Journal of Integrative Neuroscience

J. Integr. Neurosci. **2026**; 25(3): 47653
https://doi.org/10.31083/JIN47653

Original Research

Cerebellar iTBS Modulates Cortical Network Properties: An fNIRS Study

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Academic Editor: Bettina Platt
Submitted: 24 October 2025 Revised: 18 December 2025 Accepted: 27 January 2026 Published: 24 March 2026

Abstract

Background: The cortex and cerebellum have a closely connected closed-loop circuit. Intermittent theta burst stimulation (iTBS) targeting the cerebellum has shown promise in improving balance function and inducing neuroplasticity. This study investigates whether cerebellar iTBS can elicit cortical responses. **Methods**: One hundred healthy volunteers were randomly assigned to a real or sham iTBS stimulation group. Functional near-infrared spectroscopy (fNIRS) measured cortical activation during resting, walking, and unilateral support tasks. **Results**: During the unilateral support task, graph theory analysis revealed significant changes in brain network properties, suggesting a deviation from optimal small-world organization and reduced global integration. No significant changes were observed during the walking and resting-state tasks. **Conclusions**: These findings suggest that cerebellar iTBS can modulate cortical activity, though further studies are needed to confirm its clinical effects. **Clinical Trial Registration**: ChiCTR2300077916, https://www.chictr.org.cn/showproj.html?proj=207394.

Keywords: cerebellum; cerebral cortex; intermittent theta burst stimulation; functional near-infrared spectroscopy

1. Introduction

Closed-loop circuits make a close connection between the cerebellum and the cerebral cortex [1]. The cerebellum can modulate the cortex's contralateral motor and non-motor areas via the cerebello-dentato-thalamo-cortical pathway to affect motor, cognitive, or other performance [2,3]. Therefore, the cerebellum has thus been investigated over the years as a critical modulator of the activity of the cerebral cortex [4].

Different methods have explored the connections between the cerebral cortex and the cerebellum. In animal experiments, Kelly and Strick [5] injected transneuronal tracers into different regions of the cerebellum in macaque monkeys and discovered projections from the cerebellum to the M1 and prefrontal cortex (PFC). Imaging evidence from Krienen and Buckner [6] used functional magnetic resonance imaging (fMRI) to perform functional connectivity analysis between the cerebellum and seed points in the motor cortex, dorsolateral PFC, medial PFC, and anterior PFC. As a result, they constructed a provisional map of cerebellar topography based on functional correlations with the frontal cortex.

Non-invasive brain stimulation (NIBS) techniques have also been applied to explore this connection. Although cerebellum-brain inhibition (CBI) provides important evidence for cerebellar–cortical interactions [7,8], it mainly reflects changes in M1 excitability and offers limited insight into task-related cortical dynamics across multiple brain regions, suggesting an inhibitory effect of the cerebellar hemisphere on the cerebral cortex. At the same time, in a study by Koch *et al*. [9], intermittent theta burst stimulation (iTBS) was applied to the uninjured cerebellar hemisphere to address persistent balance issues in patients with chronic supratentorial stroke. This intervention resulted in significant improvements in balance function and was accompanied by cortical remodeling in the posterior parietal cortex (PPC). These findings suggest that cerebellar NIBS may influence cortical plasticity by modulating cerebellar–cortical pathways. However, whether cerebellar NIBS can directly and reliably affect cerebral cortical activity remains unclear. This uncertainty largely stems from the limitations of CBI paradigms based on motor-evoked potentials (MEPs). MEPs primarily reflect the excitability of the corticospinal tract, which integrates contributions from multiple subcortical and cortical structures, including the cerebellum, thalamus, basal ganglia, and brainstem. Moreover, hemispheric cerebellar transcranial magnetic stimulation (TMS) may also influence adjacent brainstem regions through current spread. As a result, changes in MEP amplitude cannot be unequivocally attributed to modulation of M1 or broader cortical regions. Consequently, conventional TMS-based approaches provide only indirect and spatially limited ev-

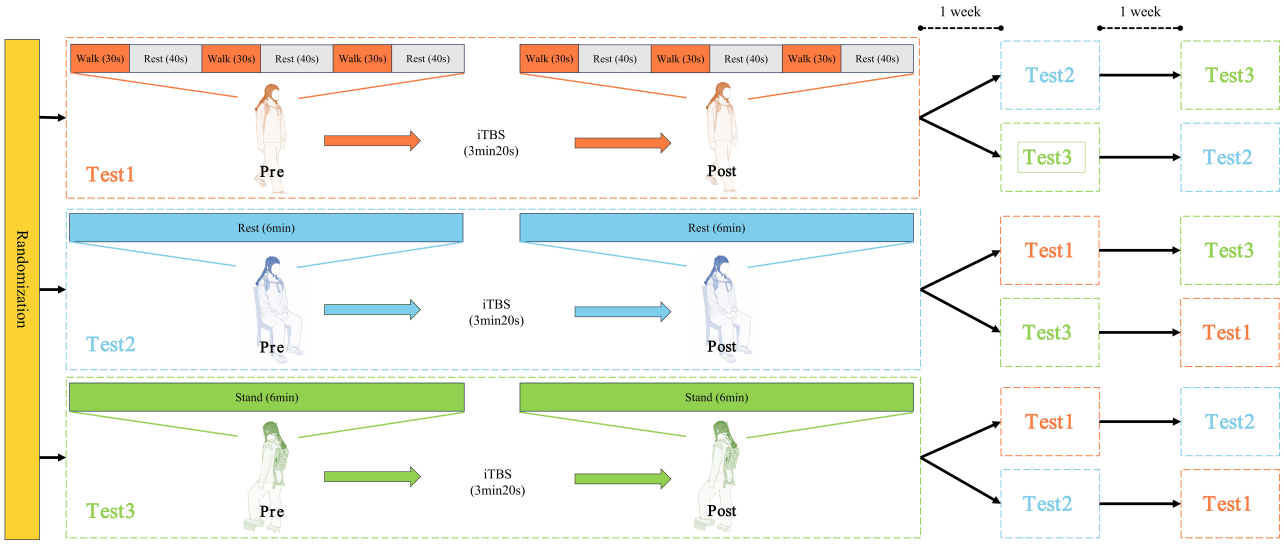

Fig. 1. The diagram of procedures. iTBS, intermittent theta burst stimulation.

idence of cortical involvement, with observations largely restricted to M1. Nevertheless, some studies have begun using magnetic resonance imaging and electroencephalography (EEG) to reveal changes in the cerebral cortex following cerebellar stimulation [10,11]. Due to equipment limitations, these observed changes have been based on the resting state. While resting-state analysis provides indirect evidence for balance function, real-time observation during balance tasks might offer more direct insights.

