Bilateral competitive processing of visual spatial attention in the human brain

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Abstract

Visual spatial attention is an essential brain function that is produced through the interactions of several cortical and subcortical regions. Using the reversible deactivation technique of transcranial magnetic stimulation (TMS) in combination with a visual stimulus detection task, we demonstrated that parietal as well as occipito-parietal cortices in the human brain contribute to spatial attentional behavior. The functional role of left- and right-hemispheric regions appeared to be mirror-symmetric, although the strength of contributions from left and right cortices might differ. Reaction times for baseline and experimental conditions suggested that

TMS interfered with an early stage of attentional processing. The experiments also demonstrated an ipsilateral enhancement of spatial attention after unilateral TMS. This observation supports a theoretical model for inter-hemispheric competition in the attentional network.

1. Introduction

Mechanisms of spatial attention underlie visual perception as well as many visual behaviors, such as search, orienting or avoidance reactions. Several cortical and subcortical regions have been implicated in attentional processing (reviewed in [1]). Knowledge about the extent and function of this attentional network in the human brain stems mainly from patients with localized brain damage who show deficits in redirecting spatial attention, mostly towards the contralesional space. Depending on whether the deficits predominantly appear for unilateral stimuli presented in contralateral space or for bilateral stimuli, such syndromes have been classified as neglect or extinction, respectively [2].

Using the "virtual lesion" technique of TMS, e.g., [3,4], we aimed to study contributions and interactions of different cortical stages in the attentional network more systematically. Reversible impairment of cortical processing by TMS can be created in an event-related way, or by prestimulation of cortical sites with 1Hz repetitive TMS (rTMS) [5]. While the mechanisms underlying TMS deactivation are not yet fully understood, reversible deactivation approaches avoid a number of conceptual difficulties posed by traditional studies of patients with permanent lesions, such as an absent baseline before lesion onset, plastic reorganization of the brain after damage and the frequent non-systematic and wide-spread behavioral impact of permanent lesions.

We used TMS deactivation approaches to (i) identify cerebral cortical regions contributing to spatial attention and (ii) explore the specific contribution of different cortical regions in the attentional network. Our experiments were guided by knowledge about the locations of lesions in neglect patients, earlier TMS studies [6], as well as the predictions from a theoretical model. This model [7-9], which was derived originally from structural information and behavioral data of studies in the cat, e.g., [10,11], suggests that spatial attention is based on a topographic neural representation of visual space and bilateral, inter-hemispheric competition. A simple prediction resulting from this concept is the disinhibition of structures in the unimpaired hemisphere through deactivation of structures in the impaired hemisphere. Such a functional release should also manifest itself in a measurable behavioral enhancement.

2. Methods

Subjects. Experiments were in line with NIH guidelines for human studies and were approved by the local Ethics Review Boards at Beth Israel Deaconess Medical Center, Boston and the Dept. of Neurology, Rostock University. Subjects belonged to two sets of healthy volunteers, consisting of 7 and 10 subjects, respectively. All subjects but one were male; the majority of them were right-handed.

Stimulus detection test. In a simple behavioral paradigm, subjects had to detect small rectangular stimuli presented briefly (for 40ms) on a cathode ray tube (CRT) monitor either unilaterally in the left or right visual periphery (lateral eccentricity approximately 25°), or bilaterally in both fields. Subjects' performance in stimulus detection was assumed to reflect the efficiency of their attentional mechanisms. Stimuli consisted of small black rectangles and stimulus presentation was interspersed with catch trials in which no stimuli were present. Subjects used their dominant hand to press one of three keys of a response box to indicate if they had detected a left, right, or bilateral stimulus. Stimulus sizes were adapted to the subjects' visual acuity and attentional capability, to be at peri-threshold stimulus strength (with a resulting median level of correct stimulus detection around 20% for small stimuli and 70% for slightly larger ones), so that correct detection during the experimental trials could vary up or down. For further details see [12].

TMS protocols. We employed two different TMS approaches. The first used an event-related design (that is, magnetic stimulation was synchronized with stimulus onset), whereas the second employed a 'chronic' repetitive TMS approach (stimulating the target site with 90% motor threshold at 1Hz for 10 minutes before experimental testing). This repetitive paradigm has been shown to result in behavioral effects consistent with transient suppression of cortical excitability, e.g., [13-16]. Consequently, we tested spatial detection performance in a block design, at baseline and after rTMS, during the window of cortical dysfunction.

