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Original Article

Rehabilitation increases cortical activation during single-leg stance in patients with chronic ankle instability

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ABSTRACT

Background: Chronic ankle instability (CAI) has been considered a neurophysiological disease, having as symptoms dysfunction in somatosensory and motor system excitability. Rehabilitation has been considered an effective treatment for CAI. However, few studies have explored the effects of rehabilitation on neuroplasticity in the CAI population.
Objective: The purpose of this study was to investigate the effects of rehabilitation on cortical activities for postural control in CAI patients and to find the correlation between the change in cortical activities and patient-reported outcomes (PROs).
Methods: Thirteen participants with CAI (6 female, 7 male, age = 33.8 ± 7.7 years, BMI = 24.7 ± 4.9 kg/m^2) received a home exercise program for about 40 min per day, four days per week and six weeks, including ankle range-of-motion exercise, muscle strengthening, and balance activities. Cortical activation, PROs and Y-balance test outcomes were assessed and compared before and after rehabilitation. Cortical activation was detected via Functional near-infrared spectroscopy (fNIRS) while the participants performed single-leg stance tasks.
Results: The participants had better PROs and Y balance test outcomes after rehabilitation. Greater cortical activation was observed in the primary somatosensory cortex (S1, $d = 0.66$, $p = 0.035$), the superior temporal gyrus (STG, $d = 1.06$, $p = 0.002$) and the middle temporal gyrus (MTG, $d = 0.66$, $p = 0.035$) in CAI patients after rehabilitation. Moreover, significant positive correlations were observed between the recovery of ankle symptoms and the change of cortical activation in S1 ($r = 0.74$, $p = 0.005$) and STG ($r = 0.72$, $p = 0.007$) respectively.
Conclusion: The current study reveals that six weeks of rehabilitation can cause greater cortical activation in S1, STG and MTG. This increase in cortical activation suggested a better ability to perceive somatosensory stimuli and may have a compensatory role in function improvement.

1. Introduction

The lateral ankle sprain is one of the most common sports injuries and 40 % of ankle sprain patients develop chronic ankle instability (CAI).[1] This condition is characterized by recurrent ankle sprains, feelings of instability and ankle joint "giving way". Furthermore, these functional deficits may persist even after surgical reconstruction of mechanical stability.[2] Recurrent ankle sprain and ankle joint "giving way" damage the ankle-joint structures, such as the anterior talofibular ligament, leading to a much higher risk of osteoarthritis in CAI patients.[3] Copers are individuals who had an initial ankle sprain, fully recovered, and not developed CAI.[4] Copers are better choices for the control group

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to determine why a portion of individuals develop CAI but others fully recovered.

Neuroplasticity is "the ability of the nervous system to change its activity in response to stimuli by reorganizing its structure, functions, or connections."[5] The effect of neuroplasticity can either be beneficial, neutral, or negative. Negative neuroplasticity appears to be the underlying mechanism of clinical deficits and poor long-term outcomes among the CAI population.[6] Numerous studies have identified CAI as a neurophysiological dysfunction, with evidence from direct neurophysiologic measures of somatosensory function and motor system excitability. In terms of somatosensory function, lots of sensorimotor impairments have been associated with CAI, including impaired balance,[7] and decreased proprioception.[8] Needle et al. found that the somatosensory cortex of CAI patients could not discriminate higher levels of load on the ankle ligaments,[9] which may potentially reduce the central nervous system's (CNS) ability to cope with joint loads.[10] Our previous study demonstrated that copers had significantly higher cortical activation in primary somatosensory cortex (S1) and superior temporal gyrus (STG) than CAI participants and uninjured controls, that might be the compensatory mechanism of copers to maintain good functions after the initial ankle sprain.[11] In terms of motor system excitability, CAI patients were found to have lower corticomotor excitability in the peroneus longus and tibialis anterior muscle[12] and longer latency in the tibialis anterior and gastrocnemius medialis muscle.[13] These deficits may cause a high risk of re-injury due to slow-motion control.