Functional near-infrared spectroscopy (fNIRS), like other brain imaging tools, can observe cortical changes at rest and can also conduct real-time monitoring during motor tasks. Red light frequencies between 700 and 900 nm were used by fNIRS, capable of detecting oxyhemoglobin (Oxy-Hb) and deoxyhemoglobin (Dxy-Hb) [12]. Compared with fMRI and EEG, fNIRS shows greater robustness to movement-related interference, which makes it particularly suitable for studying complex motor tasks [13]. Based on previous experiments [14], we conducted the resting-state data collection. By leveraging fNIRS's resistance to motion artifacts, we also performed real-time data collection during balance and walking tasks, allowing us to observe changes more directly related to balance regulation. The regions of interest (ROIs) we selected are well-aligned with the balance. The premotor cortex (PMC) and supplementary motor area (SMA) play a crucial role in both anticipatory and compensatory postural adjustments [15]. The PFC has also been shown to be involved in complex balance tasks, while the sensorimotor cortex (SMC) is responsible for executing movements and contributing to balance regulation [16,17]. Considering the cerebellar hemisphere's deeper anatomical location, we used a double-cone coil with a greater depth range for stimulation [18,19].

Therefore, the main objective of our experiment is to observe whether a single session of cerebellar iTBS can induce changes in the cerebral cortex. These changes are monitored not only at resting tasks but also in real-time during walking and unilateral support tasks, which are closely related to balance.

2. Method

2.1 Subject

A total of 100 healthy volunteers (52 in the real stimulation group) participated in this study. Participants were randomly assigned to two groups using a coin-randomization method: one group received real stimulation, while the other received sham stimulation. Six participants (4 in the real stimulation group) were excluded due to weak fNIRS signal collection, and fifteen (8 in the real stimulation group) participants did not complete all tests due to scheduling conflicts. Ultimately, 40 participants (age: 23.77 $\pm$ 9.03, gender: 15 male/25 female) were included in the real stimulation group, and 39 participants (age: 26.21 $\pm$ 10.65, gender: 13 male/26 female) were included in the sham stimulation group. As a result, these 79 participants completed all tasks. The inclusion criteria were as follows: (1) age between 18 and 70 years, (2) no history of neurological or psychiatric disorders, (3) right-handedness, and (4) signed informed consent. The exclusion criteria included: (1) any history of neuropsychological conditions such as depression, anxiety, or schizophrenia, (2) history of drug abuse, particularly substances that could pose risks for TMS or lower the seizure threshold, (3) musculoskeletal disorders, especially in the lower limbs and trunk, (4) vestibular deficits, and (5) prior participation in other TMS experiments without reporting TMS exclusion criteria.

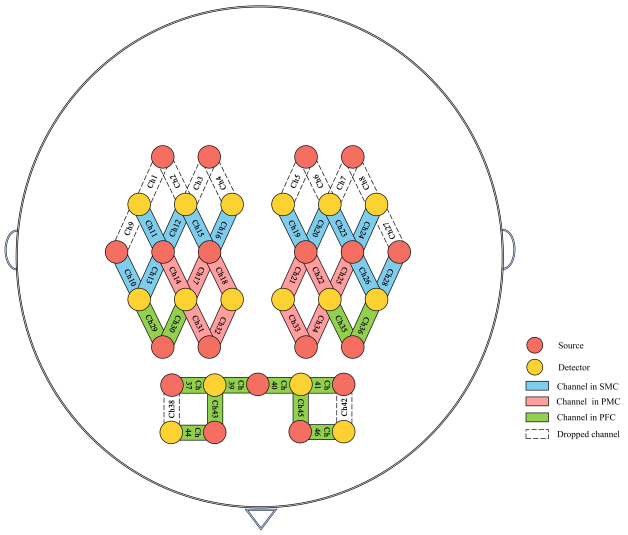

Fig. 2. The attribution of channels and division of 6 ROIs. Pink channels belong to the SMC, yellow channels belong to PMC/SMA, and green channels belong to the PFC. ROIs, regions of interest; SMC, sensorimotor cortex; PMC, premotor cortex; SMA, supplementary motor area; PFC, prefrontal cortex; ch, channel.

2.2 Procedure

Resting-state tasks are now widely used in research. In addition to this, we designed tasks related to balance. During walking, the body constantly needs to adjust balance to maintain stability and prevent falls. Furthermore, single-leg support further increases the difficulty of maintaining balance. Thus, each participant completed the following three tasks: (1) Resting state: sitting in a relaxed position on a chair for 6 minutes; (2) Walking task: walking at a preferred speed for 30 seconds, followed by 40 seconds of rest, repeated 3 times; (3) Unilateral support task: raising their leg onto a step and maintaining balance on the right leg for 6 minutes. The three tasks were performed on separate days, with a 7-day washout period between any two tasks [10]. The order of the tasks was randomized using a dice-rolling method. For each session, one task was performed first, followed by either real or sham iTBS intervention, depending on the group, and then the task was immediately repeated. Throughout all tasks, fNIRS was used to collect signal data. The procedure is illustrated in Fig. 1.

2.3 Intermittent Theta Burst Stimulation

Cerebellar stimulation was delivered using a double-cone coil (Magneuro R480, Vishee Medical, Nanjing, Jiangsu, China) connected to a 6-T magnetic stimulator, with stimulation applied to the right cerebellar hemisphere in a single iTBS session. The coil consisted of two conical windings with an outer diameter of 215 mm, an inner diameter of 140 mm, and an inter-coil angle of 105°. The stimulation site was defined anatomically as a point located 3 cm lateral to the midline and 1 cm inferior to the inion, corresponding to the external occipital protuberance. The center of the coil was located on the target point. During the iTBS application, the stimulator output intensity was set to 80% of the active motor threshold (AMT) [20]. The AMT was defined as the lowest intensity that produced a MEP of $>$200 µV in at least 5 out of 10 trials with 10% maximal voluntary contraction of abductor pollicis brevis monitored by electromyography [21]. The intermittent theta burst stimulation was administered using a standard burst-based pattern. Stimulation was delivered in 2-s trains composed of 30 pulses, with each train repeated at 10-s intervals. Within each train, pulses were arranged as ten triplets, corresponding to a theta-frequency pattern of 5 Hz, with short interpulse spacing between triplets. Across the entire session, a total of 600 pulses were applied to each participant, resulting in an overall stimulation duration of 3 min and 20 s. The sham stimulation group received stimulation at 0% of the AMT intensity.

