on intrinsic and extrinsic foot and ankle muscle volumes and strength in CAI patients. **Design:** Controlled laboratory study. **Setting:** Laboratory. **Patients:** Five young adults with CAI. **Intervention:** 12 sessions of supervised impairment-based rehabilitation that included range of motion, strength, balance, and functional exercises. **Main Outcome Measures:** Measures of extrinsic and intrinsic foot muscle volume and ankle strength measured before and after 4 weeks of supervised rehabilitation. Novel fast-acquisition MRI was used to scan from above the femoral condyles through the entire foot. The perimeter of each muscle was outlined on each axial slice and then the 2D area was multiplied by the slice thickness (5mm) to calculate muscle volume. Plantar flexion, dorsiflexion, inversion, and eversion isometric strength were measured using a hand-held dynamometer. **Results:** Rehabilitation resulted in hypertrophy of all extrinsic foot muscles except for the flexor hallucis longus and peroneals. Large improvements were seen in inversion, eversion, and plantar flexion strength following rehabilitation. Effect sizes for significant differences following rehabilitation were all large and ranged from 1.54 to 3.35. No significant differences were identified for intrinsic foot muscle volumes. **Conclusion:** Preliminary results suggest impairment-based rehabilitation for CAI can induce hypertrophy of extrinsic foot and ankle musculature with corresponding increases in ankle strength.

Key words: Magnetic resonance imaging, muscle morphology, therapeutic exercise

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Lateral ankle sprains (LAS) occur at a rate of 2.15 sprains per 1000 person years in the general public[1] and the rate is substantially higher in athletic and physically active populations.[2,3] Over 55% of all LAS patients do not seek care for their injury[4] and of those patients that do seek care, less than 7% are prescribed therapeutic exercises for the restoration of function and prevention of subsequent ankle sprain.[5] Inadequate management of acute LAS has been hypothesized as a potential mechanism of self-reported disability and recurrent ankle sprain.[5] Recurrent sprain, giving way, and self-reported disability for greater than 1 year following an initial sprain characterize the 40% of all LAS patients that develop chronic ankle instability (CAI).[6,7] Long-term consequences of recurrent ankle sprain include post-traumatic osteoarthritis,[8] decreased physical activity,[9] and lower overall quality of life.[10]

Invertor[11] and evertor[12] muscle weakness has been reported as a potential ankle sprain risk factor and four-way ankle strength deficits have been identified in some studies for CAI patients,[13,14] but not in others.[15-18] We have also recently elucidated corresponding muscle volume deficits of numerous extrinsic and intrinsic foot and ankle muscles in CAI patients.[19] Our previous results[19] suggest that inversion, dorsiflexion, and plantar flexion strength deficits are related to smaller muscles and that eversion strength deficits appear to be more neuromuscular, rather than due to muscle size, in nature. Supervised rehabilitation programs[20-23] emphasizing neuromuscular and balance training for CAI patients have been associated with improved patient-reported outcomes and sensorimotor measures, but the effects of such interventions on muscle volume have not been previously studied. Resistance band strength training and proprioceptive neuromuscular facilitation are both effective interventions for increasing ankle strength and decreasing perceived disability in CAI patients.[24] Strength training alone has been shown to improve not only strength measures, but also sensorimotor function (joint position sense)[25] and functional performance

(balance and hopping tests).[26] Up to this point, however, there is no evidence to suggest whether the improvements in ankle strength commonly seen following rehabilitation are also related to muscle hypertrophy.

Determining if hypertrophy occurs after rehabilitation and if it may be responsible for increases in measured force will allow for more informed decisions regarding the prescription of therapeutic exercise for the treatment of LAS and CAI. Analyzing muscle morphological changes in response to rehabilitation will also provide insight into the individuality or variability in muscular adaptability of CAI patients who, at baseline, may demonstrate impaired neuromuscular function[27,28] and smaller muscles[19] when compared to healthy counterparts. Therefore, the purpose of this preliminary investigation was to analyze the effect of progressive, impairment-based rehabilitation on extrinsic and intrinsic foot and ankle muscle volumes and four-way ankle strength in CAI patients. We hypothesized that CAI patients would demonstrate muscle hypertrophy and corresponding increases in muscle strength.

METHODS:

Study Design

We performed a descriptive laboratory study with a pre-post design to compare intrinsic and extrinsic foot and ankle muscle volumes and ankle strength prior to and following a 4-week progressive, impairment-based rehabilitation program for CAI patients. Evidence suggest that hypertrophy does not predominate over neural adaptations until 3-5 weeks,[29] however, we believe 4 weeks is sufficient to identify preliminary changes in muscle size in this small cohort that has demonstrated smaller muscles compared to healthy counterparts in our prior investigation.[19] Our independent variable was time (pre- and post-rehabilitation) and our dependent variables were mass*height normalized muscle volumes and mass normalized four-way ankle strength

(normalized force output for dorsiflexion, plantar flexion, inversion, and eversion). The study methods were approved by the University's institutional review board and all subjects provided informed consent prior to study participation.