Studies have proved that rehabilitation can affect both the function and the CNS.[14] Rehabilitation may also have a positive impact on neuroplasticity among CAI patients considering their benefits from rehabilitation in balance, proprioception and patient-reported outcomes (PROs).[15] Nonetheless, few studies have so far explored the effects of rehabilitation on neuroplasticity amid the CAI population.

Functional near-infrared spectroscopy (fNIRS) has been widely used in the field of rehabilitation (e.g., postural control[16] and gait rehabilitation[17]) since it is relatively robust with motion artifacts and can measure cortical function during a standing task. fNIRS is thus the most suitable method for investigating cortical activation in postural control in CAI patients and therefore it was used instead of functional magnetic resonance imaging (fMRI) in the present study.

This study was an extension of our previous work, which illustrated that copers had significantly higher cortical activation in S1 and STG compared with CAI patients.[11] The primary purpose of our study was to elucidate the effect of rehabilitation on cortical activation during single-leg stance, PROs and dynamic balance in CAI patients. The secondary purpose of the present study was to assess the association between the change in cortical activation and PROs. We hypothesized that CAI patients would present significantly greater activation in cortical areas related to balance control, better PROs and dynamic balance after rehabilitation. Additionally, we hypothesized that there might be positive correlations between the increase of cortical activation and the improvement of PROs.

2. Materials and methods

2.1. Design

We used a single-arm interventional research design to compare variables before and after rehabilitation among CAI participants. To determine their eligibility, we instructed participants to complete an online questionnaire. Fifteen individuals with CAI participated in this study with two of them withdrawing due to personal reasons. Thirteen subjects completed the rehabilitation program. According to the recommendations of the International Ankle Consortium,[18] participants must meet all the following conditions: (1) a history of at least 1 significant ankle sprain, (2) the initial sprain occurred at least 12 months prior to study enrollment, (3) the most recent injury had occurred more than 3 months prior to study enrollment, (4) history of the previously injured ankle joint "giving way" and/or recurrent sprain and/or "feelings of instability", (5) CAIT scores$<$24, (6) able to obtain complete fNIRS data, (7) age 18–65 years. Participants were excluded if they reported any of the following: (1) history of other lower extremity musculoskeletal pathology, (2) history of lower limb surgery, (3) diagnosed balance or vestibular condition, (4) history of neurological or mental disease. The study was conducted in accordance with the Declaration of Helsinki, the protocol was approved by the ethics committee of Huashan Hospital, Shanghai, China (HIRB 2016M-008) and all participants signed an approved informed consent form before participating.

This investigation is a preliminary investigation with no fNIRS data available within this population to determine the effect of rehabilitation on cortical activation. Previous investigation using 6 weeks of balance training on CAI individuals with similar outcome variables[19] (i.e. CAIT score) was used to estimate a sample size ($1-\beta = 0.9$; $\alpha = 0.05$), with 8 participants per group identified as achieving sufficient power. In order to explore the effects of rehabilitation on cortical activation as much as possible, 15 participants were recruited.

Each participant received a home exercise program and was instructed to follow this program for about 40 min per day, four days per week and six weeks. The home exercise program included ankle range-of-motion exercises, muscle strengthening, and balance activities. The program was progressive, and every participant advanced at the same pace (Table 1). Except for some bipedal tasks, all other rehabilitation tasks were only completed on the involved limb. The intervention journal was used to track the participants' compliance with the home program.

The investigator (an examiner who was not an author) performed the tests respectively before and after six weeks of rehabilitation to assess PROs, dynamic balance and cortical activation.

2.2. Test protocol

Patient-Reported Outcomes. The PROs used in this study comprised of Cumberland Ankle Instability Tool (CAIT), Karlsson-

Table 1
Outline of the rehabilitation program.