2.4 fNIRS Measurement

The NirSmart fNIRS device (NirSmart-3000A, Danyang Huichuang Medical Equipment Co., Ltd., Zhenjiang, Jiangsu, China) was used in this study. Hemodynamic activity in the prefrontal, temporal, and parietal cortices during walking was recorded using near-infrared light at wavelengths of 730 and 850 nm, with a sampling rate of 11 Hz. A total of 46 measurement channels were arranged across the cortical surface, consisting of 19 light sources and 27 detectors. The three-dimensional positions of all optodes were acquired using an electromagnetic digitization system (Patriot, Polhemus, Colchester, VT, USA; https://polhemus.cn/motion-tracking/all-trackers/patriot/). Channel locations were subsequently transformed into Montreal Neurological Institute (MNI) space and mapped onto a standard MNI brain template. Each channel was assigned to a functional region according to the Brodmann area with the highest proportional overlap. The distance between adjacent optodes was 3 cm. Further details regarding channel positions and the division of ROIs are provided in Fig. 2 and Table 1.

2.5 fNIRS Data Processing

We implemented a series of preprocessing steps on the fNIRS data using Homer2 (Homer2_UI v1.5, Massachusetts General Hospital/Harvard Medical School, Charlestown, MA, USA). Raw fNIRS signals were first converted into optical density data. Motion-related artifacts were then corrected using a cubic spline interpolation approach, with thresholds set at 6.0 for standard deviation and 0.5 for signal amplitude. To reduce physiological drift and high-frequency noise while retaining task-relevant hemodynamic components, the data were band-pass filtered between 0.01 and 0.1 Hz. The processed optical density signals were subsequently transformed into

Table 1. Relationships between ROIs, Brodmann areas, and channels.

ROI	Brodmann area	Channel
R-SMC	1	11
R-SMC	3	12
R-SMC	4	10, 13, 15, 16
L-SMC	1	24
L-SMC	3	23
L-SMC	4	19, 26, 28
R-PMC/R-SMA	6	14, 17, 18, 31, 32
L-PMC/L-SMA	6	21, 22, 25, 33, 24
R-PFC	9	29, 30
R-PFC	10	39, 43, 44
R-PFC	46	37
L-PFC	9	35, 36
L-PFC	10	40, 45, 46
L-PFC	46	41

R-, right; L-, left.

changes in hemoglobin concentration using the modified Beer–Lambert law, with a differential path length factor of 6 [22,23].

For the walking task, 30 seconds time window of changes in Oxy-Hb (ΔHBO) and Dxy-Hb (ΔHBR) during walking was used as indicators of cortical activation. The occurrence of heightened cortical activation, which coincides with a spontaneous increase in blood flow within the cortices, is referred to as neurovascular coupling [24]. The 5 seconds before the task were used as the baseline, during which participants were instructed to remain quietly standing. The walking task was repeated three times, and the ΔHBO for each participant was averaged across these three repetitions.

For the resting-state and unilateral support tasks, we performed functional connectivity (FC) analysis and graph theory analysis. FC in brain imaging refers to the temporal correlation between spatially remote neural structures [25]. The 34 channels were grouped into six ROIs, and the Oxy-Hb values from all channels within each ROI were averaged. These ROI-averaged Oxy-Hb values were then used to calculate the Pearson correlation coefficients between each pair of ROIs, which served as the FC values. Graph theory analysis is a data-driven approach that models the brain as a graph composed of nodes and edges. By calculating global and local network topological properties, it reveals changes in the brain's network topology [26].

Global properties of the brain network were computed using the GRETNA V2.0 software package (Imaging Connectomics Lab, Beijing Normal University, Beijing, China). The sparsity range was set between 0.12 and 0.40, with an interval of 0.01 and an iteration of 100 times. We used the built-in function of the GRETNA toolbox (gretna_get_rmax) to estimate the lower bound of sparsity based on the 34 used channels, which was determined to be 0.12, while the upper bound was set according to a previous study [27]. The area under the curve for each network matrix was calculated. The global properties analyzed included: (1) Global network efficiency metrics, specifically global efficiency (Eglob) and local efficiency (Eloc); (2) Small-world parameters, including clustering coefficient (Cp), characteristic path length (Lp), and normalized small-worldness (σ).

2.6 Statistical Analysis

Our fNIRS data were mainly analyzed using MATLAB R2015b (The MathWorks, Inc., Natick, MA, USA). The mixed analysis of variance (ANOVA) was applied to all results. First, regarding normality, the results of cortical activation and global properties network metrics were generally consistent with a normal distribution, with only a small number of brain regions showing mild deviations from normality. Given that the sample size in each group exceeded 30 participants, the statistical analyses are considered robust to moderate violations of the normality assumption. Second, for FC measures, more than half of the connections initially exhibited non-normal distributions. Therefore, Fisher's z transformation was applied to the FC data prior to statistical analysis. After transformation, normality was assessed using the Shapiro–Wilk test, and the vast majority of FC values were found to conform to the normality assumption. In addition, homogeneity of variance was evaluated using Levene's test, and the results indicated that the assumption of equal variances was generally satisfied across all measures. When multiple comparisons were made, the Bonferroni method was used for correction, adjusting the significance p-value to 0.05/n (where n is the number of comparisons). When significant main effects were found, further tests were conducted on the difference indicators. Paired t-tests were used within groups, and independent samples t-tests were used between groups, with the Bonferroni method applied to correct for multiple comparisons.

