Potential Corticomotor Plasticity in Those with and without Chronic Ankle Instability

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ABSTRACT

KOSIK, K. B., M. TERADA, C. P. DRINKARD, R. S. MCCANN, and P. A. GRIBBLE. Potential Corticomotor Plasticity in Those with and without Chronic Ankle Instability. *Med. Sci. Sports Exerc.*, Vol. 49, No. 1, pp. 141–149, 2017. **Introduction**: Quantifying corticomotor alterations is important to understand the neurophysiological mechanisms that likely contribute to the neuromuscular control deficits observed in patients with chronic ankle instability (CAI). Corticomotor output mapping provides further insight into the changes within the motor cortex and identifies potential changes in the area of the motor cortex associated with selected muscles. Therefore, this investigation compared the corticomotor map output for the fibularis longus (FL) muscle in patients with and without CAI. **Methods**: Eighteen CAI patients and 16 healthy controls (HC) volunteered. Transcranial magnetic stimulation was used to map the motor cortex's representation of the FL. The normalized average of three motor evoked potentials at 100% of active motor threshold intensity was recorded for each scalp site on a 6 × 6 cm grid. Corticomotor output map was compared between groups through 1) the size of the corticomotor map area, 2) the volume of the corticomotor map, and 3) the location of cortical representation. Independent *t*-tests were used to assess group differences in each mapping outcome variable. Cohen's *d* effect sizes along with 95% confidence intervals were calculated using the pooled SD values. **Results**: CAI patients exhibited less map volume ($P = 0.018$, CAI = 8.2 ± 3.2 cm^2 mV vs HC = 11.3 ± 3.9 cm^2 mV) and map area ($P = 0.046$, CAI = 12.8 ± 6.0 cm^2 vs HC: 17.4 ± 6.9 cm^2) compared with HC. **Conclusions**: The smaller map area and volume suggest a more concentrated area of neurons communicating with the FL muscle in patients with CAI. Consequently, motor cortical cells on the border of the FL excitation area are less committed to the proper function of the FL muscle and may be recruited by other surrounding areas. This may explain altered movement strategies that lead to ankle reinjury. **Key Words:** FIBULARIS LONGUS, NEUROMUSCULAR ACTIVITY, MOTOR CORTEX, TRANSCRANIAL MAGNETIC STIMULATION

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The most common lower extremity injury occurring during physical activity is a lateral ankle sprain (LAS) (12). It has been estimated that ~628,000 ankle sprains occur each year in the United States, with 60% of individuals having reported some form of ankle injury history (11,46). Unfortunately, acute LAS are often viewed as an innocuous injury that requires little treatment and have minimal long-term consequences (20). However, many patients go on to experience recurrent injuries, self-reported disability, and feeling of instability and/or "giving way" (7). This negative cascade of events is commonly termed as chronic ankle instability (CAI) (7). A growing body of research has illustrated that CAI threatens general health-related quality of life (13) and decreases physical activity levels (14). Furthermore, there is strong evidence suggesting that CAI could accelerate the onset of post-traumatic ankle osteoarthritis (6).

Impairments in the sensorimotor system have been considered to be an important factor that is responsible for activity limitations and decreased health-related quality of life associated with CAI (10). An initial LAS disrupts sensory inputs from the damaged ankle joint receptors to the central nervous system (CNS) that may chronically reorganize motor control in the corticospinal system (10). Altered reorganization of the sensorimotor system has been observed in patients with CAI (1,9,38). Specifically, there is altered spinal reflex excitability (16,28) and decreased corticomotor excitability (23,30) of the fibularis longus (FL) muscle in people with CAI. Further, these altered levels of neural excitability of the FL have been associated with physical and self-reported disability observed in people with CAI (15,30). Therefore, understanding the reorganization of descending motor pathways within the CNS will significantly improve our knowledge of the neurophysiological mechanism, which may explain the self-reported disability consistently observed in patients with CAI.

Corticomotor output mapping is a technique using transcranial magnetic stimulation (TMS) to further investigate supraspinal aspects of motor control within the corticospinal pathway (32). Briefly, focal magnetic pulses produced with TMS are applied to different scalp positions over the primary motor cortex while recording motor evoked potentials (MEP)