Task	Sets/Reps (Maximum)	Progression
Range of motion		
Gastrocnemius stretch	3 × 30s	Sitting progress to standing
Soleus stretch	3 × 30s	Sitting progress to standing
Ankle passive ROM exercise	2 × 180s	
Ankle active ROM exercise	2 × 180s	
Strengthening		
Bipedal calf raise	2/20	leg straight to slightly bent knee
Towel toe curl exercise	5/5	sets
Clamshell exercise	3/15	sets, reps
Resistance band training		
Dorsiflexion	2/20	sets, reps
Planter flexion	2/20	sets, reps
Inversion	2/20	sets, reps
Eversion	2/20	sets, reps
Planter flexion/Inversion	2/20	sets, reps
Planter flexion/Eversion	2/20	sets, reps
Dorsiflexion/Inversion	2/20	sets, reps
Dorsiflexion/Eversion	2/20	sets, reps
Balance		
Tandem Stance	4 × 30s	Eyes open to closed, surface, ball tossing at the same time
Single-leg stance	4 × 50s	Eyes open to closed, surface, ball tossing at the same time
Single-leg stance with knee lift	4 × 50s	Eyes open to closed, surface, ball tossing at the same time
Step-downs with single limb in 8 directions	4 × 40s	

Abbreviations: Reps = repetitions; ROM = range of motion.

Peterson score, Foot and Ankle Ability Measure (FAAM) and Tegner activity level. CAIT and Karlsson-Peterson scores reflect ankle symptoms, FAAM assesses the ability of daily living (ADL) and sports and Tegner activity scale measures activity levels. The minimal clinically important differences (MCID) of CAIT,[20] FAAM-ADL, and FAAM--Sports[21] were 3 points, 8 points, and 9 points, respectively. The changes of PROs were compared with MCID to assess the clinical importance of the rehabilitation program.

Dynamic Balance Testing. Y-balance test (YBT) was used to assess dynamic balance. For details, see the corresponding content of our previous article.[11] The average reach distances for the involved leg in three directions were monitored, followed by normalizing the average values based on limb length to allow comparisons across participants. The composite reach distance was the mean of normalized reach distances of the three directions.

Functional Near-Infrared Spectroscopy Testing. Participants were instructed to complete three successful trials of 30-s bipedal standing and a subsequent 30-s single-leg stance with the fNIRS recording throughout the task. For details, see the corresponding content of our previous article.[11]

2.3. Data reduction and analysis

A 64-channel fNIRS system (NirScan, Danyang Huichuang Medical Equipment Co., Ltd, China) was utilized in the present study to record the oxygenated hemoglobin (HbO) signals and the deoxygenated hemoglobin (HbR) signals over the cerebral cortex of frontal, parietal, occipital and temporal lobes of both hemispheres. The sampling frequency was 11 Hz, and the wavelengths were 730 and 850 nm. According to the requirements of the internationally-used 10/20 electrode distribution system, 24 sources and 24 detectors were used to assess cortical activation during single-leg stance. The position of the fNIRS channel was defined as the midpoint of the corresponding light source-detector pair.

The positions of fNIRS optodes and reference points (Cz, Nz, Iz, AL and AR) were identified using a three-dimensional (3D) digitizer (Fastrak; Polhemus, Colchester, VT, USA) on the standard head model. Then, the NIRS_SPM[22] was used to register the coordinate data into Montreal Neurological Institute (MNI) coordinates, and the anatomical location of each channel was consequently determined according to the Talairach Daemon.[23] The inter-participant variance of the estimated fNIRS channel was modest. Therefore, a specific channel in different participants was assumed to have a similar location.

The light intensities in the fNIRS signals were analyzed using the NIRS toolbox. In brief, the processing steps included converting raw data to optical density and converting optical density to HbO and HbR using the modified Beer-Lambert law. A general linear model (GLM) was used to estimate task-related cortical activation. The contrast between the task and baseline values was estimated, and the β-coefficient for the task-related cortical activation was calculated using the HRF models with time and dispersion derivatives. Before conducting statistical analyses, the wavelet method was used as a low-pass filter and the HRF was used as a high-pass filter to eliminate baseline drift, movement and physiological artifacts from raw data.

Next, a GLM group analysis was conducted using 2-tailed one-sample student's t-tests employing random-effect models to identify the activated channels at a group level. The false discovery rate (FDR) corrected p-value (expressed as q-value)[24] with a threshold significance at $q < 0.05$ was used to infer statistically significant findings to avoid type-1 error in multiple comparisons.