Participants

Five young adults with CAI volunteered to participate in this preliminary study (Table 1). We have previously published the baseline muscle volume and strength data on these same five CAI patients compared to age-, sex-, and limb-matched healthy controls.[19] In the current investigation, we analyze the effect of rehabilitation on these measures in the same cohort. Additionally, these 5 subjects were part of a larger sample of CAI patients in an intervention study that assessed the effects of rehabilitation on patient-reported outcomes, range of motion, balance, strength, and electromyographic measures, but not muscle volume measures.[22] Inclusion criteria was a history of more than one significant ankle sprain with the initial sprain occurring more than one year prior to study onset and current self-reported functional deficits due to ankle symptoms that was quantified by a score of <75% on the Foot and Ankle Ability Measure (FAAM) Sport scale and a score of ≥10 on the Identification of Functional Ankle Instability scale (IdFAI). Due to the small sample size and preliminary nature of this study, we utilized a lower functional threshold for inclusion as described in our previous investigation.[19] Exclusion criteria included a history of lower extremity surgery, lower extremity fracture, foot or ankle immobilization greater than 48 hours within 6 months of study onset, an ankle sprain within 6 weeks of study onset, or any other condition known to affect muscle volumetric measurements (muscular dystrophy, multiple sclerosis, etc.). Subjects were required to be physically active at least 20 minutes/day for at least 3 days/week.

Instruments

Magnetic Resonance Imaging for Foot and Ankle Muscle Volumes

Subjects were scanned on a 3 Tesla Siemens (Munich, Germany) Trio MRI scanner as previously described[19,30] from just superior of the medial and lateral femoral condyles through the entire foot. Images were acquired using a 2-D multi-slice non-Cartesian spiral gradient echo sequence with a scan time of 15 minutes per subject. Scan parameters for the shank were as follows: TE/TR/α: 3.8ms/800ms/90°, field of view: 400mm x 400mm, slice thickness: 5mm, in plane spatial resolution: 1.1mm x 1.1mm.[19] Scan parameters were identical for the foot with the exception of a smaller field of view (250mm x 250mm) and commensurately higher resolution.[19] Due to the smaller field of view for the intrinsic foot muscles, a Siemens 4-channel large flex coil was utilized to increase signal-to-noise ratio.[19]

Four-way Ankle Strength Testing

Ankle strength (dorsiflexion, plantar flexion, inversion, and eversion) was measured using a hand-held dynamometer (Accelerated Care Plus Corp, Reno, NV).

Procedures

Subjects completed a general health history questionnaire, Godin Leisure-Time Physical Activity Questionnaire,[31] FAAM Activities of Daily Living[32] and Sport scale,[33] and IdFAI questionnaire.[34] Prior to strength testing, subjects performed a 5-minute warm-up by walking on a treadmill at a self-selected pace. For each testing position, subjects were instructed to complete practice trials at 50% and then 75% of maximal effort against the tester's resistance.[22] Three 5-second maximal voluntary isometric contractions (MVICs) were completed with a 15 second rest period between trials. All three trials for an individual ankle motion were completed before

transitioning to the 50% and 75% practice trials of the next tested ankle motion. Strength testing positions were consistent with recommendations by Kelln et al.[35] for hand-held dynamometry. The MRI was scheduled within 1 week of strength testing for both pre- and post-rehabilitation time points.

Subjects were positioned in the MRI scanner supine and feet first. Axial slices for the shank were obtained contiguously in sets of 20 images from just superior to the femoral condyles distally through the most inferior aspect of the calcaneus. The research team then applied the flex coil around the feet and axial slices were obtained in sets of 20 contiguous images from just posterior to the calcaneus anteriorly through the entire foot.

Rehabilitation Protocol

We utilized the same progressive, impairment-based rehabilitation protocol as a previous study that demonstrated large improvements in strength, balance, range of motion, and self-reported function in CAI patients.[22] A detailed description of the rehabilitation protocol and individualized progression algorithm has previously been published as a supplement to the aforementioned study.[22] Briefly, the rehabilitation protocol was developed based on Donovan and Hertel's[36] paradigm for each of the four common CAI impairment domains of range of motion, strength, balance, and functional activities. Subjects completed 12 sessions of supervised rehabilitation with a certified athletic trainer. Sessions were one hour in duration and subjects completed 3 sessions per week for four consecutive weeks. Each subject's daily progression was individualized based on pre-determined criteria and the clinician's clinical expertise.[22] The progressions were individualized to ensure that each subject was challenged within each impairment domain[36] from day 1 until they completed the 12th session. All subjects completed 12

rehabilitation sessions and then returned to the lab within 48 hours for follow-up strength testing and within 7 days for the post-rehabilitation MRI.

Data Reduction

Magnetic Resonance Image Processing

A detailed and technical description of the data processing technique used in this study has been published previously.[30] Briefly, each intrinsic and extrinsic foot and ankle muscle was segmented using in-house segmentation software written in Matlab (The Mathworks Inc., Natick, MA, USA). The segmentation process required the investigator to specify 2-D contours defining the perimeter of each muscle in each axial slice. The segmentation analysis was performed by three trained research assistants who utilized a detailed slice-by-slice segmentation atlas created from a previous data set using similar scanning parameters and segmentation procedures. The inter-user variability for this process has been determined to be acceptable at <0.6%[30] and these methods have been used in numerous patient populations.[19,30,37,38] The research assistants were blinded to whether a scan was a pre- or post-rehabilitation scan during segmentation of all axial slices. A single highly trained investigator that was also blinded to group membership, to ensure consistency across all segmented images, then screened the final images. The 2-D area of each muscle for each axial slice was multiplied by the slice thickness (5mm) and summed over all slices to obtain muscle volume. Muscle volumes were normalized to the height-mass product of each subject. [19,30,38] Normalized muscle volumes ($cm^3/m*kg$) were utilized to compare pre- and post-rehabilitation muscle volumes. We compared pre- and post-rehabilitation individual muscle volumes as well as summed compartmental (anterior, lateral, deep posterior, superficial posterior) and total muscle volume for the extrinsic muscles and total intrinsic plantar muscle volumes.