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in selected musculature, generating a corticomotor output map (32). This map provides additional information about the plastic changes occurring in the motor cortex (32). Subsequently, mapping of the motor cortex can create a representation of the excitable area associated with individual muscles (45). For instance, expansion of the corticomotor area associated with the FL after an initial LAS may be observed as a result of the increase in recruitment of motor cortical cells to main function or uncovering of latent neuronal connection. The expansion or restrictions of the mapped area would indicate reorganization of the corticomotor output, influencing the efficacy of the communication from the descending corticospinal tracts responsible for voluntary movement of the FL, which is likely a contributing factor to the clinical impairments observed in CAI. Early work using TMS corticomotor output mapping technique has demonstrated increased mapping volume and area in the primary motor cortex in patients with low back injury (41) and persistent elbow pain (34). Increased mapped volume and area may blur the specific territory of the cortical representation for each muscle, possibly reducing discrete muscular activation and impairing independent fine motor control of ankle movement. Although altered muscular activations of the FL has been found in those with CAI (23,28,30), the information available on the plastic changes in the primary motor cortex in CAI population is still quite limited.

Therefore, our primary purpose was to compare the motor cortical organization of the FL between individuals with and without CAI using corticomotor output map with TMS. Researchers have reported decreased corticomotor excitability of the FL in patients with CAI (23,30), possibly requiring the CNS to expand the recruitment of motor cortical cells from the areas representing other muscles to maintain optimal neuromuscular control. Therefore, we hypothesized that individuals with CAI would have an increase in corticomotor output map area and volume. In addition, the sensorimotor system may have variations in motor control strategies that are adopted over time after LAS and severity level of self-reported instability. Therefore, our secondary aim was to determine whether the changes in cortical reorganization were associated with the number of previous LAS, the duration of time since the most recent LAS, and severity of the CAI symptoms. Exploring the influence of the length of time since a LAS occurred, the number of LAS sustained, and the severity of self-reported instability on neuromuscular characteristics of CAI may provide additional insight into mechanisms underlying postinjury neuroplasticity.

METHODS

Sample Size

To our knowledge, there is no existing study that has investigated corticomotor output mapping within a CAI population. Therefore, based on previously published data investigating similar outcome measures of corticomotor map in patients with low back pain (40) and of corticomotor excitability of the FL in participants with CAI (30), 15 participants were needed in each group to observe a 10% group difference in the outcome variable with associated power of 0.80 and strong associated effect sizes.

Participants

Eighteen participants with self-reported CAI and 16 participants with no previous ankle injury history were recruited from the university and surrounding community for the current study. Before enrolling, the primary aim of the study and the experimental procedures were explained to all participants. All participants read and signed the informed consent approved by the institutional review board, which was in accordance with the principles outlined in the Declaration of Helsinki.

All participants were free from any of the following: 1) diagnosed balance, vestibular, or respiratory disorder; 2) history of low back pain in the previous 6 months; 3) previous history of fracture or surgery in the lower extremity; 4) history of seizures; 5) history of a concussion in the past 6 months; and 6) history of neurological injuries or diseases. In addition, all participants met additional inclusion criteria for TMS in accordance with the TMS safety guidelines outlined by the National Institutes of Neurological Disorders and Stroke (31).

Inclusion criteria for the current study were based on the selection criteria for CAI established by the International Ankle Consortium (7). Participants were required 1) to have a previous history of an acute LAS (which caused swelling, pain, and/or temporary loss of function), 2) to have at least two repeated episodes of "giving way" in the previous 6 months, 3) to experience recurrent ankle sprains, and 4) to have a score of ≥5 on the Ankle Instability Instrument (AII), ≥11 on the Identification of Functional Ankle Instability (IdFAI), and ≤24 on the Cumberland Ankle Instability Tool (CAIT) (7).

Participants were included in the control group if they had the following: 1) no previous musculoskeletal and neurovascular injuries in the lower extremity, 2) no reported episodes of "giving way" or instability, and 3) a score of 0 on the AII and IdFAI and 30 on the CAIT. Healthy participants with a score of 0 on the AII and IdFAI and 30 on the CAIT were enrolled to ensure that these participants have not experienced any feelings of "giving way," weakness, or instability within their ankle.

In addition, we assessed the level of self-reported ankle functional limitations using the Foot and Ankle Ability Measure activities of daily living subscale (FAAM-ADL) and sports subscale (FAAM-S). If a participant reported a history of bilateral ankle injury, we selected the limb with the higher number of giving-way episodes and the greatest amount of self-reported functional limitations on the FAAM as the limb that would be tested.

A single investigator (P. A. G.) performed all the screening procedures for enrolling participants. Two additional investigators

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that were blinded to group membership performed the data collection and analysis. Specifically, the primary author (K. B. K.) was responsible for recording and analyzing all of the primary outcome measures, whereas the second investigator (M. T.) was responsible for measurements of spinal reflex excitability of the FL and coil placement during the TMS testing.

