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Alterations in Cortical Activation Among Individuals With Chronic Ankle Instability During Single-Limb Postural Control

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Context: Chronic ankle instability (CAI) is characterized by repetitive ankle sprains and perceived instability. Whereas the underlying cause of CAI is disputed, alterations in cortical motor functioning may contribute to the perceived dysfunction.

Objective: To assess differences in cortical activity during single-limb stance among control, coper, and CAI groups.

Design: Cross-sectional study.

Setting: Biomechanics laboratory.

Patients or Other Participants: A total of 31 individuals (10 men, 21 women; age = 22.3 ± 2.4 years, height = 169.6 ± 9.7 cm, mass = 70.6 ± 11.6 kg), who were classified into control (n = 13), coper (n = 7), and CAI (n = 11) groups participated in this study.

Intervention(s): Participants performed single-limb stance on a force platform for 60 seconds while wearing a 24-channel functional near-infrared spectroscopy system. Oxyhemoglobin (HbO2) changes in the supplementary motor area (SMA), precentral gyrus, postcentral gyrus, and superior parietal lobe were measured.

Main Outcome Measure(s): Differences in averages and standard deviations of HbO2 were assessed across groups. In the CAI group, correlations were analyzed between measures of cortical activation and Cumberland Ankle Instability Tool (CAIT) scores.

Results: No differences in average HbO2 were present for any cortical areas. We observed differences in the standard deviation for the SMA across groups; specifically, the CAI group demonstrated greater variability than the control (r = 0.395, P = .02; 95% confidence interval = 0.34, 0.67) and coper (r = 0.38, P = .04; 95% confidence interval = –0.05, 0.69) groups. We demonstrated a strong correlation that was significant in the CAI group between the CAIT score and the average HbO2 of the precentral gyrus (p = 0.64, P = .02) and a strong correlation that was not significant between the CAIT score and the average HbO2 of the SMA (p = 0.52, P = .06).

Conclusions: The CAI group displayed large differences in SMA cortical-activation variability. Greater variations in cortical activation may be necessary for similar static postural-control outcomes among individuals with CAI. Consequently, variations in cortical activation for these areas provide evidence for an altered neural mechanism of postural control among populations with CAI.

Key Words: central nervous system, balance, functional near-infrared spectroscopy, stability, cortical-activation variability.
recurrent sprains and CAI.\textsuperscript{1,3} Therefore, improving rehabilitation and intervention strategies is critical to maximizing outcomes and reducing the long-term pain and disability associated with CAI.\textsuperscript{5}

Central nervous system (CNS) adaptations after ligamentous injury may negatively influence the recovery process and be related to self-reported function, thus affecting treatment protocols, prolonging full recovery, and altering movement or balance strategies or both.\textsuperscript{6} Researchers\textsuperscript{2} have proposed several theories to explain the impairments perceived by patients with CAI and why some patients develop CAI and others do not. These theories include poor neuromuscular control, decreased muscular strength, deficits in kinesthetic awareness and balance, and mechanical laxity.\textsuperscript{2} Most traditional models framed CAI as a musculoskeletal disorder with adaptations typically occurring in the periphery rather than in the brain.\textsuperscript{6} However, recent investigators\textsuperscript{3} have suggested that CNS variations (ie, alterations in somatosensory function and corticomotor excitability) are present after acute and chronic ligamentous injuries, including lateral ankle sprains and anterior cruciate ligament (ACL) ruptures. The long-term disability associated with CAI may also demonstrate some of these CNS changes, including altered neural mapping and corticomotor activation changes.\textsuperscript{7,8} Individuals with CAI demonstrated smaller motor-evoked potentials, as well as deficits in motor thresholds, providing insight into how the descending pathways from the brain activate the ankle’s musculature to control movement.\textsuperscript{7,8} Similarly, Koski et al\textsuperscript{9} reported deviations in cortical mapping and excitability of the fibularis longus with the use of transcranial magnetic stimulation among patients with CAI compared with healthy control participants. These studies\textsuperscript{7–9} have contributed to the concept of altered neural pathways after ligamentous injury.