Four-way Ankle Strength

Strength was recorded as the maximal force (N) output during the individual MVIC trials for each ankle motion. The average over the three trials was computed for each of the four tested motions and normalized to each subject's mass (kg) and the normalized force output (N/kg) was utilized to compare pre- and post-rehabilitation strength measures.

Statistical Analysis

All dependent variables (muscle volume and strength) were compared pre- and post-rehabilitation with group means and associated 90% confidence intervals (CIs). For dependent variables where the CIs between pre- and post-rehabilitation did not overlap, it was determined there was a significant difference following rehabilitation. We also calculated Cohen's d effect sizes and associated 90% CIs to estimate the magnitude and precision of the effect due to rehabilitation. Effect sizes were interpreted as follows: ≥0.80 was large, 0.50-0.79 was moderate, 0.20-0.49 was small, and <0.20 was trivial.[39] Positive effect sizes indicate an improvement in muscle size (hypertrophy) or an increase in ankle strength. Data was analyzed using Microsoft Excel Version 14.1.0 (Microsoft, Redmond, WA).

Normative Database Comparison

Pre- and post-rehabilitation extrinsic muscle volumes were also compared to a previously established normative database for lower extremity muscle volumes.[30] The database was created as part of another project that quantified the relationship between lower extremity muscle volumes to body mass and height in 24 healthy subjects.[30] To compare muscle volumes for the subjects in our current study to the previously published normative values,[30] we calculated z-scores for each extrinsic muscle, individually for all 5 CAI subjects prior to and following rehabilitation.[19] We

then calculated the z-score change by subtracting the pre-rehabilitation z-score from the post-rehabilitation z-score for each extrinsic muscle volume to illustrate the relative change with respect to the normative database.[19,30] To our knowledge, our current study is only the second study to quantify the intrinsic foot muscle volumes using this technique and thus it was not possible to compare the CAI intrinsic foot muscles to normative values.[19] Clinical interpretation of z-scores was determined *a priori* as follows: $z \geq 3.0$: extreme hypertrophy, $3 > z \geq 2$: moderate hypertrophy, $2 > z \geq 1$: slight hypertrophy, $1 > z > -1$: normal, $-1 \geq z > -2$: slight atrophy, $-2 \geq z > -3$: moderate atrophy, and $-3 \geq z$: extreme atrophy.[19] It is important to note that the normative database comparisons are for illustrative purposes to demonstrate the individuality in patient responses and for consistency with our prior investigation with the same cohort, but for statistical comparisons to determine the effect of rehabilitation on muscle volumes, we utilized group means and 90% CIs between pre- and post-rehabilitation as described above.

RESULTS:

Muscle Volumes

Extrinsic Foot and Ankle Muscle Volumes

Rehabilitation resulted in significant hypertrophy of overall extrinsic foot and ankle muscle volume (PRE: 9.62±0.39 $cm^3/m*kg$; POST: 11.87±0.86 $cm^3/m*kg$). This overall improvement was driven by large increases in the superficial posterior and anterior compartments (PRE: 5.15±0.55 $cm^3/m*kg$; POST: 6.62±0.45 $cm^3/m*kg$ and PRE: 1.55±0.11 $cm^3/m*kg$; POST: 1.94±0.17 $cm^3/m*kg$, respectively, Figure 1). Rehabilitation resulted in large increases in all foot and ankle extrinsic muscle volumes, except for the flexor hallucis longus and peroneals (PRE: 0.87±0.22 $cm^3/m*kg$; POST: 0.66±0.18 $cm^3/m*kg$ and PRE: 0.91±0.11$cm^3/m*kg$; POST:

1.17±0.19 $cm^3/m*kg$, respectively, Table 2). Effect sizes for all significant hypertrophic gains following rehabilitation were large and ranged from 1.75 to 3.35 with 90% CIs that were entirely positive, indicating meaningful improvements in muscle size following rehabilitation for CAI.

Extrinsic Foot and Ankle CAI Muscle Volume Normative Database Comparisons

Prior to rehabilitation, CAI patients presented with slight atrophy (average z-scores of $-1 \geq z > -2$) of the flexor digitorum longus (average $z = -1.23$) and soleus (average $z = -1.45$) and moderate atrophy (average z-scores of $-2 \geq z > -3$) of the medial gastrocnemius (average $z = -2.00$), lateral gastrocnemius (average $z = -2.16$), phalangeal extensors (average $z = -2.06$), and the popliteus (average $z = -2.64$) (Figure 2a). Following rehabilitation, the average z-score for every extrinsic foot and ankle muscle was within a normal range (average z-scores of $-1 > z > 1$) compared to the normative values (Figure 2b). The z-score change is illustrated individually for each patient in Figure 3.

Intrinsic Foot Muscle Volumes

There were no significant differences following rehabilitation for any intrinsic foot muscle volumes (Table 3). Effect sizes ranged from -0.56 to 1.05 with 90% CIs that all crossed zero suggesting uncertainty about the effect of rehabilitation on intrinsic foot muscle volumes for CAI patients.

Four-way Ankle Strength

Rehabilitation significantly improved inversion and eversion ankle strength (Figure 4). Effect sizes for significant strength gains ranged from 2.03 to 2.61 with 90% CIs that were entirely positive suggesting meaningful improvements in ankle strength following rehabilitation.