Timeline analysis of both HbO and HbR signals before and after rehabilitation was performed for the activated channels in the GLM group analysis using the HomER2 toolbox. To determine task-specific cortical activity, for each participant, the differences between mean HbO and HbR during the baseline (2s before the start of the trial) and test (5–35s after the start of the trial) period were calculated and obtained average HbO and HbR concentrations. The increase of HbO concentration and the decrease of HbR concentration both indicate the increment of cortical activation.[25]

For average hemoglobin concentration before and after rehabilitation, a paired sample *t*-test was utilized, and Cohen's d effect sizes using the means and standard deviations were calculated. The strength of effect sizes was interpreted as weak ($d < 0.40$), moderate ($0.40 \leq d < 0.80$), or strong ($d \geq 0.80$).[26] Before multi-participant analysis, the fNIRS data of the left-limb-injured CAI participants was flipped horizontally about the midline. FNIRS data was analyzed using the NIRS-SPM and HomER2[27] toolboxes of MATLAB R2013b (MathWorks Inc., Natick, USA).

2.4. Statistical analysis

The Shapiro-Wilk test was used to assess the normality of the numerical variables' distributions. The Wilcoxon signed-rank test was used for paired samples to analyze the longitudinal changes of PROs and balance performances since normal distribution was not proved with the Shapiro-Wilk test for this analysis. Moreover, to investigate the relationship between the longitudinal changes in average hemoglobin concentrations and the clinical improvements of CAI, we performed Spearman's correlation analysis for ΔHbO of significant channels in paired sample *t*-test and ΔCAIT. All datasets were analyzed using the IBM SPSS Statistics 26.0 (IBM Corp., Armonk, NY, USA), and $p < 0.05$ indicated statistical significance.

3. Results

Demographic data and clinical characteristics including age, sex, BMI, the total number of ankle sprains, CAIT score and Tegner scale score are shown in Table 2.

The comparison of PROs and Y-balance test outcomes before and after rehabilitation is shown in Table 3. The CAIT ($p = 0.029$) and Tegner scale scores ($p = 0.004$) of participants were significantly improved after rehabilitation. The improvement of the CAIT score may also have clinical importance in comparison with the MCID.[28] No significant changes were detected in Karlsson-Peterson score ($p = 0.075$), FAAM-ADL ($p = 0.401$) and FAAM-S ($p = 0.421$). Participants reached further on the involved limb in the anterior ($p = 0.036$), posteromedial ($p = 0.046$) and posterolateral ($p = 0.023$) directions and had further composite reach distance ($p = 0.019$) in comparison with their baseline performances (Table 3).

The activated channels during single-leg stance were the frontal eye field (FEF), the left subcentral area, the left premotor cortex and the supplementary motor area (PM and SMA), the left S1, the left middle temporal gyrus (MTG) and the left STG. The activated channels were grouped into 7 regions of interest (ROIs) based on the FDR-corrected results from the one-sample t-tests (Table 4).

Significantly greater cortical activation was found after

Table 2
Demographics and basic characteristics of participants ($n = 13$).

Parameter	Basic information
Age[a] (y)	33.8 ± 7.7
Sex (Female/Male)	6/7
BMI[a] (kg/m^2)	24.7 ± 4.9
Injured limb (Left/Right)	4/9
CAI (Unilateral/Bilateral)	9/4
Total number of ankle sprains[a]	2.6 ± 2.5
Time since the first ankle sprain[a] (m)	79.5 ± 68.0
CAIT score[a]	12.5 ± 6.0
Tegner scale score[a]	4.1 ± 2.3

Abbreviations: CAI = chronic ankle instability; CAIT=Cumberland ankle instability tool.
[a] Values represent mean ± standard deviation.

Table 3
Patient-reported outcomes and Y-balance test outcomes.