Instrumentation

All EMG signals were collected through two surface pregelled Ag/AgCl EMG recording electrodes (EL503; BIOPAC Systems, Inc., Goleta, CA) placed 1.75 mm apart over the greatest bulk of the FL muscle, approximately 2 to 3 cm inferior to the fibular head (27). A ground electrode was placed over the ipsilateral lateral malleolus. The areas were shaved, abraded with fine sandpaper, and then cleaned with isopropyl alcohol wipes.

Spinal reflex excitability was measured using a BIOPAC stimulator module (STM100A, BIOPAC Systems, Inc.) and a 200-V maximum stimulus isolation adaptor (STIMISOC BIOPAC Systems, Inc.) that delivered a 1-ms square wave stimulus through a 2-mm shielded disk simulating electrode (EL254S; BIOPAC Systems, Inc.) to the proximal common peroneal nerve.

Corticomotor map measurements were performed using a Magstim 200 (Magstim Company, Ltd., Wales, UK) equipped with a double-cone coil configuration capable of delivering a single magnetic pulse over selected scalp sites. A 16-bit converter (MP150, Biopac Systems, Inc.) was used to process analog-to-digital signal conversion. EMG signals were sampled at 2000 Hz and amplified at a gain of 1000 (EMG100C, Biopac Systems, Inc.). EMG and stimulation signals were visualized through Acqknowledge Software (BIOPAC Version 4.1, BIOPAC Systems, Inc.).

Experimental Procedures

Participants reported to the research laboratory for a single testing session.

Spinal excitability. The maximal muscle response of the FL measured by peripheral nerve stimulation was used as a normalizing factor for the corticomotor output map measures. Spinal reflex excitability was performed using a previously published protocol (15). Briefly, participants were prone on an examination table with their knee slightly flexed and the ankle elevated and supported by a pillow. The stimulating electrode was positioned over the proximal common peroneal nerve and was shifted to find the location that elicited the largest peak-to-peak twitch response at a constant stimulus. This location was used for all subsequent testing trials. The electrical stimulus was then increased or decreased to find the largest peak-to-peak Hoffmann reflex (H_{max}). Once the intensity that produced the largest peak-to-peak H-reflex response was found, three subsequent stimuli were recorded and averaged for statistical analysis. To determine maximum M-response (M_{max}), the electrical stimulus was then increased in increments of 1.0 V until the peak-to-peak amplitude of the M-wave plateaued. Three M_{max} trials were then recorded and averaged. The H_{max}:M_{max} ratio was calculated for data analysis, representing H_{max} normalized to M_{max}.

Corticomotor output map. Participants were positioned in a Cybex II isokinetic dynamometer (CSMI, Stoughton, MA) with their hip flexed at 75°, knee flexed to 60°, and the testing ankle plantar flexed to 80°. Before testing, participants were given a Lycra swim cap (Spring Aquatics, Rothhammer International Inc. San Luis Obispo, CA) used to mark reference lines for the stimulation. The swim cap had a standard dot grid that was hand drawn with two lines: one line separating the hemispheres sagittally and the other connecting the apexes of the ears bisecting the other line. Participants performed submaximal contractions at 20% of their maximal isometric eversion contraction (MVIC) during each trail (44).

To determine the optimal stimulating location, the double-cone coil was moved in an anterior-to-posterior and medial-to-lateral direction, and a series of magnetic stimuli of 1.0 T were delivered at several locations on the grid until the largest and most consistent MEP were observed. This spot was marked and denoted as the "hot spot." After the determination of the optimal stimulating point (hot spot), the TMS coil was fixed at this location for the assessment of the active motor threshold (AMT).

Before mapping the corticomotor output, AMT was identified using a previously published method (35). Briefly, the MEP threshold was calculated by determining the peak-to-peak amplitude of the background EMG signal collected while participants performed sub-MVIC at 20% of their MVIC without magnetic stimulation (35). The cutoff threshold was set two SD above this EMG amplitude (35). AMT was determined as the lowest stimulator intensity required to elicit at least four of eight MEP with peak-to-peak amplitudes that exceeded the MEP threshold (35). AMT provides an estimate of the membrane excitability of pyramidal cells (8). A higher AMT indicates decreased corticomotor excitability, as a greater intensity of magnetic stimulation is needed to excite the pyramidal neurons in the primary motor cortex.