Self-Reported Function:

Following rehabilitation, CAI subjects demonstrated a 5.1% increase in FAAM-ADL scores and a 31.0% increase in FAAM-Sport scores (FAAM-ADL: PRE: 89.9±3.6%, POST: 94.9±7.8%; FAAM-Sport: PRE: 54.4±22.1%, POST: 85.4±5.5%). Minimal clinically important differences have been reported at 9.5% for FAAM-ADL and 28.1% for FAAM-ADL.[32]

DISCUSSION:

Following 4 weeks of progressive, impairment-based rehabilitation, CAI patients demonstrated meaningful improvements in extrinsic foot and ankle muscle volumes and concurrent improvements in ankle strength and self-reported function. We did not identify any improvements in intrinsic foot muscle volumes post-rehabilitation. This is the first study to quantify muscle morphological adaptations to rehabilitation for CAI patients. These results increase our understanding of the physiological mechanisms by which CAI patients can increase force output with rehabilitation.

Previously, we identified moderate to large deficits in muscle volumes and strength of these same subjects compared to age-, sex-, and limb-matched healthy counterparts.[19] In that same investigation we previously published the normative database comparison that represents the 'pre-rehabilitation' data of the current investigation. We have now demonstrated the potential for these morphological deficiencies to be overcome with progressive, impairment-based rehabilitation in accordance with Donovan and Hertel's[36] recommendations for the rehabilitation of CAI patients. It has been shown that strength training and subsequent improvements in force output are associated with improved joint position sense[25] and functional performance[26] and we have expanded upon this knowledge by demonstrating muscle hypertrophy can be identified following just four-weeks of rehabilitation for CAI.

Identifying muscle hypertrophy with only four weeks of rehabilitation is counterintuitive to the central dogma of resistance training for hypertrophic gains.[29,40,41] Conventional theory would suggest that strength improvements in the first weeks of training should be neuromuscular in nature followed by a progression to morphological and architectural adaptations.[42,43] Initially, this theory was based upon the observation that the initial increase in strength upon initiation of progressive resistance training occurred at a rate that far exceeded what could be explained solely by morphological adaptations.[29] This theory is based on studies of untrained individuals in which neural adaptations would be expected to be the largest.[42] Conversely, this theory suggests that if you were to take individuals that have routinely stressed their neuromuscular system prior to beginning a strength training protocol, it would not be unreasonable to see a combination of neural and structural adaptations both contributing to increased strength.[42] In CAI patients, we have previously demonstrated that traditional rehabilitation exercises (forward lunge, single limb balance, dynamic balance, and lateral hopping tasks) can result in up to 121% motor recruitment when compared to maximal voluntary isometric contractions.[44] We posit that the large neuromuscular demand placed on the shank musculature during simple functional tasks,[44] that CAI patients would be exposed to through routine physical activity prior to enrollment (based upon our inclusion criteria) in our rehabilitation protocol, may have allowed them to demonstrate hypertrophic gains with four weeks of progressive rehabilitation, however the true relationship and/or contribution of neuromuscular versus hypertrophic gains remains unclear. Non-pathological populations have seen approximately a 12% increase in quadriceps cross-sectional area after just three weeks of training,[45] compared to a 23% increase in total shank muscle volume seen in our study following 4 weeks of progressive rehabilitation for CAI. With the understanding that our CAI patients began the rehabilitation protocol with significant atrophy compared to

healthy counterparts,[19] it is no surprise that the increase in muscle size relative to their respective baseline muscle volume was greater than seen in non-pathologic populations.[45] Additionally, even though the CAI subjects saw large improvements in muscle size, when compared to the normative database, the vast majority of the individual muscles across the CAI subjects at the end of the study only approximated the average muscle size of a healthy counterpart. This may suggest that four weeks of rehabilitation was enough to demonstrate hypertrophic gains in some muscles but was likely not a long enough duration or sufficient intensity to maximize a CAI patients potential and further or continued rehabilitation may be of benefit in clinical settings. In other investigations, large improvements in quadriceps femoris cross sectional area, fascicle length, and pennation angle have also been seen after 20 and 35 days of resistance training, collectively adding credence to the increased muscle size seen in our CAI patients after four weeks of rehabilitation.[46]

Our previous results[19] on muscle volumes demonstrated a disproportional deficit in eversion ankle strength when considering the relatively normal peroneal muscle volumes seen in the CAI subjects. We postulated that this uncoupling of peroneal muscle size and eversion weakness supported the theory of peroneal neuromuscular dysfunction with CAI.[19] Similarly, in our current investigation, there were minimal increases in peroneal muscle size but large and meaningful improvements in eversion strength. This may suggest that muscles with the greatest atrophy at baseline may have the greatest potential for relative hypertrophic gains following rehabilitation and that other muscles may have greater potential for neuromuscular gains prior to demonstrating meaningful hypertrophy. Unfortunately, due to the nature of our study, we cannot delineate the absolute contribution of neural adaptations and hypertrophic gains with regards to force output after rehabilitation.

The CAI patients in our study had substantial variability in which muscles demonstrated the most atrophy at baseline and which muscles had the largest improvements in muscle size following rehabilitation. This is important from a clinical perspective because the rehabilitation protocol utilized in our study advocates for an 'assess-treat-reassess' approach so that clinicians can identify and treat each patient's specific impairments. This is useful in a clinical setting but represents a challenge in clinical research where individual improvements may become washed out or hidden within the group means and confidence intervals.

