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Short communication

Facilitation of tactile working memory by top-down suppression from prefrontal to primary somatosensory cortex during sensory interference

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ABSTRACT

Tactile working memory (WM) is improved by increasing top-down suppression of interfering sensory processing in S1 via a link from the middle frontal gyrus (MFG) to S1. Here we studied in healthy subjects whether the efficacy of top-down suppression varies with submodality of sensory interference. Navigated stimulation of the MFG-S1 link significantly improved tactile WM performance when accompanied by tactile but not visual interference of memory maintenance.

The prefrontal cortex (PFC) in general and the middle frontal gyrus (MFG) in the PFC in particular have been associated with working memory (WM)-related activity [5,7]. One potential function that the PFC has in WM is the gating of irrelevant sensory information to protect WM maintenance from interference [12]. This hypothesis is supported by earlier studies indicating that lesions of the PFC increase distractibility of WM maintenance by task-irrelevant sensory stimuli, but do not abolish WM maintenance when testing is performed under optimal conditions [2–4,11]. In line with this, the PFC has been shown to play a role in top-down suppression of irrelevant sensory information which helps protecting the contents of WM from interference [6,14].

Recently, we studied further the hypothesis that the PFC plays a role in WM by suppressing sensory interference [10]. For this purpose, we used navigated transcranial magnetic stimulation (TMS) in combination with diffusion-weighted magnetic resonance imaging (DW-MRI) and tractography that allow investigating functional anatomy of the living human brain with high precision. We found that navigated TMS attenuated somatosensory evoked potentials in the primary somatosensory cortex (S1) and improved tactile WM. The TMS-induced improvement of tactile WM occurred in spite of tactile interference during the retention period and it was observed only when TMS was applied during memory maintenance to a site in the MFG that was anatomically connected to the S1 representation area of the cutaneous test stimulus, but not adjacent to it [10]. This finding supports the hypothesis that navigated TMS improves tactile WM maintenance by increasing top-down suppression of interfering sensory processing in S1 via the MFG-S1 link.

Abbreviations: dt, distractor of tactile modality; dv, distractor of visual modality; DW-MRI, diffusion-weighted magnetic resonance imaging; HS, hotspot; MFG, middle frontal gyrus; ISI, interstimulus interval; NHS, non-hotspot; PFC, prefrontal cortex; RT, response time; S1, primary somatosensory cortex; TMS, transcranial magnetic stimulation; WM, working memory.

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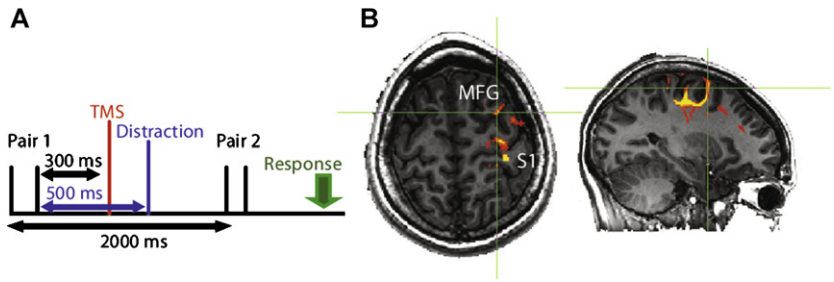

Fig. 1. (A) Experimental protocol. (B) Example of tractography in one subject. In A, vertical black lines represent cutaneous test stimuli, red line represents TMS (single monophasic pulse), and blue line distractive tactile or visual stimulation. In B, $S1_{HS}$ (the primary somatosensory representation area of the cutaneous test site) and MFG_{HS} (the middle frontal gyrus site with tractography-verified anatomical connectivity with $S1_{HS}$) are shown. Cross hair is focused on MFG_{HS}. In B, strength of connection between $S1_{HS}$ and MFG_{HS}: yellow > red. Note that to show whole path of the fiber tract connecting MFG_{HS} to $S1_{HS}$, a series of sagittal sections needs to be shown. Due to space limitation, only one sagittal section is shown here. For illustration of tractography results in other subjects, see Supplemental Figure S1.

Our recent results left open whether top-down suppression via the MFG-S1 link improves tactile WM only when WM maintenance is accompanied by tactile interference, or whether this same MFG site generates a more general top-down suppression of sensory interference, independent of its modality. Here we study whether modulation of tactile temporal WM by top-down suppression originating in the MFG site with a link to S1 varies with the modality of sensory interference. The MFG site with a link to S1 representation area of the cutaneous test stimulus was determined with DW-MRI-based tractography, and top-down suppression was induced by delivering single navigated TMS pulses to the MFG during the retention period that was accompanied by tactile or visual interference.

Experiments were performed with 12 healthy subjects (five females and seven males; age range 20–35 years). Seven of the subjects had participated also in our previous TMS study [10]. The subjects gave their informed consent before participating in the experiment, and the experiments were approved by the ethical committee of the Helsinki University Central Hospital. During the experiment, the subjects had earplugs to suppress noise.