Outcome	Pre-Rehab.[a]	Post-Rehab.[a]	ΔAfter 6 wk (95% CI)[b]
CAIT	12.5 ± 6.0	17.7 ± 6.6*	5.2 (0.8, 9.6)
Karlsson-Peterson score	64.2 ± 21.0	74.5 ± 16.3	10.3 (−1.7, 22.4)
FAAM-ADL(%)	92.3 ± 9.9	94.7 ± 7.9	2.4 (−2.7, 7.5)
FAAM-S(%)	83.2 ± 18.6	86.3 ± 17.9	3.1 (−4.6, 10.8)
Tegner	4.1 ± 2.3	5.2 ± 2.1**	1.1 (0.2, 1.9)
YBT-ANT(%LL)	63.0 ± 8.8	68.0 ± 14.7*	5.0 (−0.6,10.6)
YBT-PM (%LL)	108.3 ± 14.0	116.7 ± 12.9*	8.5 (−0.8,17.8)
YBT-PL (%LL)	112.8 ± 7.7	119.3 ± 11.1*	6.5 (1.0,12.1)
YBT-composite (%LL)	94.7 ± 9.1	101.3 ± 11.9*	6.7 (0.9,12.4)

*p < 0.05, **p < 0.01, statistically significant different from the values before rehabilitation.
Abbreviations: Δ = change; ADL = ability of daily living; ANT = anterior; CAI = chronic ankle instability; CAIT= Cumberland ankle instability tool; CI = confidence interval; FAAM = foot and ankle ability measure; LL = leg length; PL = posterolateral; PM = posteromedial; YBT= Y-balance test.
[a] Values represent mean ± standard deviation.
[b] Values represent mean (95 % confidence interval).

Table 4
Activated channels during the postural control task.

Channel	MNI coordinates (X/Y/Z)	Cortical region	BA	T-value
Ch. 2	18/38/57	FEF	8	3.1
Ch. 19	−65/-2/27	Subcentral Area	43	4.4
Ch. 20	−60/-2/41	PM and SMA	6	3.4
Ch. 21	−68/-23/30	S1	3,1,2	3.3
Ch. 37	−65/-4/-3	MTG	21	6.2
Ch. 38	−66/-4/11	STG	22	4.9
Ch. 39	−70/-27/9	STG	22	3.4

Abbreviations: BA=Brodmann's area; Ch. = channel; FEF = frontal eye field; MNI=Montreal neurological institute; MTG = middle temporal gyrus; PM = premotor cortex; S1 = primary somatosensory cortex; STG = superior temporal gyrus.

rehabilitation as indicated by the greater decrease in average HbR concentration in the S1 (channel 21, d = 0.66, p = 0.035, the difference of HbR = -0.38 μmol/L[95 % CI = −0.72, −0.03]), MTG (channel 37, d = 0.66, p = 0.035, the difference of HbR = -0.47 μmol/L[95 % CI = −0.90, −0.04]) and STG (channel 39, d = 1.06, p = 0.002, the difference of HbR = -0.59 μmol/L[95 % CI = −0.92, −0.25], Fig. 1A). No significant signal changes were observed in HbO after rehabilitation.

The longitudinal changes in average HbO concentrations (ΔHbO) in the S1 (channel 21, r = 0.74, p = 0.005) and the STG (channel 39, r = 0.72, p = 0.007) respectively presented significant positive correlations with the change of CAIT score(ΔCAIT) (Fig. 1B). No significant correlation was found between the longitudinal changes in average HbR concentrations and the ΔCAIT score.

4. Discussion

The most important finding of the present study is that rehabilitation could affect cortical activation during postural control tasks. To the best of our knowledge, this is the first study exploring the effects of rehabilitation on neuroplasticity at the cortical level in the CAI population. FNIRS was used to study the effect of rehabilitation on cortical activation for postural control and the relationship between the change of cortical activation and the change of ankle symptoms. After six weeks of rehabilitation, CAI patients have improved PROs and balance outcomes and demonstrated greater cortical activation for postural control in S1, MTG and STG. Moreover, the increase of cortical activity in S1 and STG was significantly correlated with the improvement of the CAIT score. This study associated perceptual and balance improvement with rehabilitation at the cortical level and deepened our understanding of the rehabilitation of CAI patients.

During the postural control task, CAI patients showed significant activation in FEF,[29] subcentral area, PM and SMA, S1, MTG, and STG. This result is consistent with our previous work[11] and others' research. During postural control, the information from proprioceptive, vestibular and visual constitute the afferent source to the CNS. This information is processed in the spinal cord, brain stem and cortex and then contributes to motor planning as well as to unconscious muscle activation contributing to the maintenance of joint stabilization and postural control. The significantly activated cortical regions during the postural control task were the sensory areas: FEF controls visual attention; S1 and subcentral areas have a somatosensory function; the activation of MTG and STG can reflect the vestibular activation and the processing of sensory signals[30]; PM and SMA[31] prepare and execute limbs' movement.