After the determination of AMT, a 6 × 6 cm grid (3 cm lateral–medial and 3 cm anterior–posterior) was outlined around the hot spot. The stimulator intensity was set at 100% AMT for the remainder of the testing session. Using an indicator strip corresponding with the center of the double-cone coil positioned directly over the stimulating location, three consecutive stimuli separated by 10 s were delivered before moving to the next location randomly selected by the primary investigator (40). The amplitude of the MEP at this percentage of AMT provides a reliable estimate of corticomotor excitability of the pathway between the corticospinal system and the FL (ICC = 0.86) (19). It was previously demonstrated that three stimuli at each location is sufficient to produce reliable and reproducible maps (25). The peak-to-peak MEP amplitudes for each trial were averaged at each scalp site and normalized to M_{max}.

Cortical representation of the FL was calculated using three previously used measures: 1) the location of cortical

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representation (LCR), 2) the map area, and 3) the map volume. The LCR is a valid and reliable measure used to identify map position and to measure shifts of the cortical representation of a muscle (42). LCR was calculated using the formula:

$$\text{location} = \frac{\sum a_i x_i}{\sum a_i}; \frac{\sum a_i y_i}{\sum a_i}$$

where a_i stands for the mean normalized MEP amplitude at the site with the coordinate of x_i (mediolateral) and y_i (anteriolateral) (41,42,45). Map area was defined as the number of stimulus positions whose stimulation evoked an averaged MEP greater or equal to the MEP threshold previously identified for determining AMT (42). An increase in the corticomotor map area would suggest an expansion of the cortical representation of a selected muscle. Map volume was calculated as the sum of the mean normalized MEP recorded at all scalp sites at which measureable MEP were evoked (45). Map volume is a measure of total excitability of cortical representation (41). An increase in corticomotor output map volume would indicate an increase in the cortical excitability of a selected muscle. Collectively, these parameters were calculated for each map, and the average for each group was used for statistical analysis.

Statistical Analysis

Demographic information was compared between groups using independent *t*-tests. On the basis of the analysis of the data using a Kolmogorov–Smirnov *Z* test for normality, we found that scores from selected self-reported questionnaires (AII, IdFAI, and CAIT), duration since the most recent LAS, and the number of "giving way" were nonnormally distributed ($P < 0.05$). Subsequently, a separate Mann–Whitney *U* test was performed to compare these variables between groups.

Multiple independent *t*-test was used to determine group differences for each dependent variable. Cohen's *d* effect sizes using mean and pooled SD values were calculated, along with 95% confidence intervals (CI) to determine the magnitude of group differences for each outcome variable. Effects sizes were interpreted as weak ($d < 0.40$), moderate ($0.40 \leq d < 0.80$), and strong ($d \geq 0.80$).(2)

For our secondary analysis, Pearson product moment correlations were used to assess the association between measures of corticomotor plasticity and 1) demographic information (age, height, and weight), 2) FAAM-ADL and FAAM-Sport, and 3) number of previous LAS. Spearman Rho correlations were used to assess the association between measures of corticomotor plasticity and 1) self-reported instability (AII, IdFAI, and CAIT), 2) duration since the most recent LAS, and 3) number of "giving way." Spearman Rho correlations were selected because measures of self-reported function, duration since the most recent LAS, and number of "giving way" were nonnormally distributed according to the Kolmogorov–Smirnov *Z* test for normality ($P < 0.05$). Spearman Rho and Pearson product moment were interpreted as weak ($0.0 < r < 0.25$), fair ($0.25 < r < 0.50$), moderate to good ($0.50 < r < 0.75$), or strong ($0.75 < r < 1.0$).

All significance levels were set *a priori* at $P \leq 0.05$. All statistical analyses were performed using IBM SPSS Statistics, version 21 (IBM, Corp., Armonk, NY).

RESULTS

The descriptive statistics and the associated *P* values for all key demographic variables are presented in Table 1. Participants with CAI were older and scored significantly higher on the AII and IdFAI and lower on the CAIT, FAAM-ADL, and FAAM-Sport compared with healthy controls (Table 1).

Participants with CAI had a significantly smaller map area compared with controls ($t_{32} = -2.079$, $P = 0.046$) (Fig. 1), which was supported by a moderate effect size ($d = 0.70$, 95% CI = 0.00–1.39). Similarly, map volume ($t_{32} = -2.483$, $P = 0.018$) was smaller in the CAI group compared with healthy individuals (Fig. 2), with a strong effect size ($d = 0.87$, 95% CI = 0.15–1.55) (Table 2). All other main outcome measures were not statistically significant between groups ($P > 0.05$) (Table 2).

Only map area was moderately correlated with the amount of time since the last LAS ($P = 0.037$, $\rho = -0.419$) (Fig. 3). All other correlations were not statistically significant $P > 0.05$) (Table 3).