We did not see any meaningful improvements in intrinsic foot muscle volumes following rehabilitation in our CAI patients. We did utilize short foot exercises in this rehabilitation protocol, but our results suggest that initial adaptations to the novel exercise, if any, were not that of hypertrophy. Unfortunately, we cannot speculate on whether CAI patients would need a longer duration, larger volume of exercises, greater level of resistance, or different exercises to see architectural changes in intrinsic foot muscles. Future studies should evaluate the effectiveness of intervention programs specifically aimed at improving plantar intrinsic muscle function to assess whether hypertrophy of these muscles may be accomplished.

Limitations

Limitations of this preliminary investigation include the relatively small sample size due to the high time demands of the MRI data segmentation process and analysis, the disproportionate number of females (4 out of 5), and the lack of surface electromyography of intrinsic and extrinsic foot and ankle musculature to elucidate the neural and morphological adaptations to therapeutic exercise for CAI. Future studies are needed with larger sample sizes and a control group for comparison to ensure muscle volumes are consistent over time in CAI patients. Furthermore, the lack of long-term outcomes after the cessation of rehabilitation limits our understanding of the

duration of which hypertrophic and strength gains will be maintained without continued rehabilitation. Lastly, we cannot speculate about how the results would change with a longer 8-12 week rehabilitation protocol.

Conclusion

Our preliminary results indicate that four weeks of progressive, impairment-based rehabilitation for CAI can increase extrinsic foot and ankle muscle volumes with concurrent improvements in ankle strength and self-reported function. Rehabilitation was unable to increase intrinsic foot muscle volumes. Clinicians should be aware of both the neural and morphological adaptations that can occur in response to rehabilitation for CAI patients.

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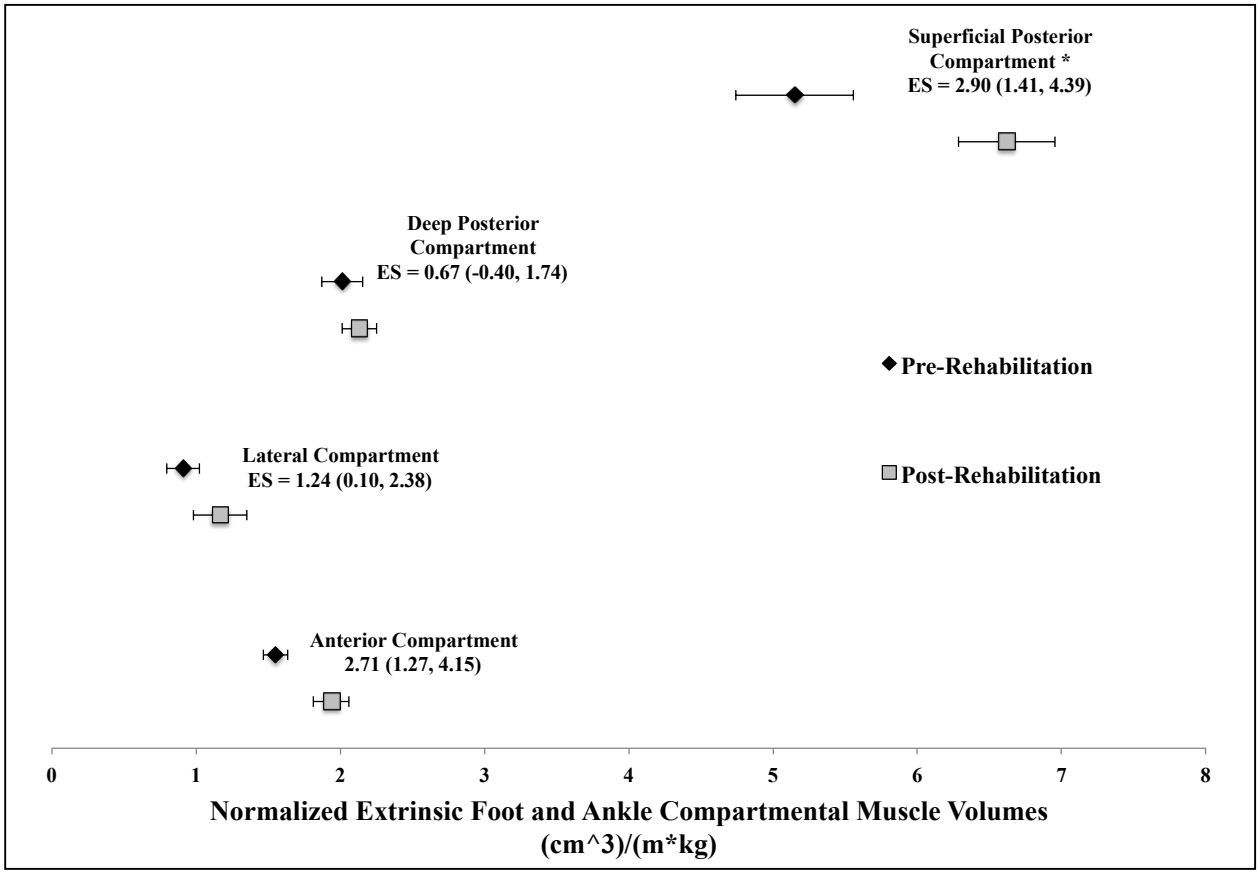

FIGURE 1. Extrinsic Foot and Ankle Muscle Compartment Volumes $\left(\frac{cm^3}{m*kg}\right)$ and Associated Cohen's d Effect Sizes and 90% Confidence Interval

*Denotes significant difference as indicated by group means and associated 90% confidence intervals that do not overlap

Positive effect size indicates lower muscle volumes with CAI

"Impairment-Based Rehabilitation Increases Lower Leg Muscle Volumes and Strength in Chronic Ankle Instability Patients: A Preliminary Study" by Feger MA et al.
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Figure 2a.

