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Research report

The study on the frontoparietal networks by continuous theta burst stimulation in healthy human subjects

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HIGHLIGHTS

- ► We examine the brain regional interactions for visuospatial attention.
- ► We use ANT paradigm to examine cTBS-induced changes in alerting, orienting, and executive control efficiency.
- ► The PPC and DLPFC regions in the right hemisphere play the crucial role in spatial orienting and resolving conflict function.
- ► There are some competitions, not only between two hemispheres, but also between different brain regions in the same hemisphere.

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ABSTRACT

Frontoparietal networks (FPNs) including the regions of the posterior parietal cortex (PPC) and dorsolateral prefrontal cortex (DLPFC) have been implicated in visuospatial attention. However, the functional interactions among different regions of dorsal FPNs remain elusive. The Attention Network Test (ANT) and continuous theta burst stimulation (cTBS) were used to investigate the functional interactions in healthy subjects. During the ANT task, subjects receiving right PPC cTBS responded significantly slower in spatial cue condition, had deficits in both alerting and orienting indices compared with those receiving either the sham cTBS or left PPC cTBS. In addition, subjects receiving left-DLPFC cTBS showed significant improvements on alerting and conflict indices whereas significant deficits on the orienting index compared with those receiving the sham cTBS. Moreover, compared with subjects exposed to the sham cTBS condition, subjects exposed to cTBS to the right-DLPFC exhibited significant decreases in the efficiency of the alerting and conflict indices whereas significant increases in the orienting index. Furthermore, there were significant differences in the alerting, orienting and conflict effect indices between subjects receiving the left-DLPFC-cTBS and those receiving the right-DLPFC-cTBS. These results suggest that the right DLPFC played a pivotal role in executive control process, whereas the right PPC was associated with orienting attentional function. The current study not only supports the model of inter-hemispheric rivalry for visuospatial attention, but also indicates inter-regional competition between the different areas of the FPNs.

1. Introduction

Visuospatial attention is an integral part of normal human behavior. Impairments in visuospatial attention significantly contribute to deficits in the execution of daily activities and functional recovery [1,2]. Visuospatial neglect is not a purely visual deficit such as hemianopia but an attentional deficit as observed in patients with hemineglect. Therefore, regaining appropriate levels of visuospatial attention in patients with brain lesions is a major rehabilitation task. However, the brain networks responsible for visuospatial attention are still not fully understood. Thus, there are no known effective therapeutic interventions for visuospatial neglect [3,4].

Abbreviations: FPNs, frontoparietal networks; PPC, posterior parietal cortex; FEF, frontal eye field; DLPFC, dorsolateral prefrontal cortex; TPJ, temperoparietal junction; IFG, inferior frontal gyrus; MFG, middle frontal gyrus; ANT, attention network test; rTMS, repetitive transcranial magnetic stimulation; cTBS, continuous theta burst stimulation; AMT, active motor threshold; EMG, electromyogram; MEP, motor evoked potentials; RTs, reaction times; ANOVA, analysis of variance.

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Visuospatial attention is regulated by a distributed structure-function network in the frontal and parietal cortices [5]. The frontoparietal networks (FPNs) have been proposed as the neurobiological substrates of visual attention. It is generally believed that dorsal FPNs projecting to the posterior parietal cortex (PPC), frontal eye field (FEF) and the dorsolateral prefrontal cortex (DLPFC) controls spatial attention ('where') whereas ventral FPNs including the temperoparietal junction (TPJ), inferior frontal gyrus (IFG) and middle frontal gyrus (MFG) mainly devotes to nospatial attention ('what') [5–7]. Indeed, damage to a region of the dorsal FPNs within one hemisphere, particularly the right hemisphere, often leads to deficits in spatial attention. Moreover, Corbetta et al. have demonstrated that the ventral FPNs lesions can cause spatial neglect through impairing normal functions of the dorsal FPNs [8]. Thus, spatial neglect is associated primarily with the damage to the dorsal FPNs, especially PPC and DLPFC. In addition, spatial neglect may be also associated with the different competing connectivity among brain regions [8–10]. There is substantial evidence from clinical and experimental studies indicating that the interhemispheric competing connectivity plays a key role in the efficient control of spatial attention by the dorsal network. However, the competing connectivity within one hemisphere and competing connectivity between related circuitry components in the dorsal FPNs have received less attention. Thus, the functions of those competing connectivity are not clear.