Assessing cortical activation allows considerable insight into the control of stability by highlighting areas of the brain that may be implicated in populations with pathologic conditions. The neural control of standing posture involves the interaction among several subsystems, including the spinal cord, brain stem, cerebellum, basal ganglia, and cerebral cortex. However, direct observations of cortical changes in these systems during such tasks are rare because of the technical difficulties associated with monitoring brain activity during movement. Researchers\textsuperscript{10} have attempted to solve this problem by having participants perform various tasks, such as mental imagery or minimal movement during ankle-mobility tasks, or repeated cycles of knee flexion and extension while lying supine in brain-imaging devices, such as that used for functional magnetic resonance imaging (fMRI). The fMRI is the criterion standard for brain-imaging studies because of its spatial resolution, but it lacks adequate temporal resolution and allows very limited movement within the device.\textsuperscript{10} Transcranial magnetic stimulation allows insight into cortical excitability via descending motor pathways but also permits minimal movement during testing. Comparatively, electroencephalography provides exceptional temporal but limited spatial resolution to identify the timing and cortical processing of an electrophysiologic response. Each of these approaches has pros and cons for investigating alterations in CNS function and these must be considered when we interpret the literature.

A recent solution to the lack of temporal resolution provided by fMRI and the inability to monitor cortical function during movement is functional near-infrared spectroscopy (fNIRS), which demonstrated robustness in recording brain activity during locomotion at a relatively low cost.\textsuperscript{10} Similar to fMRI, fNIRS measures cortical oxygen saturation occurring secondary to neuronal activation, which creates a distinct neurovascular coupling observable on various types of imaging and is the basic principle of fNIRS technology.\textsuperscript{10} Whereas fNIRS does not provide the depth of penetration or spatial resolution of fMRI, it offers better temporal resolution and tolerance of modest movements while imaging the superficial layers of the cortex.\textsuperscript{10} The fNIRS emits light from its diodes. This light penetrates the skull and is absorbed at different rates depending on the tissues, and penetrates between 1 and 1.5 cm of the cortex but does not allow measurements of deeper aspects of the brain, such as the basal ganglia.\textsuperscript{10} Given its tolerance of subtle movements, fNIRS has been used to monitor cortical activity during standing postural tasks. The prefrontal cortex and the supplemental motor area (SMA) have been identified as critical for maintaining balance among healthy individuals and among individuals with various neurologic conditions (eg, stroke, Parkinson disease, traumatic brain injury).\textsuperscript{10} Therefore, cortical activation measured with fNIRS is a potential biomarker of postural control among healthy individuals and individuals with pathologic conditions.

Chronic ankle instability is a common and debilitating condition that appears to be influenced by both peripheral and central adaptations. However, whereas central contributions during movement have important implications for populations with CAI, they have been difficult to assess because of the limited availability of advanced technology. Therefore, the primary purpose of our study was to assess cortical activation during single-limb stance using fNIRS technology in healthy control individuals, ankle-sprain copers, and individuals with CAI. Our secondary purpose was to assess the activation of the cerebral cortex and its relation to self-reported function in those with CAI. Based on these aims, we believed that, during single-limb stance, participants with CAI would demonstrate differences in cortical activation on fNIRS imaging compared with control participants and copers. Specifically, based on previous work\textsuperscript{11} in ACL-reconstructed knees, we believed that individuals with CAI would display greater cortical activation than control participants and copers.

**METHODS**

We used a cross-sectional research design to compare dependent variables across 3 groups. To determine their eligibility, we instructed volunteers to complete ankle-injury history questionnaires at our biomechanics laboratory. Eligible participants were required to be *recreationally active*, which was defined as participating in more than 90 minutes of physical activity per week that included any combination of running, walking, lifting weights, or playing a sport. Thirty-one individuals (10 men, 21 women) participated in this study (Table 1). Participants were entered into the control group (*n* = 13) if they had (1) no...
**Table 1. Demographic Data**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Control (n = 13)</th>
<th>Coper (n = 7)</th>
<th>Chronic Ankle Instability (n = 11)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex, No.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>8</td>
<td>4</td>
<td>9</td>
</tr>
<tr>
<td>Male</td>
<td>5</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>22.6 ± 2.3</td>
<td>22.0 ± 2.7</td>
<td>22.2 ± 2.6</td>
</tr>
<tr>
<td>Age, y</td>
<td>21.6 ± 2.3</td>
<td>21.0 ± 2.3</td>
<td>21.4 ± 2.6</td>
</tr>
<tr>
<td>Mass, kg</td>
<td>75.2 ± 12.2a</td>
<td>73.3 ± 9.0</td>
<td>63.4 ± 9.3</td>
</tr>
<tr>
<td>Height, cm</td>
<td>171.2 ± 11.1</td>
<td>170.1 ± 10.4</td>
<td>167.4 ± 7.9</td>
</tr>
<tr>
<td>No. of sprains</td>
<td>0.0 ± 0.0a</td>
<td>1.1 ± 0.4a</td>
<td>2.4 ± 1.4</td>
</tr>
<tr>
<td>Time since most recent sprain, y</td>
<td>0.0 ± 0.0a, b</td>
<td>3.9 ± 2.3</td>
<td>2.9 ± 2.6</td>
</tr>
<tr>
<td>Ankle rolls, No.</td>
<td>0.0 ± 0.0a, b</td>
<td>0.9 ± 0.4a</td>
<td>3.6 ± 2.8</td>
</tr>
<tr>
<td>Cumberland Ankle Instability Tool score</td>
<td>30.0 ± 0.0a</td>
<td>29.0 ± 1.0a</td>
<td>18.2 ± 5.5</td>
</tr>
<tr>
<td>Anteroposterior center of pressure, mm</td>
<td>38.0 ± 9.2</td>
<td>43.2 ± 10.0</td>
<td>40.8 ± 15.7</td>
</tr>
<tr>
<td>Mediolateral center of pressure, mm</td>
<td>30.6 ± 7.6</td>
<td>32.2 ± 7.2</td>
<td>30.7 ± 6.7</td>
</tr>
</tbody>
</table>