Methodology for magnetic resonance imaging (MRI) and determination of fiber tract connections between the MFG and S1, delivery of navigated TMS, cutaneous test stimulation, and assessment of tactile temporal WM performance have been described in detail in our earlier papers [8–10]. Briefly, DW-MRI was performed using a 3.0 T scanner (Signa VH/I Excite II; GE Healthcare, Chalfont St.Giles, UK) equipped with an 8-channel High-Resolution Brain Array head coil (GE Signa Excite, GE Healthcare, Chalfont St.Giles, UK) at the Advanced Magnetic Imaging Centre (AMI Centre, Aalto University, Espoo, Finland). Parameters used for MRI and post-processing of diffusion-weighted images are described in our recent paper [10].

An eXimia NBS Navigation system-controlled eXimia TMS Stimulator (Nexstim Ltd., Helsinki, Finland) with the Focal Monopulse 8-coil was used for delivering TMS [8]. For standardization of the intensity of TMS across the subjects in the experiments, in which TMS was applied at 120% of the motor threshold, the individual motor threshold in the thenar hand muscles (musculus abductor pollicis brevis) was determined in all subjects as described earlier [8,9]. The mean motor threshold was $54 \pm 8\%$ of the maximal output of the stimulator. Representation area of the cutaneous test site in S1 ($S1_{Hotspot}$ or $S1_{HS}$) was determined in a blocking experiment, in which electric test stimuli were delivered at threshold intensity (2.0 ± 0.4 mA) to the thenar skin of the dominant hand using a constant current stimulator as described earlier [8]. Connections between the $S1_{HS}$ and the MFG were probed with probabilistic tractography using FSL 4.0 software (FMRIB, Oxford, UK) and parameters described in our earlier study [10]. Fig. 1B shows tractography results for one subject. Tractography results for 4 other subjects are shown in Supplemental Figure S1 of the present study, for one subject in Fig. 1 of a previously published study [10], and for 6 subjects in rows 2–6 of Supplemental Figure S2 of the previously published study [10]. PFC regions with connectivity to $S1_{HS}$ were considered as possible targets for TMS in the WM study. In each subject, two regions in the MFG (one with and one without connections to the $S1_{HS}$ that were defined as MFG_{HS} and MFG_{NHS}, respectively) were selected as targets for navigated TMS. In selection of MFG_{NHS}, it was made sure that the site was in the MFG, the site had no anatomical connectivity with $S1_{HS}$, and the distance MFG_{HS}–MFG_{NHS} was more than 13 mm to reduce the possibility that TMS of MFG_{NHS} had a significant direct effect on MFG_{HS} [8]. Moreover, the coil orientation in the MFG_{NHS} condition was away from the MFG_{HS} to reduce the possibility that MFG_{HS} was stimulated in the MFG_{NHS} condition.

Influence of single monophasic TMS pulses on tactile temporal WM was assessed in a delayed discrimination task as in our previous study [10]. In the WM task, the subjects were presented pairs of twin stimuli at a retention interval of 2 s, while a single monophasic TMS pulse, when applied, was delivered 300 ms after the first twin stimulus during the retention interval (Fig. 1A). Additionally, the first cutaneous twin stimulus was followed either by a distractive tactile (dt) or visual stimulus (dv) at a delay of 500 ms (Fig. 1A). The distractive tactile stimulus was an identical electric stimulus as the single stimulus of the actual test stimulation (twice the threshold intensity) and it was delivered to the cutaneous test site through the same electrodes as the cutaneous test stimuli. Visual distraction of 64 ms duration was a three-time increase in the length of the lines of the yellow cross that served as the subject's visual fixation point against black background in the middle of a computer screen (distance between the screen and the subject: 2 m) during the experiment. In baseline control trials, there were only cutaneous test stimuli without TMS or distractive stimulation. In the WM task, the interstimulus interval (ISI) within each twin stimuli varied in a semirandom fashion from 120 to 260 ms. The variability of the ISI duration was applied both to the first (base) and second (comparison) twin stimulus of the task. The subject indicated the longer twin stimulus by pressing the button as rapidly as possible after presentation of the second pair of stimuli; this gave the response time (RT) for each trial. After completion of the study, the subjects rated the subjective difficulty of different experimental conditions as explained in detail in the results section. There were two cortical stimulation sites (MFG_{HS} and MFG_{NHS}), each of which was tested twice within the experiment. The order of testing the two brain areas ($MFG_{HS/NHS}$) was counterbalanced between and within subjects (e.g., MFG_{HS}, MFG_{NHS}, MFG_{HS}, MFG_{NHS}, or vice versa) and the order of testing 5 different stimulus conditions (dt, dv, dt + TMS, dv + TMS, baseline without TMS or dt/dv) within each of the four sessions ($2\times$ MFG_{HS} and $2\times$ MFG_{NHS}) varied in a semirandom order. Within each of the 4 sessions, each of the 5 stimulus