3. Result

3.1 Walking Task

After a single session of iTBS effects on cortical activation, significant statistical differences were observed in several ROIs. Due to 6 ROIs, the significance level for the mixed ANOVA was set at 0.05/6. The results of ΔHBO showed significant differences for the interaction factor in the left premotor cortex/left supplementary motor area (LPMC/LSMA, $F_{(1,77)} = 15.21$, $p < 0.001$, $\eta^2 = 0.016$), left prefrontal cortex (LPFC, $F_{(1,77)} = 8.31$, $p = 0.005$, $\eta^2 = 0.027$). However, no differences were observed for the time factor or group factor. Therefore, we conducted post-hoc tests on these two brain regions (Table 2). Since there were six comparisons, the significance level was adjusted to 0.05/6. The results showed that no significant differences were found in any of the groups. There

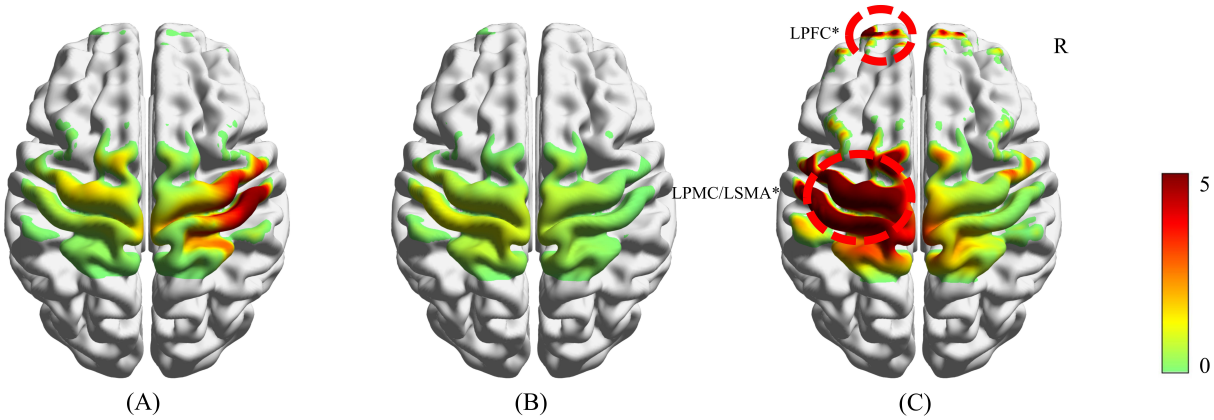

Fig. 3. F-values of mixed analysis of variance (ANOVA) of ΔHBO for the walking task. (A) Time effect; (B) Group effect; (C) Interaction effect. ΔHBO, Oxy-Hb. * with significant difference.

Table 2. The simple effect analysis of ΔHBO for in LPMC/LSMA and LPFC during walking task.

ROI		Pre (n = 40)	Post (n = 39)	*t*	*p*
LPMC/LSMA	Real	–0.011 ± 0.052	–0.004 ± 0.047	–1.218	0.231
	Sham	0.006 ± 0.053	–0.012 ± 0.052	2.573	0.014
	t	–1.381	0.661		
	p	0.171	0.511		
LPFC	Real	–0.018 ± 0.060	–0.002 ± 0.051	–2.427	0.020
	Sham	0.002 ± 0.055	–0.014 ± 0.053	2.412	0.021
	t	–1.541	1.162		
	p	0.127	0.249		

is no difference in ΔHBR. The details are shown in Fig. 3 and the **Supplementary Table 1 and Table 2.** ΔHBO and ΔHBR across all time points within walking blocks were shown for each brain region per group in Fig. 4.

3.2 Resting Task

No significant differences were observed following either real or sham iTBS intervention from the FC and graph theory perspectives. This suggests that neither real nor sham stimulation led to measurable changes during the resting task. The details are shown in Fig. 5, Fig. 6, and the **Supplementary Table 3 and Table 4**.

3.3 Unilateral Support Task

The FC analysis results showed no significant time, group, or interaction effects between the two groups of subjects (see Fig. 7 and **Supplementary Materials Table 5**). Positive results were observed only after real iTBS when analyzed using graph theory, and the significance level for the mixed ANOVA was set at 0.05. The graph theory analysis results (see Fig. 8 and **Supplementary Materials Table 6**) revealed significant time effects in the two groups for Lp ($F_{(1,77)} = 5.220$, $p = 0.025$, $\eta^2 = 0.017$) and Eglob ($F_{(1,77)} = 5.606$, $p = 0.020$, $\eta^2 = 0.017$). Additionally, significant interaction effects were observed for σ ($F_{(1,77)} = 6.785$, $p = 0.011$, $\eta^2 = 0.033$), Lp ($F_{(1,77)} = 15.469$, $p < 0.001$, $\eta^2 = 0.051$), and Eglob ($F_{(1,77)} = 18.496$, $p < 0.001$, $\eta^2 = 0.054$). Further simple effect analysis was conducted on σ, Lp, and Eglob, which exhibited interaction effects (see Table 3). The results indicated: σ significantly decreased in the real iTBS group after the intervention ($t = 3.004$, $p = 0.005$), and post-intervention σ was significantly lower in the real iTBS group compared to the control

Table 3. The simple effect analysis of σ, Lp, and Eglob during the unilateral support task.

		Pre (n = 40)	Post (n = 39)	*t*	*p*
σ	Real	0.397 ± 0.083	0.360 ± 0.059	3.004	0.005*
	Sham	0.401 ± 0.074	0.410 ± 0.070	–0.684	0.498
	t	–0.211	–3.400		
	p	0.833	0.001*		
Lp	Real	0.600 ± 0.067	0.643 ± 0.079	–4.340	<0.001*
	Sham	0.600 ± 0.062	0.588 ± 0.051	1.207	0.235
	t	–0.008	3.652		
	p	0.993	<0.001*		
Eglob	Real	0.139 ± 0.012	0.131 ± 0.013	4.761	<0.001*
	Sham	0.139 ± 0.011	0.141 ± 0.010	–1.381	0.175
	t	0.050	–3.900		
	p	0.960	<0.001*		

* with significant difference. Lp, characteristic path length; σ, normalized small-worldness; Eglob, global efficiency.

