RESEARCH ARTICLE

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Hemispheric asymmetry in visuospatial attention assessed with transcranial magnetic stimulation

Abstract Transcranial magnetic stimulation (TMS) was used to study visuospatial attention processing in ten healthy volunteers. In a forced choice recognition task the subjects were confronted with two symbols simultaneously presented during 120 ms at random positions, one in the left and the other in the right visual field. The subject had to identify the presented pattern out of four possible combinations and to press the corresponding response key within 2 s. Double-pulse TMS (dTMS) with a 100-ms interstimulus interval (ISI) and an intensity of 80% of the stimulator output (corresponding to 110–120% of the motor threshold) was applied by a non-focal coil over the right or left posterior parietal cortex (PPC, corresponding to P3/P4 of the international 10-20 system) at different time intervals after onset of the visual stimulus (starting at 120 ms, 270 ms and 520 ms). Double-pulse TMS over the right PPC starting at 270 ms led to a significant increase in percentage of errors in the contralateral, left visual field (median: 23% with TMS vs 13% without TMS, P=0.0025). TMS applied earlier or later showed no effect. Furthermore, no significant increase in contra- or ipsilateral percentage of errors was found when the left parietal cortex was stimulated with the same timing. These data indicate that: (1) parietal influence on visuospatial attention is mainly controlled by the right lobe since the same stimulation over the left parietal cortex had no significant effect, and (2) there is a vulnerable time window to disturb this cortical process, since dTMS had a significant effect on the percentage of errors in the contralateral visual hemifield only when applied 270 ms after visual stimulus presentation.

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Introduction

It is generally accepted that the parietal lobes play a major role in the network of visuospatial attention. Patients with unilateral lesions may show a large spectrum of neuropsychological deficits, e.g. impairment of perception, of directing visual and covert attention to the contralateral space. Furthermore, they may have impairments of mental representation of space (for a review, see, e.g. Rafal 1994; Lezak 1997; Heilman and Valenstein 1993). Moreover, asymmetries between right and left parietal lobe function are described: preferential right parietal activation is found in arousal, enhanced vigilance (Paus et al. 1997), global processing, as well as in visuospatial attention for the global orientation in space (Corbetta et al. 1993). The activation of the left parietal lobe seems to be more important to local processing, e.g. subsequent analysis of local features (Driver et al. 1992), for directing attention to spatial locations on the contralateral side of space, and for temporal attentional processes (Coull and Nobre 1998).

Despite this functional specialisation, visual extinction, i.e. the unawareness of contralesional visual stimuli during simultaneous presentation, seems to occur with equal frequency after right or left hemisphere lesions (Rafal 1994). The complete neglect syndrome, on the other hand (Bisiach and Luzzatti 1978; Mesulam 2000), is mainly found after right hemisphere lesions involving the temporoparietal junction, and is thought to be caused by a disruption of the network of primary attentional functions as well as of visuospatial functions.

However, it remains unclear how the parietal lobes are involved in visuospatial attention processing, and particularly the temporal dimension is not well understood. Event related potential studies show that there is evidence for early and late processing in visual attention (for a review see Luck et al. 2000). Moreover, the timing of attention processes seems to be task dependent. Many

studies showed that early attention selection might start as soon as 60–100 ms after stimulus appearance (e.g. Hillyard and Münte 1984; Mangun and Hillyard 1988). Such early sensory-evoked components are typically found to be larger when a stimulus is presented at an attended location as compared with an unattended location.

However, it seems that attention operates also in different cognitive subsystems for different tasks (Luck et al. 2000), and that attention operates at a postperceptual stage. In the real world, a typical visual scene contains many different objects, not all of which can fully proceeded with by the visual system at any given time. The late component N2pc of event-related potentials seems to be a good indicator for attentional selectivity in visual search (Eimer 1996; Woodman and Luck 1999; Hopf et al. 2000). This negative component occurs typically between 200 and 300 ms after the presentation of a visual search array. Several studies showed that the N2pc component is related to the covert orienting of visual attention before completing object recognition (Luck and Hillyard 1994a, 1994b).