TMS locations. We explored the contributions of two cortical regions to visual spatial attention, (i) occipito-parietal cortex, and (ii) parietal cortex. Locations for TM stimulation were determined within the 10-20 relative EEG coordinate system. Stimulation sites in parietal cortex were verified by post-experimental structural MRI. In the first, chronic approach, seven subjects were tested after right parietal (P4) rTMS, six subjects after left parietal (P3) rTMS. In the event-related TMS approach, ten subjects were tested on bilateral sites in occipito-parietal cortex. Here the location of stimulation was determined as the maximally effective point for inducing contra-lesional hemi-extinction (at 90% phosphene threshold). As a control, we also performed sham experiments and stimulated right primary motor cortex (M1).

3. Results

No significant changes in the subjects' detection performance were observed for sham stimulation or stimulation of M1. For both sets of deactivated cortical regions, however, we found a trend to diminished detection of unilateral stimuli opposite to the cortical TMS site. This trend was significant in the acute TMS approach. The contralesional deficit was even more pronounced for the contralateral stimulus in bilateral stimulus pairs, and led to a significant decrease in correct responses for bilateral stimuli after functional deactivation of occipito-parietal as well as parietal cortical regions. Taken together, these behavioral effects present a picture similar to the clinical syndromes of contralesional hemineglect and hemi-extinction.

We also found enhanced detection of unilateral stimuli on the side of the TM stimulation, both in terms of error rates as well as reaction times (Fig. 1). The amplification trend was seen across both sets of studies and TMS locations; however, the effects only reached statistical significance for the chronic rTMS approach. The general response trends for left and right stimulation indicated symmetrical effects, although not all observations during the two TMS approaches reached statistical significance, and effects were generally more pronounced for right-hemispheric stimulation. Different stimulus conditions and the impact of TMS deactivation could also be distinguished in terms of reaction times (presented in Fig.1 for the rTMS approach).

Results obtained during the event-related TMS approach were more difficult to interpret due to errors caused by (i) interference of the TMS discharge with the CRT stimulus display as well as (ii) TMS-induced transient visual field effects (such as phosphenes and scotomas) experienced by the subjects.

4. Conclusions

Our results provide support for the concept of a distributed, bilateral, competitive network mediating visual spatial attention in humans. Different visual cortical stages, such as occipito-parietal and parietal cortex, contribute to the functioning of this network, each probably within the context of their individual functional roles. It appears likely that even more stations are involved, e.g., [17]. Largely mirror-symmetric effects for the deactivation of left- and right-hemispheric sites indicated the principal similarity of attentional processing in both hemispheres, although processing may be partly lateralized to the right hemisphere.

The results also suggested that the behavioral consequences resulting from the local impact of event-related TMS and 1Hz rTMS are comparable, even though at least the latter approach also results in global changes of neural activation patterns [18].

The obtained reaction times allowed us to address another question: Are incorrect unilateral responses for bilateral stimuli more similar to correct unilateral detection or to correct bilateral detection? In other words, are both stimuli of a bilateral pair first processed by the brain after which the response to one of them is omitted, or is the initial processing of one stimulus suppressed altogether? The present results lend support to the latter hypothesis, as incorrect unilateral responses to bilateral stimuli were found to be significantly faster than correct bilateral responses. The finding suggests an interference of parietal cortical TMS with an early stage of attentional processing, and is in line with simple feedforward models of evoked attention, such as [19].

Future experiments should aim to replicate the results obtained for event-related TMS of occipito-parietal cortex, due to the technical difficulties we experienced. Additional experiments could use either a chronic rTMS paradigm, or a modified event-related approach that minimizes interference of the TMS field with the stimulus display through the use of a projection system. We are, however, encouraged in our interpretation of the current results by independent findings [20,21] that also suggest involvement of occipito-parietal regions in attentional processing.

Enhanced ipsilateral stimulus detection was seen in error rates as well as reaction times and was found across studies and locations, hinting on the general nature of competitive inter-hemispheric interactions in spatial attention. It will be an interesting challenge for the future to determine the exact structural basis of the competitive inter-hemispheric interaction. Is it being mediated directly between the homotopic parietal and occipital sites? Alternatively, competition might be created via a number of intermediate stages (even subcortical ones, as in the cat, [7,10]), or just between some of the cortical pairs. These effects could then be transmitted ipsilaterally to other cortical regions in the network [17].