Visuospatial attention includes three different functional components: the alerting, orienting, and executive control networks [11]. The Attention Network Test (ANT) has been widely used to investigate the integrity of separable neural systems for alertness, spatial orienting, and executive control of attention [12]. Recently, noninvasive brain stimulations such as transcranial magnetic stimulation (TMS) are becoming important tools in investigating the brain function [13,14]. As a "virtual lesion" technique, continuous theta burst stimulation (cTBS), a novel rTMS paradigm, provides an ideal tool for exploring the roles of different brain regions in visuospatial attention [3]. In the current study, we combined cTBS and the ANT paradigm to investigate interactions of neural structure-function networks and models of visuospatial attentive mechanisms.

2. Methods

2.1. Participants

The total study sample comprised 80 healthy subjects (40 male, 40 female; aged 19–23 years; education: 13–15 years). Subjects were divided into two groups, a frontal group and a parietal group, in accordance with sex for the DLPFC and the PPC stimuli studies, respectively. All participants were right-handed according to the Oldfield Handedness Questionnaire [15]. They had normal or corrected-to-normal vision and no significant current medication or psychiatric histories. Study protocols were approved by the Ethical Committee of the First Affiliated Hospital of Sun Yat-sen University. Each subject gave informed consent prior to the testing session.

2.2. Experimental design

Subjects in the ANT experiment were tested for a total of four separate testing sessions, with an interval of 3–5 days between each session. Each session included 40 s cTBS followed by 30 min ANT task (Fig. 1). Subjects randomly received either real or sham cTBS to one side of hemisphere and then real or sham cTBS to the other side (left DLPFC or PPC if they had started with right and vice versa). Session order by side (right or left) and type of stimulation

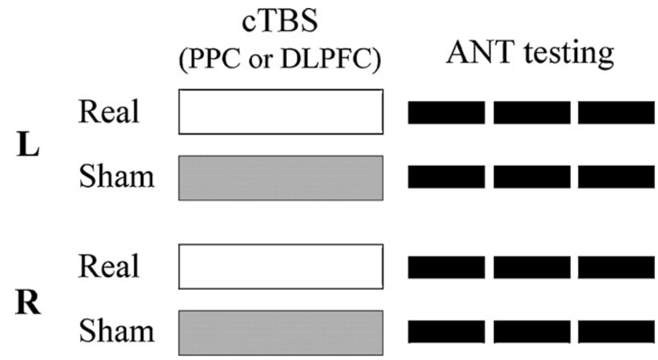

Fig. 1. Experimental design. Subjects attended on four separate sessions in which they received sham and real cTBS conditioning to their left and right side (either PPC or DLPFC), followed by ~30 min ANT testing starting immediately after the end of cTBS conditioning. Subjects were allocated to each session in a counterbalanced order. (L, left; R, right).

(real or sham) were counterbalanced across subjects in the frontal and parietal lobe groups generating. This generated one between session factors (site of cerebral cortex) plus two within-session factors (side and type of cTBS conditioning). We hypothesized that the effects of cTBS conditioning might be hemisphere dependent.

2.3. Experimental task

2.3.1. Behavioral study

The ANT task was used to study the effects of cTBS over the DLPFC or PPC on reaction times and attention network efficiency [12]. A fixation cross was first displayed for 400 ms at the onset of each trial followed by a warning cue for 100 ms. Following a short fixation period of 400 ms after the cue, a target was displayed simultaneously either above or below the fixation cross. The target immediately disappeared after a response was made, but the time window for participants' responses was no longer than 1700 ms. A fixation cross appeared in the center throughout the entire experiment. Each trial persisted for 4000 ms on average. The different cue configurations were as follows: no cues; double cues (two asterisks were displayed 5° above and 5° below the fixation cross); center cues (the asterisk was presented at the same location as the fixation cross); and spatial cues (either above or below the fixation cross). The spatial cues were always the valid cue conditions. The flanker stimuli consisted of: congruent flankers pointing in the same direction as the central target arrow; incongruent flankers pointing in the opposite direction; and neutral flankers. A single arrow subtended 0.58° of visual angle and the contours of adjacent arrows or lines were separated by 0.06° of visual angle. The stimuli subtended a total of 3.27°. The target was presented in one of two locations, either 1.06° above or below the fixation cross. The three different target types were equally distributed in trials containing each of the different cue conditions.

The ANT was conducted in a dimly lit, quiet room. Stimuli were presented using E-Prime (Psychology Software Tools) on a Lenovo personal computer running Window XP, presenting to a 17-inch monitor. Participants were comfortably seated ~65 cm in front of the computer screen and instructed to press the left or right mouse button corresponding to the direction of the target arrow as quickly and accurately as possible. Participants performed a total of three blocks of trials, each block lasting ~8 min. A practice block of 24 trials with full-feedback on accuracy and speed of response was followed by three feedback-free experimental blocks with 96 trials per block (4 cue conditions × 2 target locations × 2 target directions × 3 flanker conditions × 2 repetitions). Participants were allowed to rest for ~5 min between blocks.