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Short Communication

Sequential Roles of Primary Somatosensory Cortex and Posterior Parietal Cortex in Tactile-visual Cross-modal Working Memory: A Single-pulse Transcranial Magnetic Stimulation (spTMS) Study

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ABSTRACT

Background: Both monkey neurophysiological and human EEG studies have shown that association cortices, as well as primary sensory cortical areas, play an essential role in sequential neural processes underlying cross-modal working memory.
Objective: The present study aims to further examine causal and sequential roles of the primary sensory cortex and association cortex in cross-modal working memory.
Methods: Individual MRI-based single-pulse transcranial magnetic stimulation (spTMS) was applied to bilateral primary somatosensory cortices (SI) and the contralateral posterior parietal cortex (PPC), while participants were performing a tactile-visual cross-modal delayed matching-to-sample task. Time points of spTMS were 300 ms, 600 ms, 900 ms after the onset of the tactile sample stimulus in the task.
Results: The accuracy of task performance and reaction time were significantly impaired when spTMS was applied to the contralateral SI at 300 ms. Significant impairment on performance accuracy was also observed when the contralateral PPC was stimulated at 600 ms.
Conclusion: SI and PPC play sequential and distinct roles in neural processes of cross-modal associations and working memory.

Introduction

Working memory refers to cognitive processes to maintain and store information in the short term (usually for seconds) for subsequent goal-directed actions [1]. Both association cortices (especially the fronto-parietal loop) and the primary somatosensory cortex (SI) have been suggested to be important in tactile working memory [2–4].

Association cortices are the most prominent candidates for integrating information from different sensory modalities [5]. Meanwhile, growing evidence that neurons in primary sensory cortices respond to stimuli of different sensory modalities has requested reconsideration of the functional role of sensory cortices in multisensory information processing [6,7]. A recent study has reported anatomical and electrophysiological evidence showing direct interactions between primary visual and somatosensory cortices (VI and SI) [8], which indicates feedforward and lateral projections from one primary sensory cortex to another. This has expanded our understanding of cross-modal modulation of activity in primary sensory cortices. Traditionally, this modulation was thought to be induced by feedback projections from higher cortical areas to primary sensory areas [6].

All these studies suggest that primary sensory cortices participate in cross-modal working memory that involves active maintenance of cross-modal information and cross-modal information transfer, which has been further supported in human and non-human primate studies by showing that the activation of

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somatosensory brain regions is influenced by subsequent associated non-tactile (visual) stimuli in tactile-visual cross-modal delayed matching-to-sample tasks [7,9,10]. Nevertheless, there is still a lack of causal evidence linking SI activity with behavioral performance in tactile cross-modal working memory tasks, or evidence showing whether there is a sequential hierarchical order of processing in the cortical network of tactile cross-modal working memory, of which SI is an early constituent part.

In this study, we addressed these issues using single-pulse TMS (spTMS) at different time points to determine the time course of the involvement of cortical areas during a given cognitive process. We proposed that the cortical processes of cross-modal working memory, including cross-modal information processing and transfer, would start from SI. This assumption fits in with the proposed cortical dynamics and hierarchical structures of the perception–action cycle [11].

Materials and methods

Participants

Thirteen individuals participated in the study (8 females and 5 males, 18–25 years, mean 22.0 years). All of them were fully informed of potential risks of TMS experiments, and then signed written consent forms. One participant was excluded due to poor task performance (<50% accuracy). The experimental protocol was approved by the Institutional Review Board of East China Normal University.

