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Research article

Continuous theta burst stimulation inhibits the bilateral hemispheres

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HIGHLIGHTS

- cTBS at the left hemisphere reduces the MEP of right hand for more than 30 min.
- cTBS at the right hemisphere also reduces the MEP of right hand.
- cTBS at the left hemisphere inhibit the activity of bilateral motor cortex.

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ABSTRACT

Transcranial magnetic stimulation induces changes in the cerebral cortex functions, either unilaterally or bilaterally. Here, we combined evoked potential recording and functional brain imaging to analyze the modulating effects of continuous theta burst stimulation in bilateral motor regions of the adult human cortex. We detected concurrent inhibition of the bilateral motor regions following stimulation, as evidenced by both the electrophysiological and imaging results. Our findings supported the notion that magnetic stimulation is able to modulate the contralateral hemisphere through the callosal connectivity.

1. Introduction

Non-invasive brain stimulation, especially transcranial magnetic stimulation (TMS), is widely used in the management of psychiatric diseases including depression, schizophrenia, compulsive disorder, addiction, and sleep disorders [1–7]. TMS is also useful in measuring brain functioning when combined with evoked potential recording or brain imaging approaches [8–12]. Repetitive TMS or TMS stimulation in the theta burst mode results in long lasting functional changes in the brain. For instance, continuous theta burst stimulation (cTBS) procedures represent one useful approach in TMS to suppress the brain function transiently [13].

The present study combined prolonged motor evoked potential (MEP) recording and brain imaging approaches to reveal the effects of cTBS in the bilateral hemispheres.

2. Materials and methods

2.1. Participants

A total of 36 healthy young participants were included in this study. Of these, 17 were male participants aged 20–34 years and 19 were female participants aged 20–33 years (Table 1). The included participants met the following inclusion criteria: (1) healthy, (2) no metal implants in the head or heart, (3) no epilepsy history, and (4) no history of central neurological system diseases such as cerebral stroke or traumatic brain injury. All the participants had a good rest before the TMS procedure. The recruited participants were volunteers and they signed a written informed consent form. The study was approved by the Huashan Institutional Review

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Table 1
Overview of the characteristics of the included participants. All the participants were healthy and right-handed.

Acronym	Gender	Age	Handness	Intensity of TBS (machine intensity%)
GX	F	21	Right	75
WL	M	34	Right	50
CWQ	M	23	Right	50
ZYS	F	21	Right	43
CYY	M	23	Right	45
ZW	M	20	Right	41
YWL	F	21	Right	55
FLB	M	22	Right	50
NZB	M	22	Right	43
JYY	F	21	Right	45
CXY	F	22	Right	50
SF	M	35	Right	50
ZXX	F	21	Right	30
SJH1	M	20	Right	60
ZSW	M	20	Right	70
YX	F	20	Right	30
CYN	F	33	Right	55
SYL	F	25	Right	60
ZL	F	21	Right	30
LQ	F	22	Right	55
LMY	F	22	Right	30
HQN	F	20	Right	65
ZCY	M	23	Right	50
SSH	M	21	Right	70
CYH	M	23	Right	55
XJ	F	20	Right	28
JYY	F	21	Right	40
LYZ	F	24	Right	70
ZDL	M	22	Right	70
YJC	F	22	Right	47
ZCY	M	23	Right	55
LMX	F	21	Right	40
SJH2	M	22	Right	40

Board and all procedures complied with the rules of human medical research.