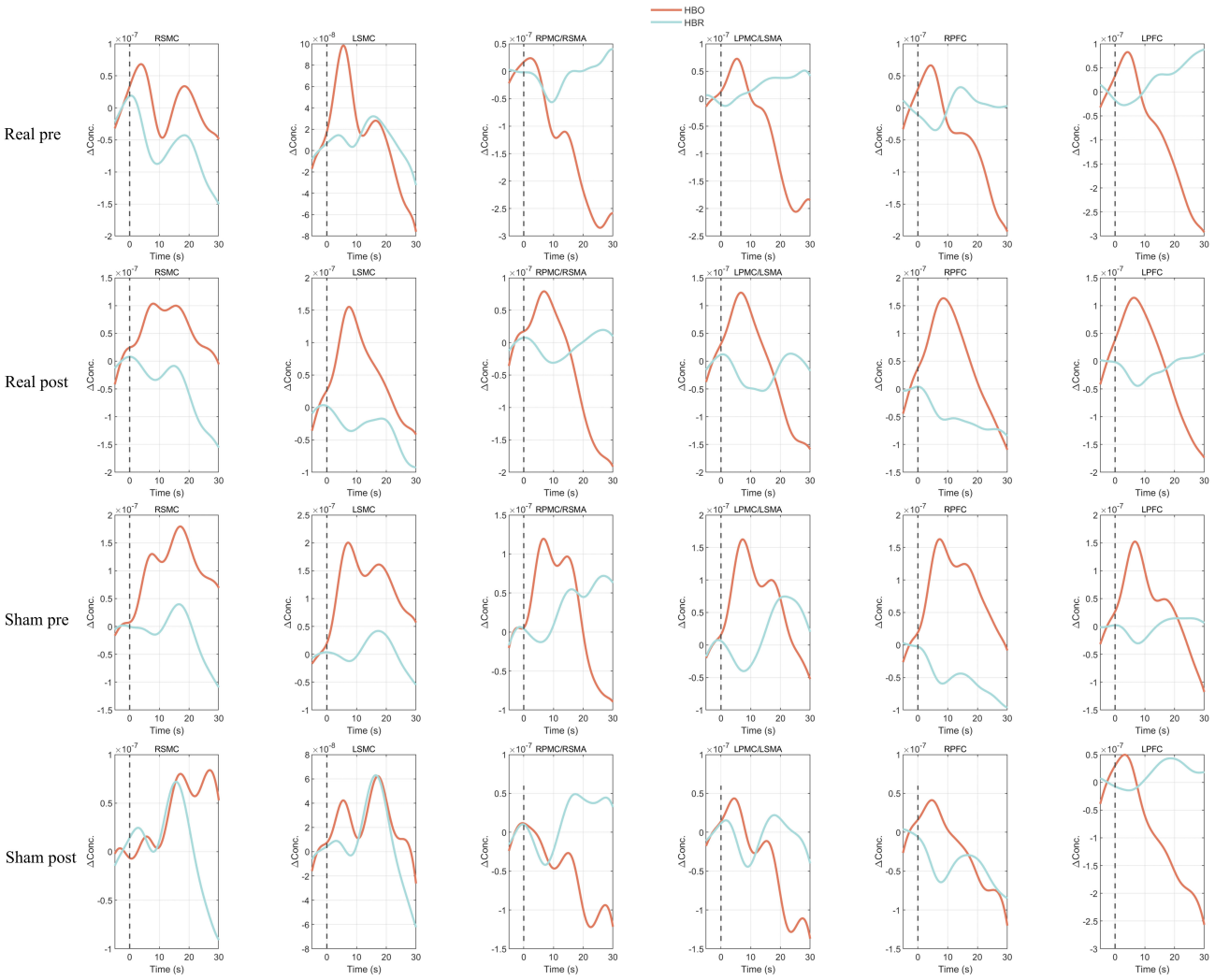

Fig. 4. ΔHBO and ΔHBR across all time points during walking task in 6 ROIs. ΔHBR, Dxy-Hb.

group (t = –3.400, p = 0.001). Lp significantly increased in the real iTBS group after the intervention (t = –4.340, $p <$ 0.001), and post-intervention Lp was significantly higher in the real iTBS group compared to the control group (t = 3.652, $p < 0.001$). Eglob significantly decreased in the real iTBS group after the intervention (t = 4.761, $p < 0.001$), and post-intervention Eglob was significantly lower in the real iTBS group compared to the control group (t = –3.900, $p < 0.001$).

4. Discussion

This study aimed to investigate whether cerebellar iTBS induces a cortical response, thereby validating the feasibility of a closed-loop cerebellar-cerebral cortex circuit using NIBS techniques. Significant differences in graph theory metrics were observed before and after the unilateral support task, while no significant differences were found during the walking and resting-state tasks. In contrast, the sham stimulation group exhibited no differences across any of the tasks.

During the walking task, we found significant interaction factors in LPFC and LPMC/LSMA. However, further simple effect analysis of these two brain regions revealed no significant differences. This pattern likely reflects diverging trends between groups, which is sufficient to produce a significant interaction term but insufficient to yield statistically significant simple effects under conservative multiple-comparison correction. From the results, we observed that the real stimulation group showed an increasing trend in ΔHBO levels after the intervention, whereas the sham stimulation group exhibited a slight decrease in activation compared to baseline. We speculated that the iTBS could elicit the activation of the contralateral cortex to some extent. It should be noted, however, that this speculation remains tentative and requires further validation. Tan *et al.* [16] found that cerebellar iTBS can enhance cortical excitability. This study applied iTBS to the cerebellar vermis and observed its immediate effects on cortical excitability during balance tasks in healthy individuals, revealing that a single session of cerebellar ver-