*a Different from the chronic ankle instability group (P < .05).

*b Different from the coper group (P < .05).

history of lateral ankle sprain; (2) no history of their ankle giving way; and (3) a Cumberland Ankle Instability Tool (CAIT) score ≥28, indicating good function and no perception of instability. Inclusion criteria for the coper group (n = 7) were (1) a history of a moderate to severe lateral ankle sprain, including inflammatory symptoms (pain, swelling, discoloration, or non-weight bearing or partial weight bearing) and disruption of sport or physical activity; (2) ≤1 episode of giving way and no history of ankle sprain in the 12 months before the study; and (3) a CAIT score ≥28, indicating good function and no perception of instability. We defined a coper as an individual who had sustained an initial ankle sprain, fully recovered, and not developed CAI. Inclusion criteria for the CAI group (n = 11) were (1) a history of a moderate to severe lateral ankle sprain, including inflammatory symptoms (ie, pain, swelling, discoloration, non-weight bearing or partial weight bearing) and disruption of sport or physical activity; (2) ≥2 episodes of giving way at the ankle in the 12 months before the study; and (3) a CAIT score ≤24, which suggested impaired ankle function. Volunteers were excluded if they (1) had a history of lower limb surgery or fracture; (2) had a joint sprain or injury in the lower extremity at the time of the study; (3) had any other health problem that may have affected their balance or well-being; (4) were pregnant; (5) had a history of a balance or vestibular disorder; (6) had a substantial history of a condition that impaired cognitive function, such as a learning disability or concussion; or (7) were taking medications that might have affected their cognition (ie, narcotics, antidepressants, antianxiety agents). The researchers were not blinded to injury status before fNIRS testing.

All participants provided written informed consent, and the study was approved by the University of Nebraska Medical Center Institutional Review Board.

**Instrumentation**

A 24-channel continuous-wave fNIRS system (model ETG-4000 Optical Topography System; Hitachi Medical Corp, Tokyo, Japan) was used to record neurovascular changes (Figure 1). Specifically, we recorded oxyhemoglobin (HbO₂) over the superior parietal lobe, precentral gyrus (PreCG), postcentral gyrus (PostCG), and SMA. The HbO₂ is the amount of saturation of oxygenated hemoglobin of the local blood vessels in the superficial layers of the cortex. We used 2 wavelengths (approximately 695 and 830 nm) to record the changes in oxygenated hemoglobin concentration. The fNIRS system was calibrated before each testing session to ensure accurate measurements. The testing setup on the force platform (Balance Master System 8.4; NeuroCom, Clackamas, OR) with the functional near-infrared spectroscopy system affixed to the head.
830 nm) at 10 Hz to sample the data and measure cortical activity. The fNIRS electrode was secured on the participant’s head based on the international 10/20 system, with the vertex of the head (Cz) located beneath the center of the front 2 rows of optodes. The vertex of the head was found by a single researcher (not an author) who located the intersecting point of the midpoint between the left and right preauricular areas and the midpoint between the bridge of the nose and external occipital protuberance.