Experimental paradigm

Participants sat in front of a 17-inch CRT monitor (IBM C220P CRT; resolution 800 × 600 pixels; refresh rate 60 Hz), with a chin support situated 0.87 m away from the monitor. A complete experimental trial (as in Fig. 1A) started with a gray fixation-cross (lasting 1000–1500 ms) centered on the monitor. The cross then turned red and stimulus-1 (S-1), a 200-ms tactile vibration (selected pseudo-randomly from four frequencies, 30 Hz, 40 Hz, 60 Hz or 100 Hz, based on the equal sensation contours for vibration [12]), was immediately applied to the subject's left index finger. A delay interval of 1000 ms followed the offset of S-1 when the cross turned back to gray. The delay ended with the onset of stimulus-2 (S-2) that was selected pseudo-randomly from four amorphous texture-pattern pictures of identical size (visual angle 8° × 8°) and black-white contrast [13]. Each of the four tactile stimuli was assigned to be associated with one of the pictures, and vice versa. These assignments were counter-balanced across subjects. After the offset of S-2, the participant was instructed to report whether S-2 matched S-1 by pressing one of two buttons as quickly and accurately as possible. The interval between trials was randomly set as 3–4 s. Each participant performed three training blocks (with feedback of performance information, a correct or incorrect response) to learn these paired associations, and then performed six experimental TMS blocks (without feedback). Each block consisted of 48 arranged trials (24 "match" trials and 24 "non-match" trials).

Tactile stimulator

A permanent magnetic vibrator (LDS V101 vibrator; probe diameter, 6.4 mm) driven by an LDS PA25E Power Amplifier (Brüel & Kjær Sound & Vibration. Measurement A/S, Denmark) was used as a vibration stimulator in this study. The amplitude of vibrations at different frequencies was restricted to the same level (vertical displacement, ±0.049 inches).

TMS protocol

TMS was delivered with a Magstim Rapid2 stimulator and a 70-mm figure-eight-shaped coil (The Magstim Company, Ltd., Whitland, UK). Individual anatomical T1-weighted magnetic resonance images (MRI) were acquired with 3T Siemens Trio (TR = 2530 ms, TE = 2.340 ms, inversion time = 1100 ms, flip angle = 7°, FOV = 232*256 mm, 170 sagittal slices, 1 mm thickness) at ECNU MRI Research Center. These images were then imported into BrainSight 2.0 (Rogue Research Inc., Montreal, Canada) for stereotaxic registration of the TMS coil with the participant's brain areas.

Resting motor threshold (MT) was measured by the minimal intensity necessary to elicit a visible movement of the right hand of the participant in 5 of 10 stimulation pulses applied to the left motor hand area [14]. The strength of TMS was then designed with 110% MT individually (mean: 73% maximum machine output, standard deviation: 10%).

The motor hand area was also marked for each participant within Brainsight. The left SI (ipsilateral SI, iSI) was localized 2 cm posterior to the motor spot [15]. The contralateral SI (cSI) was localized as a mirror point of iSI toward the sagittal plane of the brain. The contralateral posterior parietal cortex (cPPC) was localized 1 cm posterior and 2 cm lateral from the cSI [16]. Averaged Talairach coordinates (*x*, *y*, *z*) of the above three locations were iSI (−34 mm, −38 mm, 50 mm), cSI (34 mm, −38 mm, 50 mm), and cPPC (46 mm, −47 mm, 50 mm) (as in Fig. 1B). In cPPC, the average position stimulated was located in the right inferior parietal lobule. The TMS coil was held to the head of the participant with a custom coil holder and was oriented tangentially to the scalp. Single-pulse TMS was then delivered over the iSI, cSI and cPPC (two experimental blocks for each stimulating brain site) when the participant performed the task (the order of blocks assigned randomly for each participant). Three different stimulating time points (STPs: 300 ms, 600 ms, and 900 ms after the onset of S-1) for TMS were based on our previous ERP findings [10]. Within each block, 48 trials were equally divided into three groups in line with the STPs, and in each group, the four vibration frequencies were arranged pseudo-randomly, with each of them having 4 trials.

White noise (80 dB) was generated by Adobe Audition 3.0 (Adobe Systems Inc., USA) and delivered through two loudspeakers on each side of the CRT monitor to attenuate the influence of sounds from the vibrations and TMS. Earplugs were also used for this reason.

Paradigms and spTMS delivery were programmed using Psychtoolbox-3 (www.psychtoolbox.org) based on Matlab R2010b (MathWorks, MA, USA).