Transcranial magnetic stimulation (TMS) is a non-invasive technique, which allows interference with cortical processing by briefly disrupting a cortical region. It is an ideal tool with which to study the temporal organisation of complex processes (Cracco et al. 1999; Walsh and Rushworth 1999), and to determine functional relevance in time of a cortical region. It has been shown (Amassian et al. 1989; Miller et al. 1996; Epstein and Zangaladze 1996; Epstein et al. 1996; Kamitani and Shimojo 1999) that single-pulse TMS over the occipital cortex induces visual suppression if applied at critical time intervals after target presentation, and repetitive TMS (Pascual-Leone et al. 1994) induced contralateral visual extinction by stimulating the parietal lobes. Furthermore, TMS over the parietal cortex disturbs the performance in a visual search task (Walsh et al. 1999).

The aim of the present study was to perform a temporal mapping of parietal lobe function in a complex visuo-spatial attention and recognition task. By using the double-pulse (dTMS) technique with an interstimulus interval (ISI) of 100 ms, the right or left parietal lobes were stimulated at corresponding coordinates during a forced-choice recognition task. The subjects had to identify a pattern of two simultaneously flashed symbols during the short presentation time of 120 ms, out of four possible arrangements. The symbols were always presented in both visual hemifields.

Materials and methods

Subjects

Ten healthy subjects, four women and six men, were examined. Their mean age was 32 years (range 22–40 years). None of them took psychoactive medicaments. The local ethics committee approval had been obtained for the study and subjects gave their informed consent to participate in the study. Handedness was assessed by the Oldfield questionnaire (Oldfield 1971). Nine subjects were right handed and one subject was ambidextrous.

Subjects were seated in front of a 17-inch screen at a distance of 60 cm. The eye level was aligned to the mid-height and mid-width of the screen. The chin was set on a chinrest and the head was fixed during the experiment by using a Velcro band across the forehead.

Preliminary experiments (results not shown in detail)

Three preliminary experiments were performed in three out of the ten subjects before all subjects were tested in the main experiment. In the first preliminary experiment, we used the same experimental design as was used in the study by Pascual-Leone et al. (1994). In brief, a small asterisk was presented either in the left, right or both visual hemifields. Repetitive TMS trains of five pulses at 25 Hz were applied with the beginning of target presentation. In contrast, we applied dTMS instead of repetitive TMS. The ISI was always 100 ms, and stimulation started 120 ms, 270 ms, or 520 ms after simultaneous presentation of the visual targets in both hemifields. Double-pulse TMS in this experiment had no effect on performance; in particular, no visual extinction of the contralateral visual target was induced.

In the second preliminary experiment, we used the symbol combination paradigm as described in the main experiment (see below). In this experiment, symbol combinations appeared without additional gridlines, and the symbols were always presented at the same spatial location in the right and left hemifield. Double-pulse TMS applied at the same time intervals as in the first preliminary experiment had no effect on symbol recognition at any interval.

The third preliminary experiment differed from the previous one by overlaying horizontal gridlines of 8×8 cm to the symbol combination. Double-pulse TMS at the mentioned timing had no effect on symbol recognition at any stimulated interval.

Main experiment

In the main experiment (Fig. 1), the task started with a central fixation of randomly changing letters for a variable time interval of 1000–3000 ms. Simultaneously with the extinction of this central fixation point, a combination of the two symbols with the overlaid horizontal gridlines was simultaneously presented in both visual hemifields for 120 ms. In contrast to the preliminary experiments, the symbol combination was displayed now at various and random positions on the left and right side of the screen. A 6-cm large, vertical zone in the centre of the screen, which corresponded to 5.9° of visual angle, was spared. Four combinations of simultaneously presented symbols were possible, each of 2×2 cm dimensions (1.9° of visual angle): (1) >>; (2) <<; (3) <>; and (4) ><. According to the four possible combinations of the two simultaneously presented symbols, four key responses were attributed, and the subjects were instructed to respond by pressing the corresponding key press within 2000 ms after the extinction of the central fixation point. The next trial started with the appearance of the central fixation point. Each subject was individually trained without stimulation until 70–80% of correct responses was achieved (generally between 20 and 40 trials). All trials were performed in blocks of ten symbol presentations, and the subject decided individually when to continue the experiment after performing a block. In each subject, four to six blocks for each interval and stimulation side were acquired for each experiment. The subjects were examined in three sessions each lasting about 45 min, and in each session trials with and without stimulation were performed.