Procedures

Once the fNIRS was in place, participants completed a 60-second baseline trial while sitting in a chair. After the baseline trial, they completed 5 successful trials of single-legged stance on a force platform (model Balance Master System 8.4; NeuroCom, Clackamas, OR) that collected center-of-pressure (COP) data at 100 Hz (Figure 1). Participants were instructed to maintain their balance with their eyes open and hands on their hips for 60 seconds, and they rested for approximately 1 minute between trials. Among individuals who indicated bilateral instability, the limb with the lower CAIT score was used as the test limb. Participants could remove their hands from their hips if necessary to maintain upright stance; however, falling, touching down on the opposite limb, or bracing on the force-platform surround resulted in a failed trial. If a participant failed a trial, the test was stopped, he or she was given time to rest, and the trial was reattempted until 5 successful trials were completed. Individuals were allowed to familiarize themselves with the force-platform surround and the fNIRS headgear but did not have any formal practice trials. Given the potential for artifact movement to create excessive noise within the fNIRS system, we chose single-limb stance rather than a more dynamic movement. Our results suggested that the CAI group demonstrated greater variability in SMA activation, whereas higher values for the SD HbO2 indicated greater levels of cortical activation. These differences and relationships highlight a potentially altered cortical-activation strategy among individuals with CAI.

DISCUSSION

The CAI group demonstrated greater variability in SMA cortical activation than the control and coper groups, suggesting a potentially altered cortical-activation strategy to maintain single-limb balance. For the CAI group, cortical activation in the PreCG and possibly the SMA was strongly correlated with the CAIT, signifying that individuals with CAI who self-reported poorer function also had lower levels of cortical activation. The SMA is an important structure in motor-planning and movement strategies. Our results suggested that the CAI group demonstrated greater variability in SMA cortical activation compared to the control and coper groups, suggesting a potentially altered cortical-activation strategy to maintain single-limb balance. For the CAI group, cortical activation in the PreCG and possibly the SMA was strongly correlated with the CAIT, signifying that individuals with CAI who self-reported poorer function also had lower levels of cortical activation.
group may have had a positive cortical adaptation with greater variations in SMA activation, resulting in similar static postural outcomes as the control and coper groups. Whereas static postural control was not different among the 3 groups in our study, the findings of a recent meta-analysis supported alterations in movement strategies during dynamic tasks relative to static balance among those with CAI. Authors of many of these studies have pointed to altered preparation for movement or feed-forward movement planning, and altered SMA activity indicates that such feed-forward control is affected. Therefore, this variation in cortical activation may be an adaptive change that plays a role in successfully negotiating dynamic tasks.

Similar to the SMA, the HbO PostCG standard deviation demonstrated a comparable, though nonsignificant, pattern across participants. Analysis of the data spread in Figure 2 shows a similar dichotomy in the PostCG compared with the SMA in the CAI group: 4 participants demonstrated a relatively higher SD HbO than the rest of the pools. To further support this notion, calculated effect sizes for these data also displayed moderate to large differences between the CAI and the control (r = 0.374; 95% CI = 0.01, 0.65) and coper (r = 0.838; 95% CI = 0.69, 0.92) groups. Changes in PostCG cortical activation during single-limb stance showed that somatosensory perceptions may be affected among those with CAI compared with copers. Similarly, in a recent meta-analysis, Song et al found that use of somatosensory perceptions was altered among individuals with CAI. Specifically, individuals with CAI tended to rely on vision more than and may integrate sensory information differently from those without a history of ankle sprain. Needle et al observed that participants with CAI did not have increased somatosensory cortex activation compared with controls but had earlier somatosensory activation during joint loading. When combined with previous research, our results further contribute to the theory of

Table 2. Oxyhemoglobin in the Supplementary Motor Area, Precentral Gyrus, Postcentral Gyrus, and Superior Parietal Lobe Across Groups

<table>
<thead>
<tr>
<th>Oxyhemoglobin, mmol/L</th>
<th>Group</th>
<th>Control</th>
<th>Coper</th>
<th>Chronic Ankle Instability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Supplementary motor areas</td>
<td>Average 0.012 ± 0.160</td>
<td>-0.015 ± 0.043</td>
<td>0.132 ± 0.322</td>
<td></td>
</tr>
<tr>
<td></td>
<td>SD 0.150 ± 0.120a</td>
<td>0.095 ± 0.035a</td>
<td>0.580 ± 0.731</td>
<td></td>
</tr>
<tr>
<td>Precentral gyrus</td>
<td>Average 0.013 ± 0.062</td>
<td>0.001 ± 0.029</td>
<td>0.081 ± 0.056</td>
<td></td>
</tr>
<tr>
<td></td>
<td>SD 0.133 ± 0.076</td>
<td>0.085 ± 0.039</td>
<td>0.132 ± 0.039</td>
<td></td>
</tr>
<tr>
<td>Postcentral gyrus</td>
<td>Average 0.001 ± 0.029</td>
<td>0.001 ± 0.029</td>
<td>0.001 ± 0.029</td>
<td></td>
</tr>
<tr>
<td></td>
<td>SD 0.120 ± 0.088</td>
<td>0.078 ± 0.033</td>
<td>0.251 ± 0.219</td>
<td></td>
</tr>
<tr>
<td>Superior parietal lobe</td>
<td>Average 0.004 ± 0.023</td>
<td>0.003 ± 0.034</td>
<td>0.022 ± 0.050</td>
<td></td>
</tr>
<tr>
<td></td>
<td>SD 0.097 ± 0.066</td>
<td>0.065 ± 0.036</td>
<td>0.100 ± 0.058</td>
<td></td>
</tr>
</tbody>
</table>

a Different from the chronic ankle instability group (P < .05).