DISCUSSION

The current study investigated the corticomotor representation of the FL muscle using TMS mapping technique between individuals with and without CAI. We hypothesized

TABLE 1. Key demographic outcomes for CAI and healthy participants (mean ± SD).

	CAI (*n* = 18)	Healthy Control (*n* = 16)	*P*
Age (yr)	23.8 ± 3.6 (F: 14 vs M: 4)	21.1 ± 2.2 (F: 10 vs M: 6)	*P* = 0.035*
Height (cm)	169.6 ± 7.5	168.6 ± 13.4	*P* = 0.708
Weight (kg)	73.13 ± 12.03	66.51 ± 10.2	*P* = 0.066
AII	6.3 ± 1.7	0.0 ± 0.0	*P* < 0.001*
IdFAI	19.8 ± 4.3	0.0 ± 0.0	*P* < 0.001*
CAIT	14.7 ± 5.0	30.0 ± 0.0	*P* < 0.001*
FAAM-ADL (%)	88.82 ± 6.0	100.00 ± 0.0	*P* < 0.001*
FAAM-Sport (%)	72.7 ± 11.7	100.00 ± 0.0	*P* < 0.001*
No. LAS	4.46 ± 2.6	0.0 ± 0.0	*P* < 0.001*
Time since last LAS (months)	51.6 ± 43.4	0.0 ± 0.0	*P* < 0.001*
No. "giving way"	10.6 ± 16.5	0.0 ± 0.0	*P* < 0.001*
Godin leisure-time exercise	55.3 ± 18.1	66.5 ± 30.1	*P* = 0.195

*Statistically significant between group difference.

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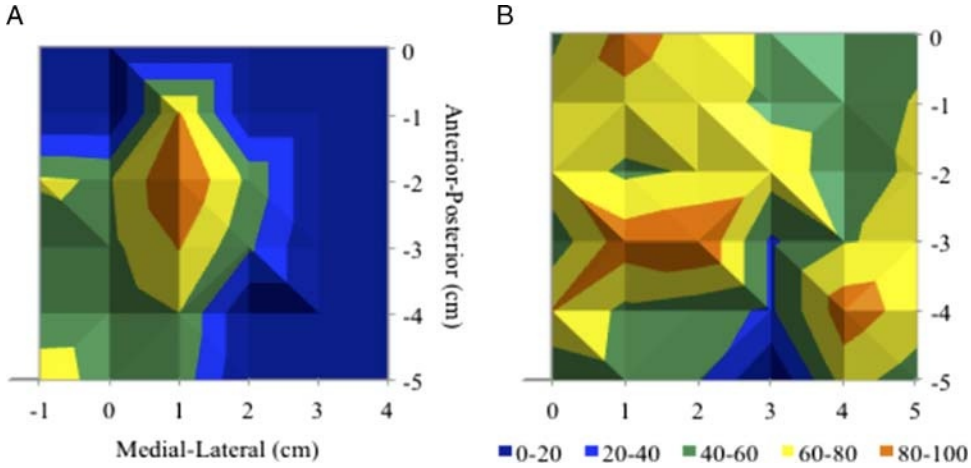

FIGURE 1—Corticomotor output map area. Representation of a participant identified as having CAI (A) vs healthy control (B). The areas of mapping are divided into five areas that are determined based on percentages of M_{max}: 1) area ≥80%, 2) 80% < area ≥60%, 3) 60% < area ≥40%, 4) 40% < area <20%, and 5) area ≤ 20%.

that corticomotor area and output volume of the FL would be larger in participants with CAI compared with those without to compensate for the decreased neural excitability previously reported (30). However, the primary findings of the current investigation were that individuals with CAI exhibited decreased corticomotor map area (Fig. 1) and volume (Fig. 2) representation of the FL compared with healthy controls. Furthermore, it appears that the excitable area within the motor cortex associated with the FL was more restricted in participants with CAI as the length of time since LAS increased (Fig. 3) but was not associated with levels of self-reported instability and function (Table 3). These findings provide unique insight into the sensorimotor adaptations associated with CAI. Specifically, the decreased corticomotor map area and volume suggests that individuals with CAI have a decreased corticomotor representation of the FL.

The ability of the motor cortex to self-organize is critical to allow individuals to successfully adjust to the changes in the task and environment. Previous studies have observed altered movement patterns in patients with CAI (37), indicating that the presence of CAI may be associated with alterations within the CNS to cope with the organismic, task, and environmental constraints placed on individuals with CAI. The findings obtained from the current study provide novel insight into the supraspinal adaptations of the CNS that may occur in response to ankle joint injury. Corticomotor output map volume provides an estimate of total cortical excitability of a selected muscle (41,45). Therefore, the decreased corticomotor output map volume would suggest that individuals with CAI might have greater difficulty in producing voluntary motor commands to the FL. Furthermore, we used corticomotor output map area to provide an estimate of the size of the cortical representation of a muscle (42). The smaller corticomotor output area would imply that individuals with CAI might have fewer cortical neurons devoted to the activation and control of the FL muscle.