Statistical analysis

Accuracy and reaction time (RT) were defined respectively as the percentage of correct responses in each condition and the interval between the offset of S-2 and the subject's correct response. They were analyzed by two-way repeated measures analysis of variance (RMANOVA), with LOC (stimulating sites) and STP as within-subject factors. After a significant interaction effect was observed, the post-hoc paired *t*-test was executed and the false-discovery-rate (FDR) was corrected. Performance in the third training block was extracted as a baseline and compared with that in each TMS condition (at each STP and LOC) using the paired *t*-test.

All statistical analyses were performed with Statistica 6.0 (StatSoft, Inc., Tulsa, USA).

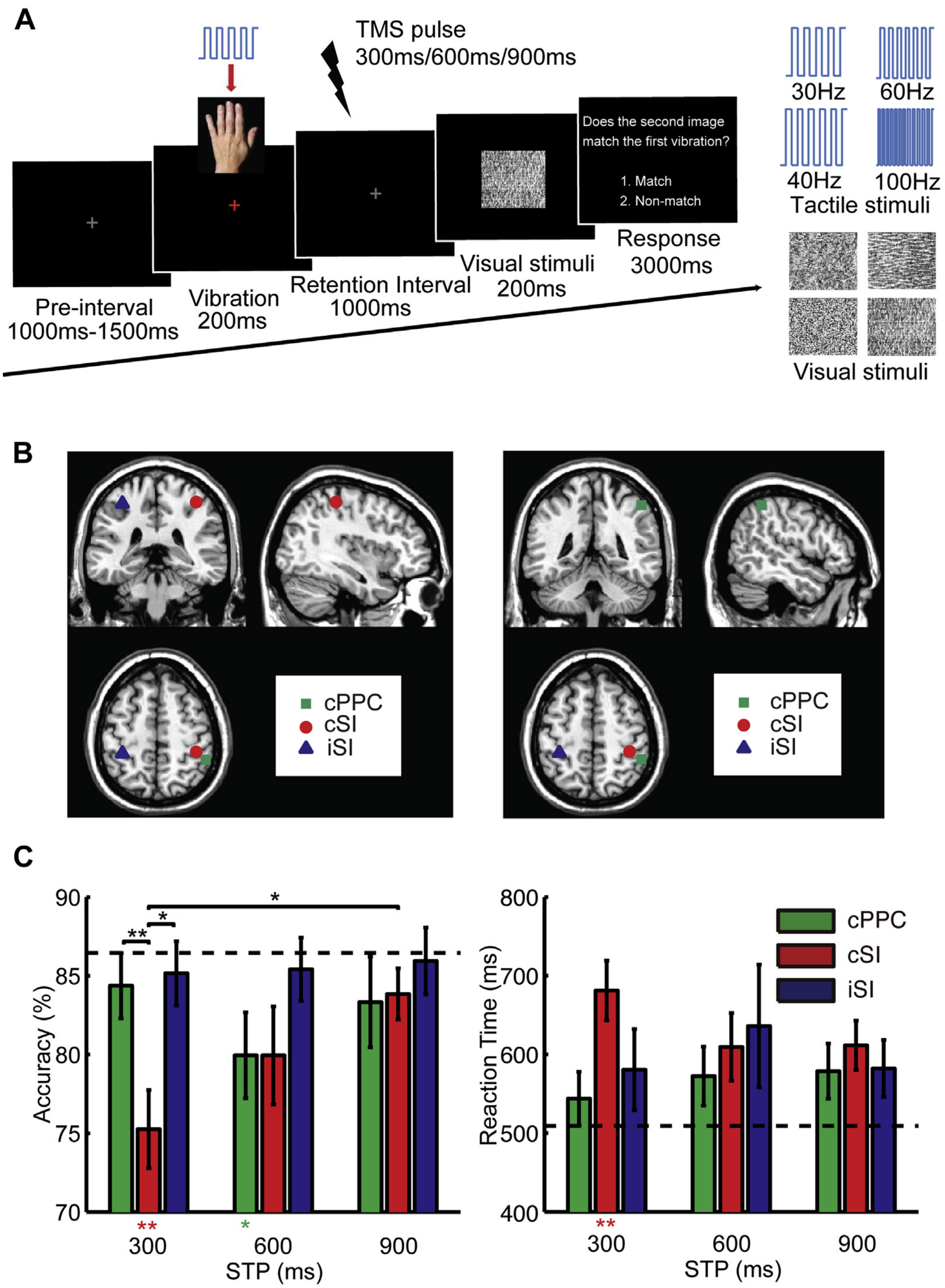

Figure 1. (A) Schematic diagrams of the cross-modal working memory task. spTMS is delivered at 300 ms, 600 ms, or 900 ms after the onset of the tactile sample stimulus. (B) Stimulating sites of spTMS. (C) The accuracy of behavioral performance (left) and reaction time (right) at different STPs and stimulating sites. Dashed lines represent non-TMS performance baselines. Error bars indicate SEs. Colored asterisks below the horizotal axis indicate the significant difference in each condition compared with the baseline (*$P < 0.05$, **$P < 0.01$).(For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Results

RMANOVA for accuracy exhibited a significant main effect of LOC ($F_{2,22} = 4.90$, $P = 0.02$, $\eta_p^2 = 0.31$) and a significant interaction ($F_{4,44} = 2.79$, $P = 0.04$, $\eta_p^2 = 0.20$) between LOC and STP, while the main effect of STP was marginal ($F_{2,22} = 3.17$, $P = 0.06$, $\eta_p^2 = 0.22$). The planned contrast comparison showed that stimulation on cSI and cPPC impaired the task performance significantly ($P < 0.05$), compared with that on iSI. The post-hoc *t*-test (FDR corrected) showed that stimulation at 300 ms on cSI decreased the accuracy significantly compared with that on iSI ($P < 0.05$) and on cPPC ($P < 0.01$) (Fig. 1C).

Compared with baseline performance, the paired *t*-test analysis revealed that stimulation on cSI at 300 ms significantly decreased the accuracy by an average of 11.2% ($t_{11} = -3.91$, $P < 0.01$, Cohen's $d = 0.8$), and stimulation on cPPC at 600 ms significantly decreased accuracy by an average of 6.5% ($t_{11} = -2.48$, $P < 0.05$, Cohen's $d = 0.6$) (Fig. 1C).