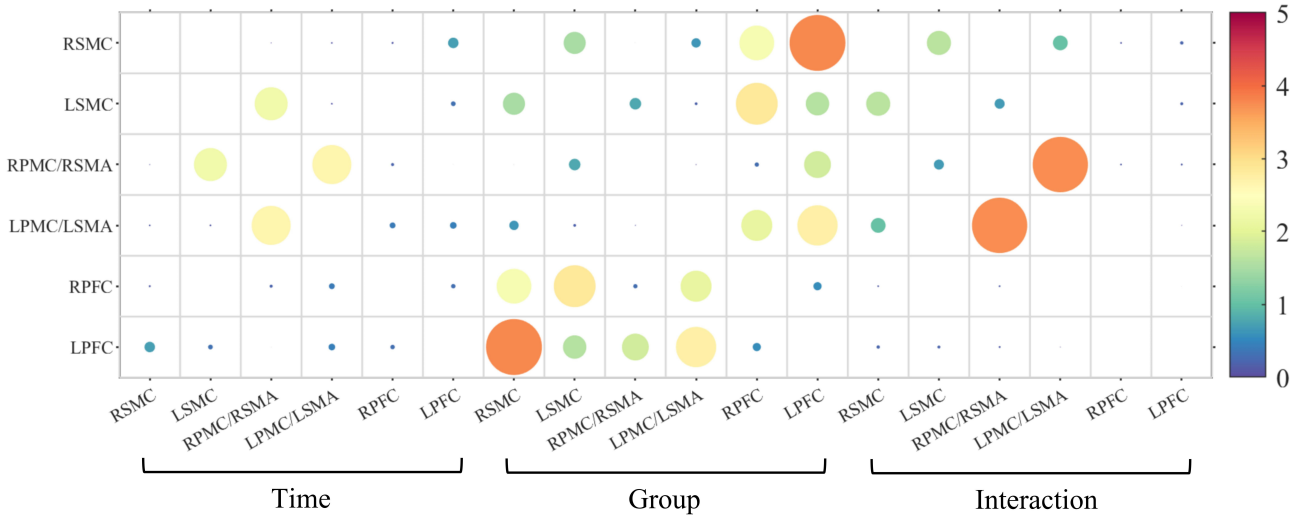

Fig. 5. Functional connectivity (FC) of F-values in mixed ANOVA for the resting task.

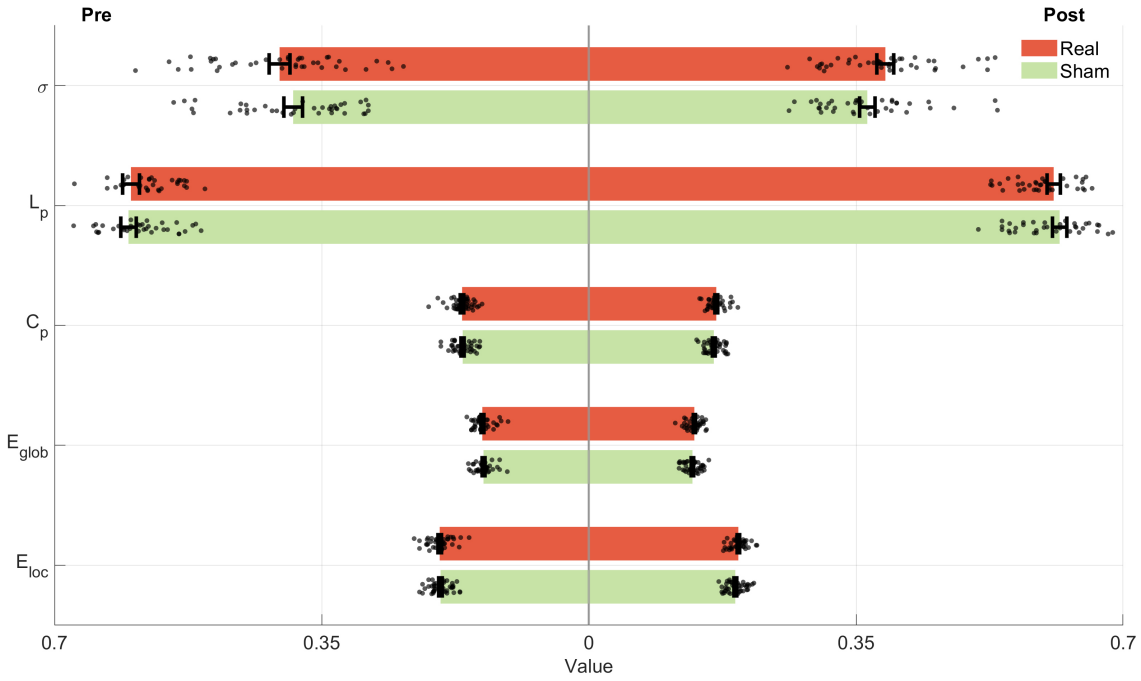

Fig. 6. The graph theory metrics of pre- and post- iTBS for the resting task.

mis iTBS could increase cortical excitability in the bilateral SMA during balance tasks in healthy adults. The discrepancy between our findings and those reported by Tan *et al.*'s study [16] may be partly attributed to differences in cerebellar stimulation sites. Tan *et al.* [16] targeted the cerebellar vermis, which has strong bilateral connections with the SMA [28]. In contrast, the present study stimulated the cerebellar hemisphere, which predominantly influences the contralateral cortex via the dentato–thalamo–cortical pathway. Consequently, hemispheric stimulation may produce more distributed or subtle cortical network modulation rather than focal increases in SMA excitability. These differences highlight the importance of stimulation site selection when interpreting the cortical effects of cerebellar iTBS. Similarly, another study [29] used TMS combined with EEG to assess cortical changes induced by cerebellar iTBS, showing that TMS-evoked potentials significantly increased after a single iTBS intervention. This metric is associated with intracortical inhibitory networks, suggesting a relative increase in cortical excitability. Other studies [30,31] have indicated that when excitatory NIBS protocols (such as high-frequency repeated transcranial magnetic stimulation [rTMS] or iTBS) are applied to the cerebellar hemispheres, they may activate superficial stellate