Functional competition between different brain structures, as seen here, might be a general principle of brain function [22] and may help to explain the 'paradoxical' behavioral enhancement or recovery observed after various brain lesions [23]. Future studies will have to describe systematically the specific contributions that different neural components make in the widely distributed network for spatial attention, and should explore their functional interactions.

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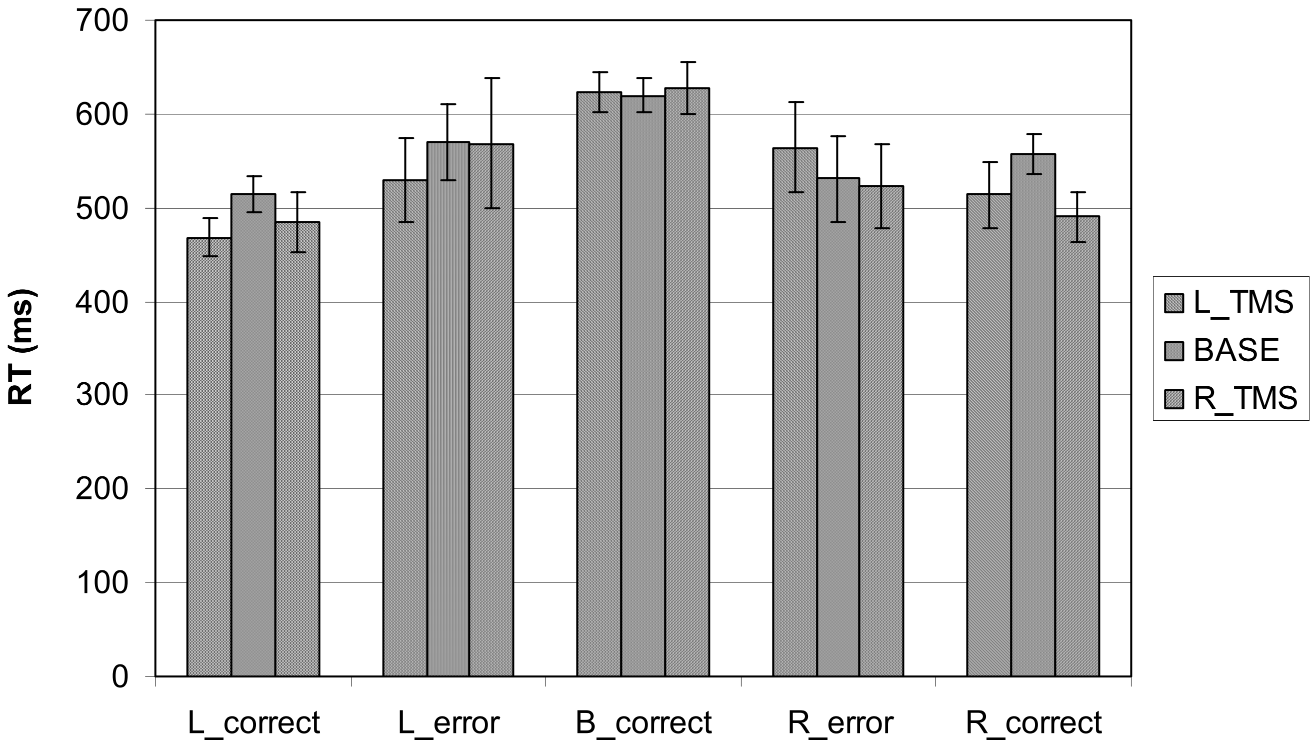

Hilgetag et al., Figure 1.

Figure 1. Average reaction times and standard error for correct bilateral, as well as for correct and incorrect unilateral responses at baseline and after rTMS of parietal regions P3 (“L_TMS”) and P4 (“R_TMS”) in the chronic rTMS approach. “L_correct”, “B_correct” and “R_correct” denote reaction times for the respective correct detection responses. “L_error” and “R_error” indicate reaction times of incorrect left and right detection responses for presented bilateral stimuli (involving extinction of the contralateral stimulus). Correct unilateral responses were significantly faster than bilateral responses ($p<0.05$). After rTMS, incorrect responses for only the ipsilateral stimulus in bilateral stimulus pairs were also significantly faster than correct bilateral responses. Left- and right-hemispheric TMS generally introduced mirror-symmetric reaction time effects, and speeded up detection of ipsilateral stimuli.