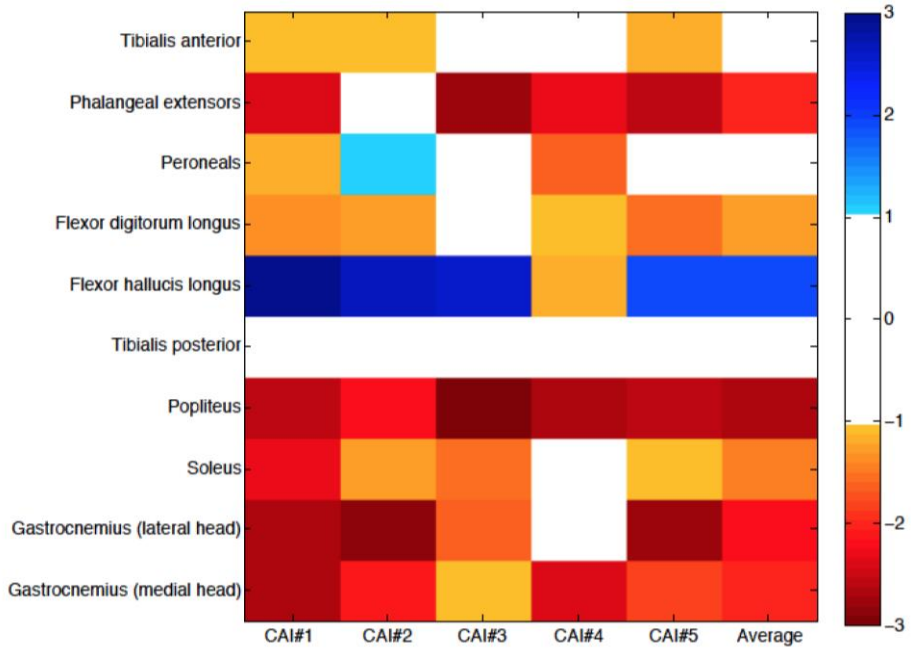

Figure 2b.

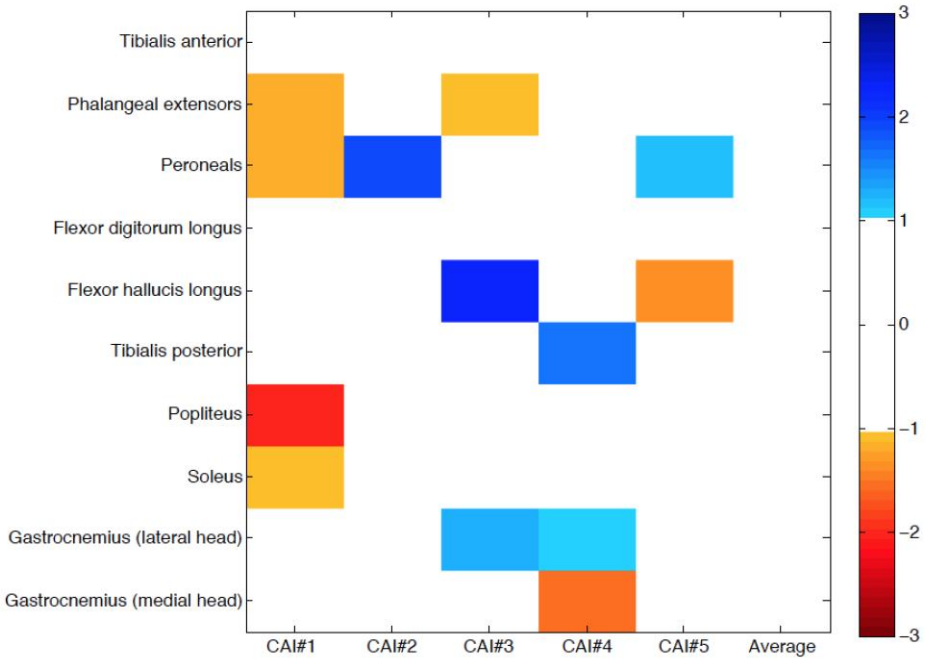

FIGURE 2. Normative database z-score comparisons for each muscle, individually for each CAI subject, prior to (2a) and following (2b) impairment-based rehabilitation