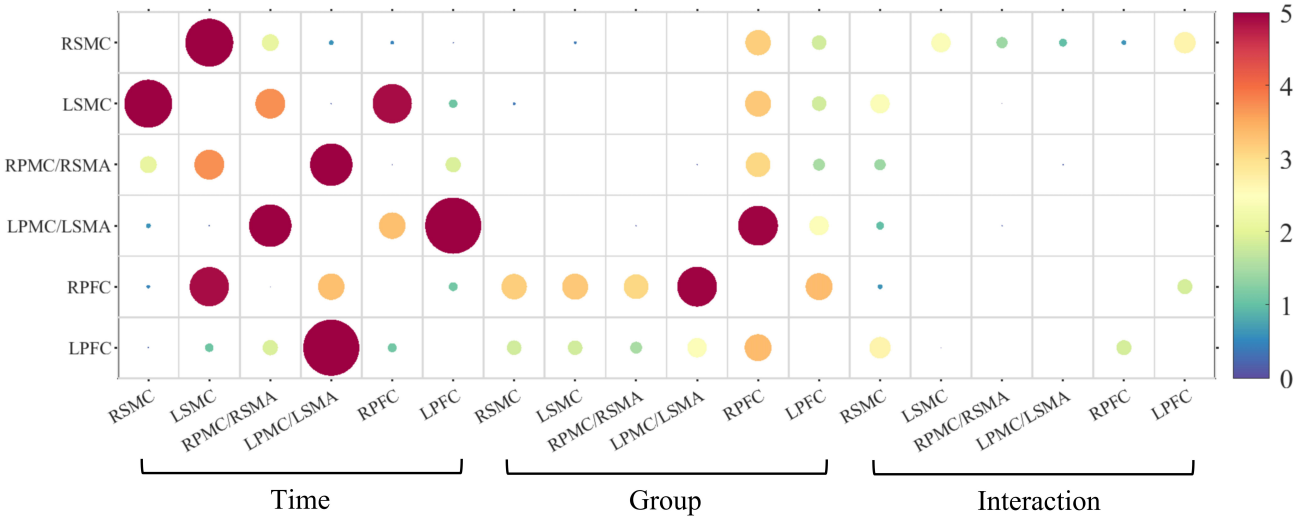

Fig. 7. FC of F-values in mixed ANOVA for the unilateral support task.

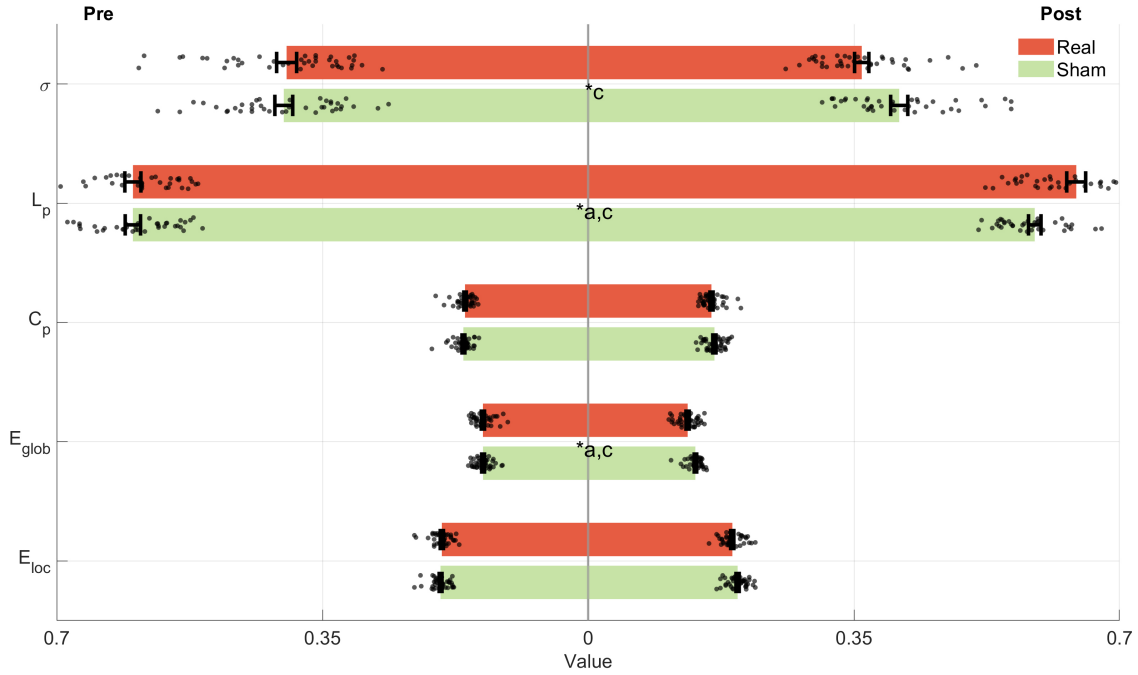

Fig. 8. The graph theory metrics of pre- and post- iTBS for the unilateral support task. *a, intervention factor with a significant difference, *b, group factor with a significant difference; *c, interaction factor with a significant difference. Cp, clustering coefficient; Eloc, local efficiency.

and basket cells, leading to inhibition of Purkinje cells. The reduced inhibitory synaptic connections between Purkinje cells and the deep cerebellar nuclei result in increased excitatory synaptic connections from the deep cerebellar nuclei to the motor cortex via the ventral thalamus [5], thereby enhancing cortical excitability. In the left sensorimotor cortex (LSMC), no tendency was observed in this study, which may be related to the walking task design itself. Walking tasks primarily involve lower limb movements, and the sensory and motor cortices for the lower limbs are anatomically located in the ventromedial regions of the precentral and postcentral gyri [32]. This area is relatively deep and may lie beyond the detection range of fNIRS [33]. In the study by Koenraadt *et al.* [34], it was also found that ΔHBO in S1 and M1 during walking showed little difference compared to the baseline state. Quiet standing constitutes an active postural control state rather than a passive rest condition, due to the sustained anti-gravity muscle activity and ongoing balance adjustments required. Thus, the design of the baseline state requires further consideration—a point

overlooked in current research. Furthermore, walking is a highly automated task primarily reliant on subcortical automatic mechanisms, suggesting that the motor cortex's contribution may not differ significantly between standing and walking states.

An interesting phenomenon observed during walking, regardless of whether the stimulation was real or sham, was that participants exhibited smaller changes in cortical blood flow compared to the resting state. It is well known that the centers controlling walking are primarily governed at lower levels of the neuroaxis, including brainstem regions, spinal pattern-generating circuits, and cerebellar circuits. These structures generate patterns of intermuscular and interlimb coordination, promoting the automation of walking and minimizing reliance on cortical control [33]. Disruption of these structures can lead to significant consumption of cortical resources, as demonstrated in stroke and Parkinson's disease patients [35]. In the study by Koenraadt *et al*. [34], it was found that participants exhibited decreased activation in the SMA and PFC during normal walking compared to resting states. However, during precision stepping, activation in the SMA and PFC increased compared to resting states. When walking requires more control, the activation of motor control-related cortices, such as the PFC and SMA, also correspondingly increases. In our results, the significant interaction factor in activation was particularly evident in the LPFC and LPMC/LSMA, further suggesting that the changes in activation during normal walking compared to resting states may be closely related to walking automation. Additionally, even though we emphasized maintaining natural conditions during data collection, it remains uncertain whether the collected resting state truly represents rest. The observer effect also plays a significant role in this context. This factor may also lead to participants exhibiting higher activation during resting states.