Control experiment

Finally, after obtaining significant results in the main experiment with dTMS starting at 270 ms, we tested the subjects again in a control experiment with single-pulse TMS. The issue of this ex-

Fig. 1 The main paradigm. After presentation of the central fixation point, a combination of two symbols was shown for 120 ms. During a 2-s period, the subject had to respond by pressing the corresponding key
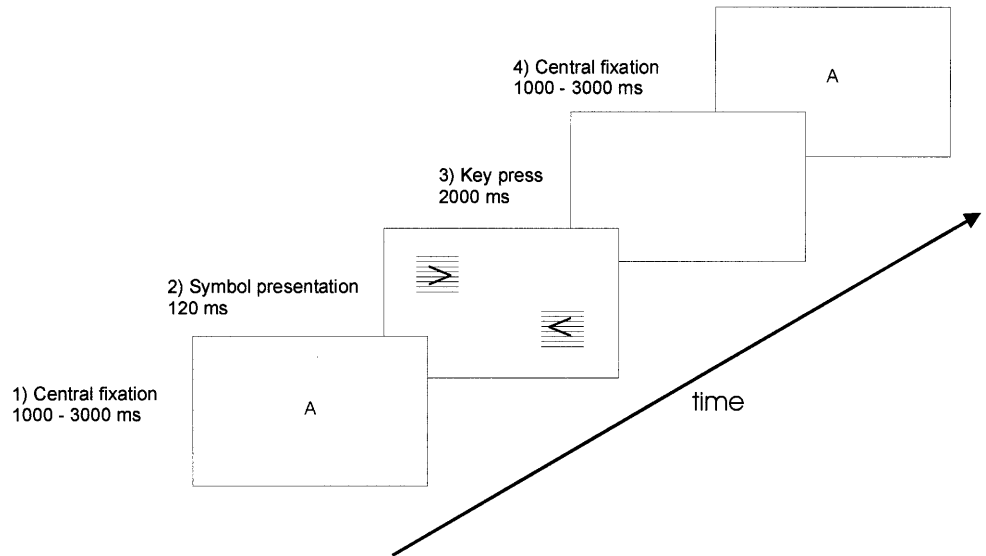
periment was to test whether single-pulse TMS over the right parietal cortex at 270 ms or 370 ms (i.e. corresponding to the timing where dTMS pulses were applied) was effective in inducing a significant increase in errors of the contralateral side.

TMS parameters and stimulation localisation

TMS was applied by using a MagStim high-speed stimulator (Magstim Co., Wales, UK) with a 90-mm non-focal, circular coil. The motor threshold was determined by muscle twitching of the subject's relaxed small hand muscles. The magnetic pulse intensity was fixed to 80% of the stimulator's maximal output and corresponded to 110–120% of the observed motor threshold. The coil position to stimulate the parietal cortex was determined according to the international 10-20 system of electrode placement (P3, P4). The inducing current in the coil segment overlaying the parietal target region flowed in the posterior direction, and the handle of the coil was posteriorly oriented. Double-pulse TMS was applied with 100 ms ISI starting at 120 ms, 270 ms, and 520 ms after the onset of the presentation of the symbols during right parietal cortex stimulation and at 120 ms and 270 ms during left parietal cortex stimulation.

Data analysis

The percentage of response errors was analysed and the percentage of response errors on the left or right side of the visual field (i.e. in which hemifield the symbol had been misinterpreted: left, right or both) was calculated. The absence of a key response was counted as an error in both hemifields.