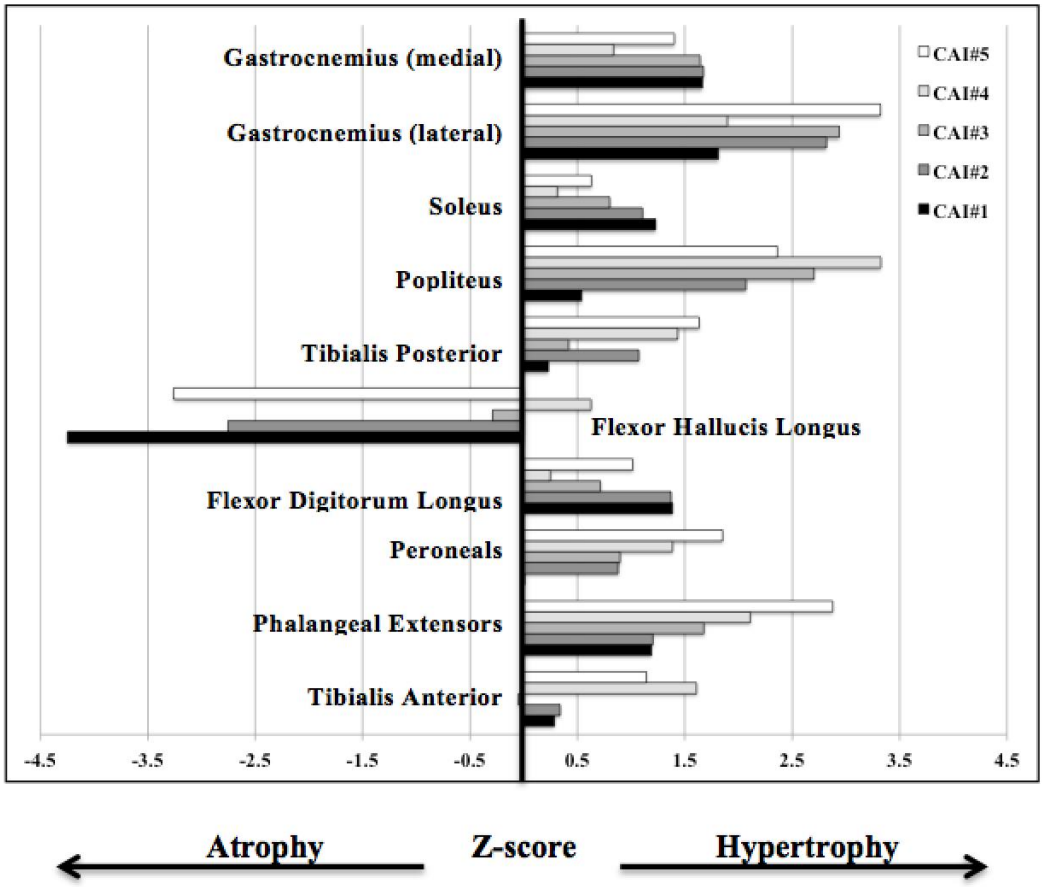

FIGURE 3. Change in z-score (post z-score – pre z-score) due to rehabilitation for all extrinsic foot and ankle muscles individually for each subject

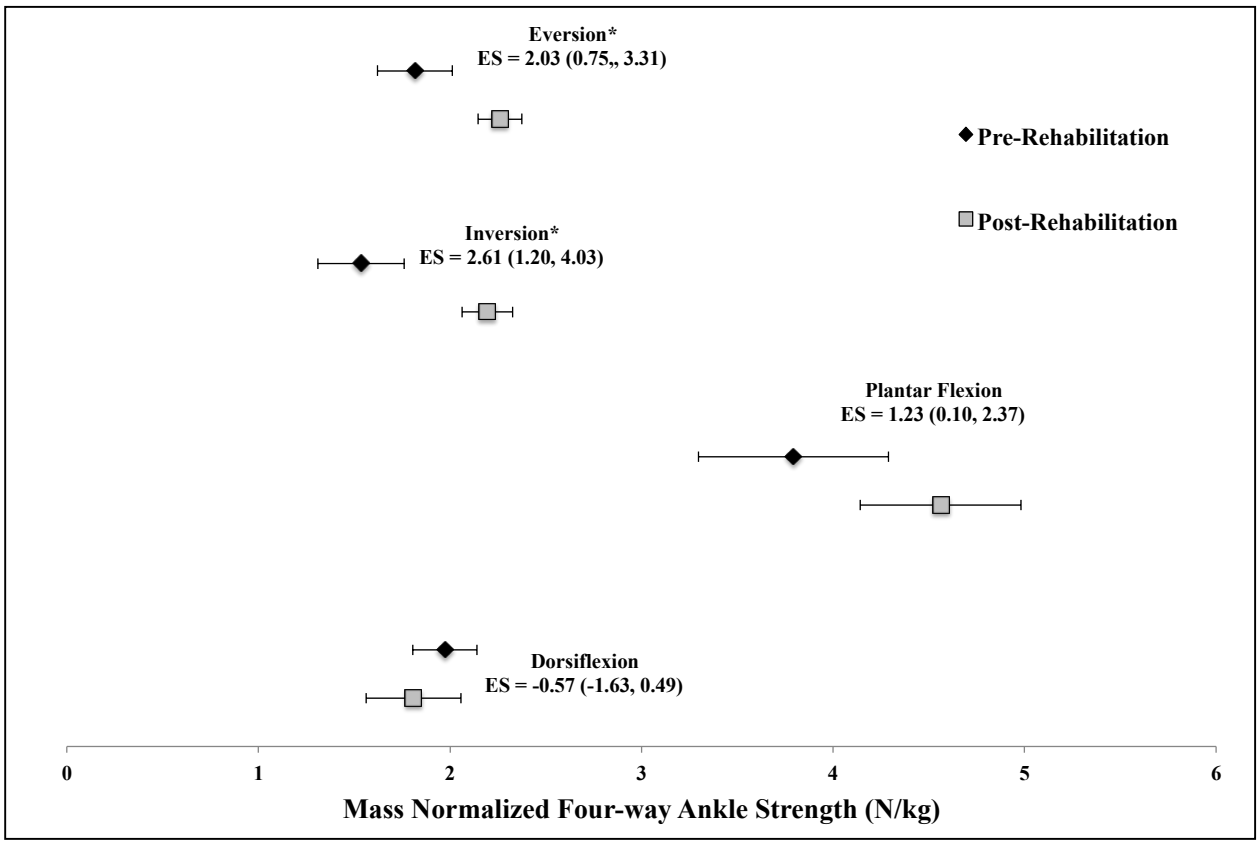

FIGURE 4. Four-way Ankle Strength Measures N/kg and Associated Cohen's d Effect Size and 90% Confidence Interval