In the balance task, we designed a unilateral support task to engage participants in postural control. We observed an increase in σ and Lp, and a reduction in Eglob. A healthy brain network typically exhibits small-world organization, characterized by an optimal balance between local specialization and global integration [36]. In the present study, changes in key graph-theoretical metrics—including Lp, Eglob, and σ—were used to evaluate alterations in network organization during the unilateral support task. Specifically, increased Lp together with reduced Eglob indicates decreased efficiency of global information transfer, while changes in σ reflect deviations from an optimal small-world configuration [26,37]. Current research [38–40] has shown that this efficient brain network balance can be disrupted in some neurological diseases. Our results indicate that after a single session of iTBS, the brain network seems to deviate from optimal small-world organization and reduced global integration [26]. In healthy individuals, the brain typically maintains a state of balanced stability. Although NIBS techniques have demonstrated positive effects on functional improvement in stroke patients, potentially based on the interhemispheric inhibition theory [41], which involves inducing cortical reorganization towards a pattern observed in healthy brains, our NIBS approach may disrupt the originally balanced brain network in healthy individuals. Katagiri *et al*. [42] found that a single session of anodal and cathodal transcranial direct current stimulation (tDCS) on the cerebellum suppressed the acquisition of postural control skills in healthy individuals compared to sham stimulation. Thus, for healthy individuals, it indicated that a single session of iTBS may disrupt the existing balance of the brain network.

For the resting-state results, we did not observe any positive outcomes at the levels of FC or graph theory metrics. One possible reason for this could be the relatively low spatial resolution of fNIRS, which may have limited our ability to detect changes in FC within the observed brain regions. Wang *et al*. [11] investigated changes in swallowing-related brain regions using resting-state fMRI after a single session of iTBS on the cerebellar hemisphere. They found changes in the middle temporal gyrus, precuneus, and superior frontal gyrus that could not be detected by fNIRS. Additionally, it is not only our study that failed to find significant results in the resting state. Thomson *et al*. [43] also reported similar findings. They suggested that the hemodynamic response induced by sub-threshold repetitive TMS in a single trial is generally very mild and may be masked when averaging epochs, which presents a challenge for fNIRS-based measurements. Regarding FC during the single-leg support task, no significant differences were observed. Currently, no studies are exploring whether cerebellar iTBS can induce changes in functional connectivity between brain regions. However, we speculate that there may be functional changes between the cerebellum and the cerebral cortex, which warrant further investigation using fMRI in future research.

Our study still has certain limitations. First, there are inherent limitations of near-infrared spectroscopy, which cannot detect subcortical structures that also participate in the cerebellar-cortical circuitry. Second, this study only intervened with healthy individuals, and no research has confirmed that cerebellar NIBS improves balance function in healthy people. We assessed the balance function (Berg Balance Scale) of all participants before and after the intervention and found both full scores without any differences, so we did not mention this result. We speculated that the scale we selected has low sensitivity among healthy individuals. Future experiments should use more precise balance measures for further observation. Third, leg dominance was not formally assessed, and all participants performed the unilateral support task using the right leg. Although this approach ensured task standardization, future studies should consider evaluating lower-limb dominance and counterbalancing the supporting leg to examine potential laterality effects. Fourth, we did not perform within-task time-course

analyses (e.g., early vs. late epochs) because subdividing the recording may reduce the robustness of connectivity and graph metrics and would require concurrent behavioral/physiological fatigue measures for reliable interpretation. Furthermore, in recent years, fNIRS systems equipped with short-separation channels have been increasingly adopted, as they provide important advantages for improving signal specificity and reducing motion-related and systemic physiological artifacts. The incorporation of such hardware designs facilitates more accurate separation of cortical hemodynamic responses from superficial and non-neuronal signals. Future studies may therefore consider employing fNIRS systems with short-separation channels to further enhance data quality during dynamic motor tasks.

5. Conclusions

This study provides evidence that cerebellar iTBS can induce cortical responses, supporting the hypothesis of a cerebellar-cerebral cortex circuit involved in balance regulation. The changes in brain network properties during the unilateral support task indicate that iTBS may disrupt the efficient balance of brain networks in healthy individuals. However, no significant effects were observed during the walking and resting tasks, which may be due to the limitations of fNIRS in detecting subtle functional connectivity changes. Overall, these findings contribute to our understanding of the neural mechanisms underlying cerebellar NIBS and its potential therapeutic applications in improving balance. Further research is required to explore the clinical relevance of these findings.

Availability of Data and Materials

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

Author Contributions

CG and AG contributed equally to this work. CG, AG, TW, and SZ conceived and designed the study. CG, AG, QW, JS, CK, and YS performed the research, including participant recruitment, assessment, and data collection. CG and AG analyzed and interpreted the data and drafted the manuscript. QW, JS, CK, and YS contributed to data curation and provided critical feedback on the manuscript. TW and SZ supervised the study, provided important intellectual input, and critically revised the manuscript for important intellectual content. TW and SZ also took primary responsibility for the overall coordination of the study and communication during the research and publication process. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

This study was approved by the Changzhou De'an Hospital Human Ethics Committee (CZDALL-2023-013) and registered with the China Clinical Trial Registration Center (ChiCTR2300077916) on November 23, 2023. The research was conducted in accordance with the principles embodied in the Declaration of Helsinki and in accordance with local statutory requirements. Prior to participation, all participants provided written informed consent and received financial compensation.

Acknowledgment

We are sincerely grateful to all the researchers (excluding the co-authors) and participants for their valuable contributions to this study.

Funding

This work was supported by the National Natural Science Foundation of China (NSFC) (Grant No. 82302882) and the Key Medical Discipline Project of Jiangsu Province (No. XK201110).

Conflict of Interest

The authors declare no conflict of interest.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.31083/JIN47653.

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