We did not find differences in spinal reflex excitability or AMT of the FL muscle between groups. Early reports

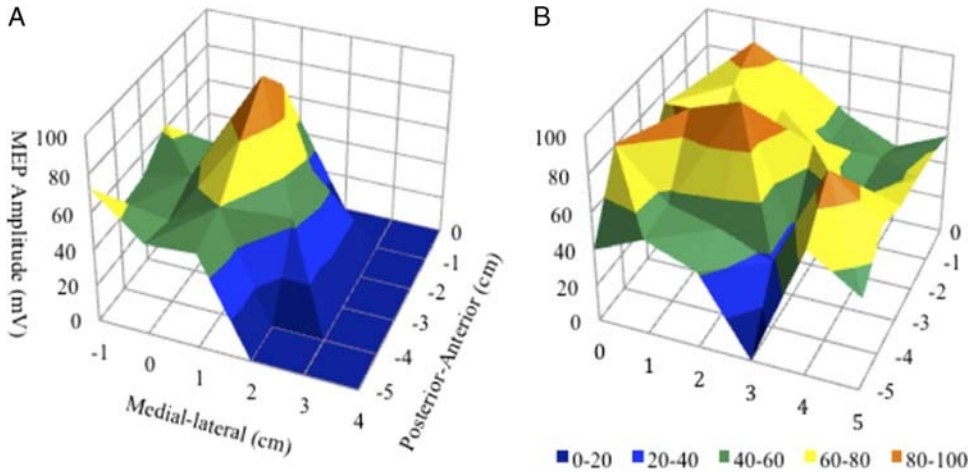

FIGURE 2—Corticomotor output map volume. Representation of a participant identified as having CAI (A) vs healthy control (B). The areas of mapping are divided into five areas that are determined based on percentages of M_{max}: 1) area ≥80%, 2) 80% < area ≥60%, 3) 60% < area ≥40%, 4) 40% < area <20%, and 5) area ≤ 20%.

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TABLE 2. Mean ± SD and effect sizes (95 CI) for all main outcome measures.

	CAI (n = 18)	Healthy Control (n = 16)	P	Effect Size (95% CI)
AMT (%)	36.3 ± 6.2	39.2 ± 6.6	P = 0.203	0.45 (−0.22 to 1.12)
Normalized MVIC (N·kg^{-1})	0.16 ± 0.06	0.19 ± 0.08	P = 0.174	0.43 (−0.26 to 1.10)
MEP threshold	0.17 ± 0.12	0.16 ± 0.07	P = 0.800	−0.10 (−0.77 to 0.58)
LCR (x) (cm)	1.38 ± 0.80	1.30 ± 0.80	P = 0.759	−0.10 (−0.77 to 0.58)
LCR (y) (cm)	1.19 ± 0.89	1.41 ± 0.77	P = 0.440	0.26 (−0.42 to 0.93)
Corticomotor map volume* (cm^2 mV)	8.22 ± 3.2	11.3 ± 3.9	P = 0.018	0.867 (0.15 to 1.55)
Corticomotor map area* (cm^2)	12.8 ± 6.0	17.4 ± 6.9	P = 0.046	0.71 (0.00 to 1.39)
H:M ratio	0.21 ± 0.21	0.15 ± 0.11	P = 0.377	0.36 (−0.36 to 1.06)

*Statistically significant between group difference.

suggest that a decrease in spinal reflex excitability (24) and resting motor threshold (30) was present in patients with CAI compared with healthy controls; however, more recent reports have been unable to detect differences in spinal reflex excitability or AMT of the FL (23). The absence of changes in spinal reflex excitability in the presence of decreased corticomotor area and volume may indicate CAI is associated with more supraspinal alterations. Furthermore, the level of AMT was determined at the site of optimal excitation where differences in AMT may be too subtle to identify. Rather, differences in excitability on the border of the FL excitation area may be more prominent and associated with the presence of CAI.