Figure 2. Scatter-box plot of cortical-activation standard deviations in cortical activity of A, the supplementary motor area, B, the precentral gyrus, C, the postcentral gyrus, and D, the superior parietal lobe across groups.
an altered sensorimotor strategy among individuals with CAI.

Analyzing the variability of biological signals, such as COP during stance, may provide greater detail about postural control than simply comparing the means of this time series. Humans naturally sway during static stance, resulting in an inherent variability during the COP time series. Variability in movement patterns, such as standing posture, used to be considered error or random noise. However, variability is increasingly considered to be a marker of health in biological systems. Therefore, if movement shows such characteristics, the neural control of such variable patterns would also demonstrate variable characteristics and thereby characterize healthy posture as separate from pathologic posture. Hence, among patients with musculoskeletal impairments, presenting the variability of cortical activation alongside more traditional linear measures may provide greater understanding of the neural control mechanisms. In future studies, researchers should investigate these signals using both linear and nonlinear analyses of variability.

Brain networks are known to be coupled in a highly nonlinear manner. Analyzing the means of time series is therefore unlikely to provide valuable insight into the neural control of posture. When an individual performs a postural task with additional cognitive load, the synchronization among different cortical sites undergoes a major shift anteriorly to use frontal cognitive resources and reduce

Figure 3. Raw data from a single channel over the supplementary motor area of representative participants from the A, control, B, coper, and C, chronic ankle instability groups.
activity, especially during postural tasks. Given that the organizing system, the brain has demonstrated complex neuronal oscillations in the brain are strongly related to the modulation of proprioceptive feedback, it is intuitive to hypothesize that such neural control of posture would be affected among individuals with CAI.

The correlation analysis also revealed a positive relationship between the average cortical activation in the PreCG and the CAIT score, suggesting that cortical activity in the motor cortex may affect function and perceived instability in participants with CAI. Levels of cortical activity in the motor cortex may influence function among participants with CAI who have lower CAIT scores. The SMA showed a similar trend in demonstrating a relationship between ankle function and cortical activation. Whereas this is a preliminary study and no researchers have directly observed cortical activation among participants with CAI, previous studies of alternative populations may provide interesting comparisons. For example, in a cohort of children with cerebral palsy, participants who displayed higher levels of somatosensory cortical activity during fNIRS evaluation also displayed greater function and mobility.

The authors believed that such neural control of posture would be affected among individuals with CAI.

CONCLUSIONS

Individuals with CAI demonstrated large differences in the variability of SMA cortical activation. Cortical activation may also be positively related to self-reported function. Corticomotor postural-control strategies in individuals with CAI may differ because of altered motor strategies, as indicated by modifications in SMA activation. Consequently, for the SMA, variations in cortical activation provide evidence for an altered neural mechanism of postural control in populations with CAI.

Because this was a preliminary study with a relatively small sample size, the results should be confirmed among larger samples. Correspondingly, the CAI group was predominantly female (n = 9), which was likely the reason for the lower mass in this group. Thus, further studies should be aimed at a more diverse sample to improve the generalizability of our results and outcomes. More experimental control, such as blinding, would also improve the design. Researchers should examine the effectiveness of rehabilitation strategies and their ability to moderate cortical-activation strategies among those with CAI. In subsequent work, investigators may also want to explore data using more advanced nonlinear analyses, such as sample entropy and detrended fluctuation analysis, to provide greater insight into the complexity of the time-series signals.

ACKNOWLEDGMENTS

Throughout this project, Dr Mukherjee was supported by the following funding sources:

National Institute of General Medical Sciences/National Institutes of Health (NIH; P20GM109090 subproject #5347), National Aeronautics and Space Administration Established Program to Stimulate Competitive Research grant (80NSSC18M0076), and an American Heart Association award (18AIREA33960251). Funding for this project was provided by grant P20 GM109090 from the NIH, grants R01HD090333 and R01AG049868 from the NIH (Dr.
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