Statistical analysis of the influence of the different stimulation intervals on percentage of response errors was performed by the Friedmann test. The Wilcoxon signed ranks test was used to compare the percentage of response errors with and without stimulation. Furthermore, the Bonferroni correction was made for multiple testing.

Results

Figure 2 shows the effect of dTMS over the right and left parietal cortex. The Friedmann test revealed a significant difference in the percentage of response errors during the different stimulus conditions when dTMS over the right
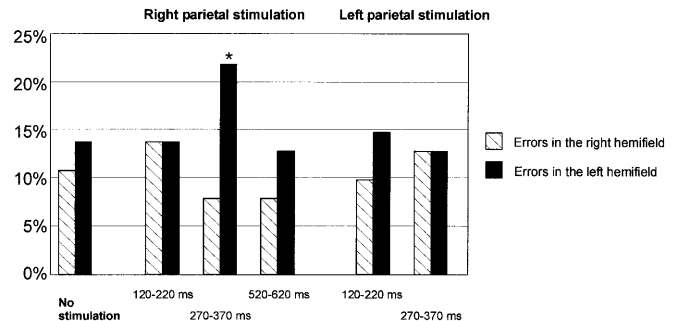

Fig. 2 Bar graphs showing the median percentage of errors for the different stimulation intervals and stimulated sides. Percentage of errors contralateral to the stimulated right parietal cortex was significantly increased after double-pulse TMS applied starting at 270 ms (*P=0.0025). Double-pulse TMS over the left parietal cortex had no significant effect. Finally, single-pulse TMS over the right parietal cortex at 270 ms or 370 ms had no significant effect on the percentage of errors

parietal cortex ($P<0.001$), but not when the left parietal cortex, was stimulated. Without stimulation, the median percentage of response errors in the right hemifield was 11% (range: 6–20%), and in the left hemifield 14% (range: 4–20%). Response errors in both hemifields occurred rarely, with a median of 6% (range: 0–10%).

A significant *contralateral* increase in percentage of response errors was found with dTMS over the right parietal cortex at 270 ms (median 22.2%, range 5–26%, P=0.0025, Wilcoxon signed rank test, Bonferroni's correction, $P<0.05$) compared to without stimulation. Double-pulse stimulation over the right parietal cortex at 120 ms [median (range) for errors in the right hemifield: 14% (3–28%) and for errors in the left hemifield: 14% (8–21%) respectively] or 520 ms [8% (5–23%) for errors in the right hemifield and 13% (5–23%) for errors in the left hemifield] had no significant effect on the percentage of response errors. The percentage of response errors in both hemifields always remained low during dTMS

(median for 120 ms: 5%; for 271 ms: 8%; and for 520 ms: 5%).

In the *control experiment*, single-pulse TMS had no significant effect on ipsi- or contralateral percentage of response errors [median for TMS at 270 ms: 18% (14–23%) in the left hemifield and 12% (7–23%) in the right hemifield; for TMS at 270 ms: 16% (10–20%) in the left hemifield and 10% (0–15%) in the right hemifield].

Discussion

In this study we performed a temporal mapping of visuospatial attention processing in the posterior parietal lobes. The main results were: firstly, there is a distinct time interval during which TMS interferes with parietal attentional processing, since dTMS with an ISI of 100 ms applied at 270 ms over the right PPC significantly increased the percentage of response errors in the contralateral visual hemifield. Earlier or later dTMS application had no significant effect, suggesting a specific effect in time. Secondly, the observed effect was hemispheric-specific since stimulation at 270 ms over the left parietal cortex had no significant effect on contralateral percentage of response errors.