We acknowledge that the retrospective design of our study limits our ability to link the causality between decreased corticomotor area and volume and the development of CAI. Because of the retrospective design, it remains unknown whether CAI participants exhibited decreased corticomotor area and volume before their index LAS, or if these alterations occur after joint damage and are linked to the development of CAI. Moreover, it is difficult to determine whether the findings in the present study are beneficial or harmful to participants with CAI. It is reasonable to speculate that the decreased corticomotor area and volume might be a protective mechanism to allow patients with CAI to have more focused and finite motor control of the FL muscle to prevent further joint injury and joint dysfunction. Further investigation into the association between these supraspinal alterations and motor control is needed to understand what implications these findings have on motor output in patients with CAI.

With the primary motor cortex having strong connections with the somatosensory cortex, peripheral afferent information arising from somatosensory structures surrounding the ankle joint can have a significant influence on the stability and reorganization of the corticomotor output (32). Impairments in the somatosensory system at the damaged ankle joint after an initial ankle sprain may lead to sensory reweighting of the sensorimotor system to use other areas and structures available to compensate for the loss of sensory inputs from the damaged structures (21). Needle et al. (26) found that, compared with healthy individuals, the activation level of the somatosensory cortex in those with CAI was not different during ankle joint loading. Interestingly, the authors reported a positive correlation between cortical activation and ankle joint displacement in healthy individuals, but not in those with CAI (26). This adds evidence that individuals with CAI may rely on other forms of sensory information, rather than from the ankle joint mechanoreceptors, which could be evidence of somatosensory plasticity. Further, Terada et al. (36) found that individuals with CAI could use unimpaired somatosensory areas during a functional task to adjust for changes in a task demand. However, this somatosensory plasticity still may not provide enough sensorimotor reorganization to cope with organismic constraints in a CAI population because this consequence would reduce the total degrees of freedom available from sensory inputs to appropriately modulate motor outputs and movement (22). Therefore, altered sensory inputs along with potential somatosensory reorganization associated with CAI might create changes to the corticomotor representation of the FL. However, it is important to recognize that we did not directly measure sensory inputs and their association with the mapping parameters used in the current investigation. More research is needed to further to investigate the association between sensory information and map parameters.

In addition to the altered sensory information, movement variability may also explain the deficits found in the present study. Previous authors have identified deficits within the

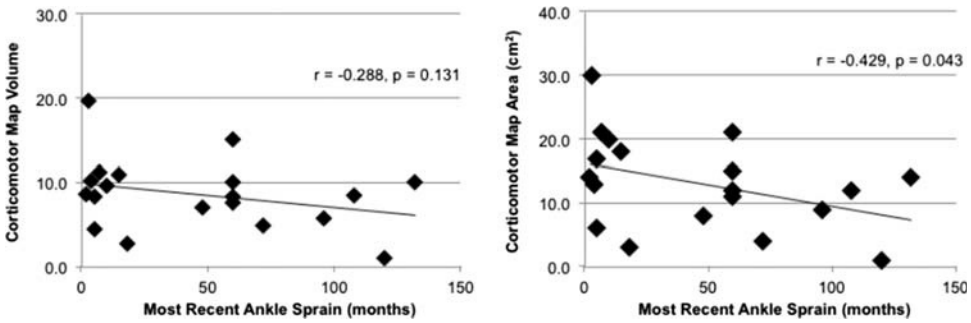

FIGURE 3—Association between corticomotor map volume and area and most recent ankle sprain.

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TABLE 3. Association between measures of corticomotor plasticity and self-reported outcome measures.

	Corticomotor Map Area		Corticomotor Map Volume	
	r/ρ	P	r/ρ	P
Age (yr)	$r = -0.215$	$P = 0.189$	$r = -0.299$	$P = 0.106$
Height (cm)	$r = -0.107$	$P = 0.331$	$r = 0.048$	$P = 0.423$
Weight (kg)	$r = -0.172$	$P = 0.241$	$r = -0.141$	$P = 0.282$
AII	$\rho = -0.000$	$P = 0.499$	$\rho = -0.030$	$P = 0.452$
IdFAI	$\rho = 0.154$	$P = 0.265$	$\rho = 0.107$	$P = 0.332$
CAIT	$\rho = 0.187$	$P = 0.221$	$\rho = 0.160$	$P = 0.244$
FAAM-ADL (%)	$r = 0.008$	$P = 0.487$	$r = -0.001$	$P = 0.498$
FAAM-Sport (%)	$r = 0.076$	$P = 0.378$	$r = -0.114$	$P = 0.321$
No. LAS	$\rho = -0.016$	$P = 0.475$	$\rho = -0.188$	$P = 0.221$
Time since last LAS (months)*	**$r = -0.419$**	**$P = 0.037$**	$r = -0.337$	$P = 0.079$
No. "giving way"	$\rho = -0.228$	$P = 0.173$	$\rho = 0.213$	$P = 0.191$