The cortical activation of S1 was increased after six weeks of rehabilitation. S1 is a primary receptor of bodily sensory data from skin, joints, ligaments, muscles and tendons relayed by thalamic radiations. Healthy people rely heavily on somatosensory during postural control tasks.[32] However, the mechanoreceptors located in ankle ligaments of CAI patients were damaged due to recurrent ankle sprain and ankle "giving way", resulting in decreased bodily sensory data of the ankle joint. Previous studies found that the somatosensory cortex of CAI patients is not able to discriminate higher levels of load on the ankle ligaments,[9] which may potentially reduce the CNS ability to cope with joint loads[10] and increase the risk of a recurrent ankle sprain. Combined with previous studies, our findings further illustrate that six weeks of rehabilitation can increase the cortical activation of S1 during the single-leg stance and may subsequently allow patients to appropriately position their joints to avoid injury and to cope with balance tasks better.

Furthermore, six weeks of rehabilitation could increase the cortical activation of STG and MTG as well as the vestibular input. MTG and STG are parts of the multisensory vestibular cortical areas.[33]Moreover, increased activation of STG was observed when participants relied more on vestibular function.[34] Fu et al. suggested that CAI patients may have vestibular malfunction,[32] while Hilgendorf found that four weeks of vestibular-ocular reflex training improved dynamic postural stability among CAI patients.[35] Both of these results indicate that the CAI patients can benefit from the improvement of vestibular function, with this finding being also demonstrated in our study. The balance ability of CAI patients had significantly improved after six weeks of rehabilitation and the brain areas related to vestibular input presented greater activation. It is thus hypothesized that MTG and STG plays a compensatory role in the rehabilitation process of CAI patients.

The increased cortical activation due to rehabilitation is associated with the improvement of ankle symptoms. Significant positive correlations were observed between the ΔHbO concentrations in S1, STG and the ΔCAIT score, suggesting that the cortical activation of S1 and STG plays an important role in postural control in CAI patients. Our previous work found that CAI's activation of S1 and STG during the single-leg stance was lower than that of the coper group, which might be the underlying cause of CAI's dysfunction and the important influencing factor for copers' better recovery.[11] Combined with our previous study, this finding further illustrated that the increased activation of S1 and STG was beneficial for CAI patients. Future rehabilitation should focus more on enhancing the CAI patients' perception. For example, early mobilization instead of prolonged immobilization after ankle sprains, starting balance training as soon as weight bearing can be tolerated and developing more complex balance-training protocols is beneficial to restoring perception.[36] Future studies could also try to use neuromodulative therapies (e.g. transcranial magnetic stimulation, transcranial electrical stimulation and transcranial direct current stimulation) to enhance the cortical activation of S1 and STG and find out whether these therapies can assist the treatment of CAI. Bruce et al. treated CAI patients with