For RT, RMANOVA exhibited a significant interaction effect ($F_{4,44} = 3.28$, $P = 0.02$, $\eta_p^2 = 0.23$) between LOC and STP. The post-hoc paired *t*-test (FDR corrected) revealed no significant difference between conditions. However, compared with baseline, the paired *t*-test analysis showed a significant impairment of RT with stimulation on cSI at 300 ms ($P < 0.01$) (Fig. 1C).

Discussion

Our previous EEG studies on cross-modal working memory [10] have revealed two ERP components around 300 ms and 600 ms after the onset of S-1 in recordings from parietal electrodes. These components most likely represent neural processes of cross-modal information transfer and cross-modal associations between two stimuli (tactile vs. visual). The present study has further indicated the causal role of SI and PPC in these sequential processes.

Stimulation of both cSI and cPPC decreased the performance accuracy in the cross-modal working memory task, compared with the performance baseline. Specifically, cSI stimulation was most prominent at STP 300 ms, while cPPC stimulation was at STP 600 ms. As expected, under the same experimental condition, control iSI stimulation did not affect participants' performance at any time point. Stimulation of cSI showed the significant effect on task performance 300 ms earlier than cPPC did, which indicates that cSI plays an essential role in the early stage of cross-modal associations, and that information processing during the cross-modal task relies on SI first and then PPC. The result fits in with the proposed cortical dynamics and hierarchical structures of the perception–action cycle [11].

We did not observe any TMS stimulation effect at STP 900 ms in our study. Neural processes after 900 ms have been suggested to be related to working memory maintenance [10], and to be possibly located in the prefrontal cortex (PFC) [17,18].

Recently, studies have focused on the involvement of primary sensory cortices in working memory [19] and multimodal processing [6]. Our results here give new evidence showing the important role of SI in an early stage of cross-modal associations, which has also been suggested in our previous human EEG studies [9]. The present study (the role of SI in tactile cross-modal working memory) extends the finding of early involvement of SI in tactile uni-modal working memory by Harris and his colleagues [4], and also works in concert with our monkey neurophysiological data [3,7].

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