*Statistically significant correlation.

descending corticospinal pathways of the FL within individuals with CAI, which has been suggested to result in greater difficulty in generating a motor command to the FL (30). This loss of motor control of the FL likely leads to compensatory movement strategies to protect the ankle, as researchers have previously shown altered proximal joint kinematics during gait (3,37), balance (5), drop landing (36,38), and muscular activation patterns (43) in individuals with CAI. These altered movement and muscular activation patterns identified likely reflect the attempt by individuals with CAI to overcome the inability to effectively use the ankle musculature, relying more heavily on the proximal joint musculatures to prevent further injury and to remain functional (4). Certainly, these compensatory movement strategies may be associated with the reorganization of the corticomotor output map found in the present study. Specifically, decreased reliance on the ankle musculature may disrupt neuronal connections associated with the FL. Previous authors have demonstrated joint immobilization reduces the area of the motor cortex associated with the target muscle (17,18). The authors speculated this decrease in corticomotor area might be attributable to the inactivity and disuse of the muscle. Subsequently, the compensatory movement strategies placing a high demand on proximal joint musculatures could increase recruitment of nearby neuronal connections, thereby invading the area of the motor cortex originally representing the FL muscle. Therefore, decreased activity of the FL and increased demand on the proximal joint musculature may be associated with decreased corticomotor output map area and volume in participants with CAI. Future research comparing the corticomotor output between different musculature is required to confirm this speculation.

Furthermore, we found a moderate and negative association between the corticomotor map area and the length of time since LAS, indicating that the excitable area within the motor cortex associated with the FL was reduced as the length of time since participants with CAI experienced the most recent LAS increased (Fig. 3). These results are in line with earlier work by Liepert et al. (18) who found that the motor cortex representation of the tibialis anterior was negatively correlated with the amount of time the ankle joint was immobilized. However, previous investigations have found increased map volume in the primary motor cortex in patients with other musculoskeletal conditions, including chronic low back pain (41) and persistent elbow pain (34). The differences between these previous investigations and the current study might be explained by the presence of pain. Schabrun et al. (34) found corticomotor map volume was positively correlated with the level of the worst pain within the previous 6 months. Although we did not record the level of ankle joint pain that participants with CAI had experienced in the previous 6 months, the primary symptoms reported by participants with CAI were feelings of "giving way" and joint instability, but not joint pain. Joint instability may not be a primary source of elbow and chronic low back pain. Therefore, differences in the primary symptoms between CAI and chronic elbow or low back pain may explain why patients with CAI presented differently in the corticomotor map volume than patients with the previously mentioned musculoskeletal pathologies (34,41). Furthermore, CAI is a unique pathological condition that alters sensorimotor control (10). Damage to the lateral ankle ligamentous complex from an initial ankle sprain has been shown to be associated with disruption of sensory input that may chronically create a centrally mediated alteration in neuromuscular function (10). Previous studies reported that decreased map area and volume in patients with neurologic disorders impairs sensorimotor control (33,39). Therefore, while often regarded as a musculoskeletal pathology, CAI likely exhibits unique sensorimotor alterations.

Although it remains unknown whether the decreased corticomotor map area and volume is beneficial or a harmful adaptation, the findings do have clinical implications. Researchers have found skilled motor training is associated with enlarged corticomotor output (29). Therefore, clinicians should consider implementing a goal-oriented therapeutic intervention program and is progressed in difficulty by manipulating the environment or task to introduce new movement strategies for patients with CAI. Ideally, this will allow them to learn to cope with unanticipated changes in their surrounding environment.

Limitations

This study was not without limitation. First, the spatial representation required for corticomotor output mapping is often larger than the true anatomical representation, making it difficultly to understand the true cortical representation of the FL muscle. Second, we observed differences in age between the CAI and the control groups, potentially influencing our findings. Previous studies have reported age-related changes in corticomotor representations. However, we found nonsignificant, weak correlations between age and the selected TMS measures ($r < 0.40$, $P > 0.05$). These data indicate that perhaps the presence of CAI, rather than age differences, may contribute to altered corticomotor representation of the FL.

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CONCLUSION

The purpose of this study was to compare the corticomotor outputs of the FL muscle between those with and without CAI. These data demonstrate that individuals with CAI have decreased overall corticomotor excitability and a more concentrated cortical representation of the FL muscle compared with healthy individuals. Further, the length of time since their last injury and corticomotor output area was negatively correlated in individuals with CAI. These results provide novel insight into the potential altered reorganization of the corticomotor output of the FL and the influence of chronicity. Further investigation into the functional relevance of decreased corticomotor output map area and volume should continue.

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