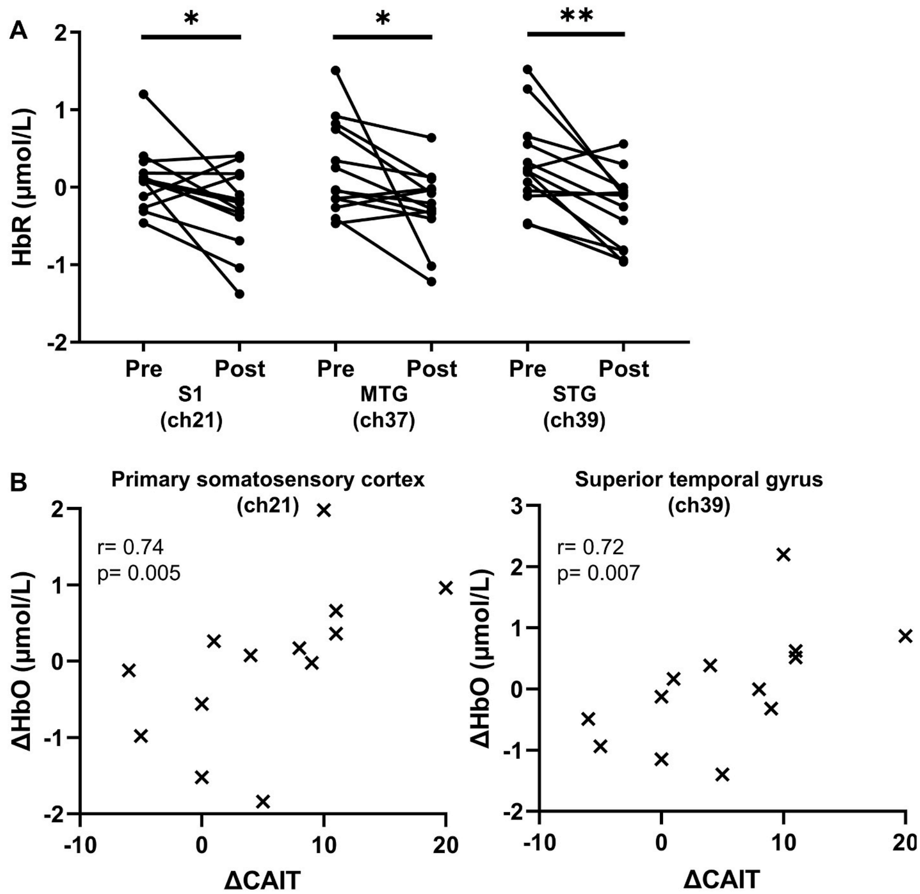

Fig. 1. Cortical activation associated with rehabilitation. **(A)** The scatterplots of cortical activity of the primary somatosensory cortex (S1), the middle temporal gyrus (MTG) and the superior temporal gyrus (STG) showed significantly greater cortical activation by a greater decrease of the average HbR concentration. **(B)** Correlation analysis between cortical activation changes and ankle symptoms. Significant positive correlations were found between ΔCAIT and ΔHbO in S1 and STG respectively. *, $p < 0.05$; **, $p < 0.01$.

Abbreviations: Δ = change; ΔHbO = longitudinal changes in average oxyhemoglobin concentrations; CAIT=Cumberland ankle instability tool; HbR = deoxyhemoglobin; MTG = middle temporal gyrus; S1 = primary somatosensory cortex; STG = superior temporal gyrus.

four-week eccentric training and anodal transcranial direct current stimulation (aTDCS) and reported a significant improvement in cortical excitability, PROs and functional performance.[37] In addition, the cortical activation of S1 and STG during postural control tasks measured by fNIRS may be used to assess the effect of treatment in the future.

The present study has several limitations. Firstly, as an extension of our previous work,[11] this study lacks a control group, however, due to the similarity of the fNIRS testing, we can refer to the conclusion of the previous study. Secondly, the sample size of this study is small, however, we still found significant differences in cortical activation before and after rehabilitation and may provide a reference for sample size estimating for future studies using similar methods. Thirdly, as an exploratory study, our rehabilitation protocol included training of the range of motion, muscle strength and balance, making it difficult to determine which rehabilitation procedure mostly contributed to neuroplasticity. Future studies should use more specific rehabilitation methods as an intervention to assess their influence on neuroplasticity. Finally, because of the low penetration depth of fNIRS, it was impossible to evaluate deep brain regions, such as the basal ganglia, brain stem and cerebellum. However, the 64 channels were fully used to maximize the coverage of the cortical regions of interest.

5. Conclusions

The present study revealed that 6 weeks of rehabilitation improved the PROs, balance outcomes and led to greater activation of S1, MTG and STG. Moreover, the increase of the cortical activation of S1 and STG significantly correlated with the improvement of ankle symptoms. Future studies could use fNIRS technology to further clarify the neuroplasticity of CAI and to solve important clinical issues, such as the selection of the most powerful rehabilitation procedures for neuroplasticity.

Institutional review board statement

The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the local ethics committee.

Informed consent statement

Informed consent was obtained from all subjects involved in the study. Written informed consent has been obtained from the patient to publish this paper.

Declaration of competing interest

The authors have no conflicts of interest relevant to this article.

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