2.2. TMS procedures

The TMS was applied using the Yiruide CCY-II TMS instrument (Wuhan, China) with a round coil; the MEPs were recorded as previously described [11]. Briefly, the MEPs were recorded by the self-contained MEP recording system in the Yiruide transcranial magnetic stimulator and analyzed with an affiliated MEP-analysis software (Wuhan, China) [28]. Before the stimulation, the resting motor threshold (RMT) was measured. The recording electrode was placed on the first dorsal interosseous (FDI) and the minimal intensity that can induce at least five MEPs with a wave amplitude >50 μv during 10 stimulations was regarded as the RMT. The intensity of the following single-pulsed TMS was 120% RMT. Once the location of the coil was decided, two researchers observed and remembered the position of the coil. During the course of the MEP recording, the researcher who was responsible for maintaining the angle and position of the coil was blinded to the amplitude of the MEP wave and 12 MEPs were evoked at an interval of 8 s. If the researcher deemed that the position of the coil changed during the recording course, the two researchers should make a consensus decision together. After adjusting the position of the coil, another 12 MEP waves were recorded consecutively. The MEPs were recorded twice at baseline and 5 min, 10 min, 15 min, 30 min, 45 min, 60 min, and 75 min after the cTBS intervention (Fig. 1). During the waiting session, the participants were instructed to remain silent and were prohibited from playing games or falling asleep. The cTBS protocol was performed according to the protocol described by Huang et alfor 40 s and 600 pulses. The intensity of cTBS was 70% RMT.

2.3. MRI acquisition

A German Siemens 3.0 T Trio Tim MRI system was used to acquire the structural and functional MRI data. A 12-channel head coil was utilized. Before the scanning, the healthy volunteer was placed on a noise cancellation earphone (Minnesota Mining and Manufacturing company, USA). The head of the volunteer was fixed with custom-fit foam pads to minimize the movement of the head. During the scanning, the participant was instructed to lie on the back in a state of relaxation and rest, close the eyes, remain clear-headed, and avoid thinking of anything. The high-resolution T1-weighted structure data were collected using the same parameters as described previously [14]: resolution = $1.0 \times 1.0 \times 1.0$ mm; TR = 2530 ms; TE = 2.34 ms; inversion time = 1100 ms; flip angle = 7°; number of slices = 192; sagittal orientation; field of view (FOV) = 256×256 mm^2, matrix size = 256×256, and slice thickness = 1 mm. Before and after the cTBS session, the resting-state fMRI images were collected using a T2*-weighted gradient spiral pulse sequence. The fMRI parameters were as follows: resolution = $3.4 \times 3.4 \times 3.5$ mm; repetition time = 2000 ms; echo time = 30 ms; flip angle = 90°; number of slices = 33; transverse orientation; FOV = 220×220 mm^2; matrix size = 64×64; slice thickness = 3.5 mm; total number of frames = 210. Thirty minutes after the cTBS protocol, the resting-state fMRI images were acquired again using the same parameters. During the waiting time, the participant was instructed to have a rest without talking and without activity.

2.4. fMRI data preprocessing

The Data Processing Assistant for Resting-State fMRI (DPARSF) pipeline analysis (http://www.restfmri.net/forum/DPARSF) was used to preprocess the fMRI data as described previously [15,26]. Briefly, the Digital Imaging and Communications in Medicine (DICOM) files were first converted into Neuroimaging Informatics Technology Initiative (NIFTI) images and the first 10 time-points were discarded in order to eliminate the influence of the initial instability of the machine. Subsequently, we performed the slice timing in order for the collecting time of every slice to remain consistent in a repetition time period. In addition to slice timing, we made the correction of head motion and discarded the data with more than 2 mm drifting and more than 2° spinning. Subsequently, we normalized the data with the echo planar image templates using the Statistical Parametric Mapping (SPM) software and entered them in the Montreal Neurological institute space. In the following step, we smoothed the data with an 8-mm full width at half maximum Gaussian kernel to raise the noise-to-signal ratio (only for the Amplitude of Low-Frequency Fluctuation [ALFF] and fractional ALFF [fALFF]). Subsequently, we removed the linear trend of time courses and performed the temporally band-pass filtering (0.01–0.1 Hz) (fALFF expected). Finally, we removed the influence of head motion, whole brain and white matter signals, and cerebrospinal fluid on the low frequency synchronous oscillation signal utilizing the linear regression.

2.5. Regional homogeneity (ReHo) analysis

The ReHo value was expressed using the Kendall's coefficient of concordance (KCC), which represents the local consistency of the selected voxels and their neighboring voxels in the same time series [27]. Here, 27 individual voxels formed a cluster. Since ReHo reflected the synchrony of the local neuronal activity, the present study was performed within the gray matter mask, i.e., the KCC value of each voxel in the gray matter mask. When the center of the cube was located at the edge of the gray mask, only the voxels in the gray matter mask and its nearest neighbors were calculated.