*Denotes significant difference as indicated by group means and associated 90% confidence intervals that do not overlap

Positive effect size indicates lower muscle volumes with CAI

TABLE 1. Subject Demographics

	CAI Mean ± SD N=5
Age	23.0 ± 4.0
Sex	1M:4F
Height (cm)	165.4 ± 8.8
Mass (kg)	66.5 ± 7.3
Number of ankle sprains	3.2 ± 1.6
Time from last sprain (months)	27.8 ± 21.2
FAAM ADL	89.9 ±3.6
FAAM sport score	54.4 ± 22.1
IdFAI	24.0 ± 3.8
Godin Leisure Time Physical Activity Scale	51.8 ± 23.0

Abbreviations: CAI=Chronic Ankle Instability, SD=Standard Deviation, FAAM=Foot and Ankle Ability Measure, ADL=Activities of Daily Living, IdFAI=Identification of Functional Ankle Instability

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TABLE 2. Extrinsic Foot and Ankle Muscle Volumes $\left(\frac{cm^3}{m*kg}\right)$ and Associated Cohen's d Effect Sizes

Extrinsic Muscles	Pre-Rehabilitation Mean (90% CI)	Post-Rehabilitation Mean (90% CI)	Cohen's d Effect Size (90% CI)
Tibialis Anterior	0.92* (0.90, 0.95)	1.09* (1.01, 1.18)	1.93 (0.67, 3.19)
Phalangeal Extensors	0.63* (0.53, 0.72)	0.84* (0.75, 0.96)	1.75 (0.52, 2.97)
Peroneals	0.91 (0.80, 1.02)	1.17 (0.98, 1.35)	1.24 (0.10, 2.38)
Flexor Digitorum Longus	0.16* (0.15, 0.18)	0.23* (0.21, 0.25)	2.82 (1.35, 4.29)
Flexor Hallucis Longus	0.87 (0.71, 1.02)	0.66 (0.53, 0.79)	-1.04 (-2.14, 0.07)
Tibialis Posterior	0.86* (0.79, 0.92)	1.05* (0.96, 1.14)	1.84 (0.60, 3.08)
Popliteus	0.13* (0.12, 0.14)	0.19* (0.17, 0.21)	2.56 (1.16, 3.96)
Gastrocnemius Medial Head	1.62* (1.50, 1.75)	2.03* (1.87, 2.18)	2.12 (0.82, 3.42)
Gastrocnemius Lateral Head	0.90* (0.78, 1.03)	1.34* (1.19, 1.49)	2.38 (1.02, 3.74)
Soleus	2.62* (2.40, 2.84)	3.25* (3.09, 3.41)	2.42 (1.05, 3.79)

* Denotes significant difference as indicated by group means and associated 90% confidence intervals that do not overlap

Abbreviations: CI=Confidence Interval

Positive effect size indicates increased muscle volume following rehabilitation

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TABLE 3. Intrinsic Foot Muscle Volumes $\left(\frac{cm^3}{m*kg}\right)$ and Associated Cohen's d Effect Sizes

Intrinsic Foot Muscles	Pre-Rehabilitation Mean (90% CI)	Post-Rehabilitation Mean (90% CI)	Cohen's d Effect Size (90% CI)
Abductor Hallucis	0.21 (0.17, 0.25)	0.21 (0.18, 0.24)	0.01 (-1.03, 1.05)
Adductor Hallucis Obliqus	0.07 (0.06, 0.08)	0.06 (0.05, 0.08)	-0.56 (-1.62, 0.50)
Adductor Hallucis Transversus	0.02 (0.01, 0.02)	0.03 (0.02, 0.03)	1.05 (-0.06, 2.16)
Flexor Hallucis Brevis	0.06 (0.05, 0.07)	0.09 (0.06, 0.12)	0.90 (-0.19, 1.99)
Abductor Digiti Minimi	0.16 (0.14, 0.18)	0.16 (0.13, 0.18)	-0.18 (-1.22, 0.87)
Flexor Digiti Minimi	0.08 (0.06, 0.10)	0.07 (0.06, 0.08)	-0.45 (-1.50, 0.61)
Extensor Digitorum Brevis	0.08 (0.06, 0.10)	0.10 (0.07, 0.14)	0.64 (-0.53, 1.70)
Flexor Digitorum Brevis	0.20 (0.16, 0.23)	0.21 (0.17, 0.24)	0.19 (-0.85, 1.23)
Interosseus	0.17 (0.14, 0.20)	0.20 (0.18, 0.23)	0.81 (-0.27, 1.89)
Quadratus Plantae	0.13 (0.10, 0.16)	0.14 (0.12, 0.16)	0.40 (-0.65, 1.45)
Total Plantar Intrinsic Foot Muscle Volume	1.09 (0.95, 1.23)	1.16 (1.05, 1.27)	0.39 (-0.66, 1.44)

* Denotes significant difference as indicated by group means and associated 90% confidence intervals that do not overlap

Abbreviations: CI=Confidence Interval

Positive effect size indicates increased muscle volume following rehabilitation