These results suggest that dTMS interfered with visuospatial attention processing in the parietal cortex, but did not induce visual suppression or extinction. Previous studies (Amassian et al. 1989, 1998) have shown that induction of visual suppression crucially depends on TMS application early after visual presentation. Amassian et al. (1989) found that single-pulse TMS over the occipital cortex 80–100 ms after stimulus presentation induced contralateral suppression, and, by combining two or three pulses (Amassian et al. 1993), the effective interval for visual suppression was delayed. However, when the first pulse was later than 100 ms, i.e. after 120 ms applied, contralateral visual suppression did not occur. In our experiments, early TMS application had no effect on contralateral percentage of response errors. Moreover, visual extinction can be induced by early repetitive TMS over the parietal cortex. Pascual-Leone et al. (1994) induced visual extinction of contralaterally presented visual targets at a constant position by repetitive TMS over right and left parietal cortex starting the stimulation simultaneously with the visual presentation. By using the same experimental design, we were not able with dTMS in our preliminary experiments to induce visual extinction.

The effect of dTMS was hemispheric specific, since only stimulation of the right parietal cortex but not over the left parietal cortex had a significant effect on percentage of response errors in the contralateral hemifield. Such a right hemispheric dominance of visuospatial abilities is also found in patients with permanent lesion of the parietal cortex (e.g. von Cramon and Kerkhoff 1993).

Only few studies used TMS to explore visuospatial attention mechanisms (Sabatino et al. 1996; Ashbridge et al. 1997; Walsh et al. 1999), and they were mainly investigating the interference with attention processes of visual search. However, the results were not unequivocal. Sabatino et al. (1996), e.g. stimulated continuously over the temporal lobes with 0.5 Hz during a verbal and a visuospatial cancellation task and was not able to influence performance of a search task using low-frequency TMS. However, during prefrontal stimulation, task performance was even better. Ashbridge et al. (1997) used a visual search array, which was presented for 750 ms, and stimulated the parietal cortex 100 ms or 160 ms after stimulus onset. Reaction time was increased when the right parietal cortex was stimulated at 100 ms, and stimulation at 160 ms increased reaction time when the target was absent. In a second study (Walsh et al. 1999), they showed that magnetic stimulation over the left parietal cortex decreased reaction time when the target was presented in the left hemifield. However, in both studies TMS did not affect the error rate.

Finally, a recent rTMS study by Rushworth et al. (2001) found a similar right hemisphere dominance of parietal lobe stimulation during an attentional paradigm.

A conspicuous although somewhat expected feature of this study is the relatively late vulnerable time window for the TMS interference that we found. In contrast to classical visual attention tasks where early sensory attention selection mechanisms are expected, the task we used included different cognitive components such as object recognition, working memory and response selection.

Therefore, late attention mechanisms may be much more important in our experiment. There is evidence from event related potential (ERP) studies during more complex tasks showing similar critical time intervals to what we found: The N2pc component, an indicator of attention selectivity, is typically observed between 200 and 300 ms after the array presentation. The component is also related to covert orienting of visual attention before the completion of object recognition (Luck and Hillyard 1994a, 1994b), and becomes more activated in attentional filtering processes such as in visual discrimination tasks (Eimer 1996). Woodman and Luck (1999) found in a visual search task the most important attention-related changes in ERP components were observed between 200 and 300 ms after visual presentation. In a target detection task (Menon et al. 1997), significant activation of the parietotemporal cortex was found even 285–610 ms after stimulus onset. For object recognition, a critical time interval of about 250 ms after target presentation was determined by EEG coherence analysis (Mima et al. 1999). Finally, Yamaguchi et al. (2000) showed that right parietotemporal region and left posterior temporal region were differentially activated during acttentional allocation to global and local features of a visual scene. These effects started around 240 ms after presentation. Taking all these studies together, the vulnerable time window for disrupting attention processing as observed in our experiment would correspond well with the timing found in ERP studies in complex visual search tasks.

In conclusion, the current results of the TMS interference suggest a critical visuospatial attention process of a recognition task controlled by the right parietal cortex 270 ms after visual presentation. Furthermore, a hemispheric asymmetry was found, since only stimulation over the right parietal cortex significantly disrupted the performance.

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