

A bilateral competitive network for visual spatial attention in humans

Claus C. Hilgetag^{*1}, Rolf Kötter^{2,3}, Hugo Théoret⁴, Joseph Claßen⁵, Alexander Wolters⁵, Alvaro Pascual-Leone⁴

¹School of Engineering and Science, International University Bremen, Campus Ring 1, 28759 Bremen, Germany; C.Hilgetag@iu-bremen.de;

²C. & O. Vogt Brain Research Institute and ³Dept. of Anatomy II, Heinrich Heine University, Universitätsstr. 1, 40225 Düsseldorf, Germany;

⁴Beth Israel Deaconess Medical Center and Harvard Medical School, Dept. of Neurology, 330 Brookline Avenue, Boston, MA 02115, USA;

⁵Department of Neurology, Rostock University, Gehlsheimer Str. 20, 18147 Rostock, Germany.

*To whom correspondence should be addressed.

Abstract

Visual spatial attention is an essential brain function that is produced through the interaction of several cortical and subcortical regions. Using transcranial magnetic stimulation (TMS, an experimental technique for producing ‘virtual lesions’) in combination with a visual stimulus detection test, we demonstrated that parietal as well as occipito-parietal cortices in humans contribute to spatial attentional behavior. The functional role of left- and right-hemispheric regions appeared to be mirror-symmetric, although the strength of the left and right contributions may differ. The experiments also demonstrated an ipsilateral enhancement of spatial attention after unilateral TMS. This observation supports a theoretical model for interhemispheric competition in the attentional network.

A bilateral competitive network for visual spatial attention in humans

C.C. Hilgetag, R. Kötter, H. Théoret, J. Claßen, A. Wolters, A. Pascual-Leone

Abstract

Visual spatial attention is an essential brain function that is produced through the interaction of several cortical and subcortical regions. Using transcranial magnetic stimulation (TMS, an experimental technique for producing ‘virtual lesions’) in combination with a visual stimulus detection test, we demonstrated that parietal as well as occipito-parietal cortices in humans contribute to spatial attentional behavior. The functional role of left- and right-hemispheric regions appeared to be mirror-symmetric, although the strength of the left and right contributions may differ. The experiments also demonstrated an ipsilateral enhancement of spatial attention after unilateral TMS. This observation supports a theoretical model for interhemispheric competition in the attentional network.

Introduction

Visual spatial attention is neural function that underlies perception as well as many visual behaviors, such as visual search, orienting or avoidance reactions. It is based on wide-ranging brain networks including different cortical and subcortical stages (reviewed in [1]). Knowledge about the extent and function of this network 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]. However, systematic and reliable studies are difficult to carry out in patients with permanent brain lesions, because of the non-systematic, wide-spread behavioral impact of the lesions and because the patients’ behavioral baseline before the onset of their impairment is not normally known [3]. Experimental ‘virtual lesion’ techniques such as transcranial magnetic stimulation (TMS) [4] can offer a practical alternative [5].

We used TMS approaches to explore (i) which cerebral cortical regions contribute to spatial attention and (ii) how matching bilateral regions interact. Our experiments were guided by

No presentation preference.

knowledge about the locations of lesions in neglect patients, earlier TMS studies, as well as the predictions from a theoretical model. This model [6-8], which was derived originally from structural information and behavioral data of studies in the cat, suggests that spatial attention is based on a topographic representation of visual space and bilateral, inter-hemispheric competition. A simple prediction resulting from this 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.

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 were two sets of healthy volunteers, consisting of 7 and 10 subjects respectively. All subjects but one were male, and the majority of them were right-handers.

Stimulus detection test. In a simple behavioral paradigm, subjects had to detect small rectangular stimuli briefly (for 40ms) presented on a computer monitor either unilaterally in the left or right visual periphery (lateral eccentricity approximately 25°), or bilaterally in both. The 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 stimulus was present. Subjects used their dominant hand to press one of three keys of a response box to indicate whether 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 [9].

TMS protocols. We employed two different TMS approaches. The first used an acute design (that is, the magnetic stimulation was synchronized with the stimulus presentation) whereas the second one used a 'chronic' repetitive TMS approach (stimulating the target site at 1Hz for 10 minutes). This repetitive paradigm has been shown to result in behavioral effects consistent with transient suppression of cortical excitability, e.g., [10-13]. We tested spatial detection

No presentation preference.

performance in a block design, at baseline and after rTMS during the window of cortical dysfunction.

TMS locations. We tested the contribution of two cortical regions to visual spatial attention, (i) occipital and occipito-parietal cortex, and (ii) parietal cortex. The locations for stimulation were generally determined within the 10-20 relative EEG coordinate system. One of the locations (in parietal cortex) was verified by post-experimental structural MRI. In the first group of subjects, seven of the subjects were tested after right parietal (P4) rTMS, six subjects after left parietal (P3) rTMS. For the acute approach performed with the second set of subjects, ten of the subjects were tested on bilateral sites in occipital and occipito-parietal cortex. 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).

Results

No significant changes in the 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 TMS-induced cortical deactivation. This trend was significant in the acute TMS approach. The contralesional deficit was even more pronounced for the contralateral stimulus in presented bilateral stimulus pairs, and led to a significant decrease in correct responses for bilateral stimuli after functional deactivation of occipital as well as parietal cortical regions. Taken together, these behavioral effects present a picture similar to the clinical syndromes of hemi-neglect and –extinction.

We also found an enhancement of detection of unilateral stimuli on the side of the TM stimulation. This amplification was seen across studies and locations, hinting on the general nature of competitive inter-hemispheric interactions in spatial attention. The response trends for left and right stimulation indicated symmetrical effects, although not all observations during the two TMS approaches reached statistical significance.

No presentation preference.

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., [14], and we plan to use TMS for testing the contributions of further cortical regions.

It will also 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 matching parietal and occipital sites? Alternatively, competition might be created via a number of intermediate stages (even subcortical ones, as in the cat, [6, 15]), or just between some of the cortical pairs. These effects could then be transmitted ipsilaterally to other cortical regions in the network [14].

Functional competition between different brain structures, as seen here, might be a general principle of brain function [16] and may help to explain the ‘paradoxical’ behavioral enhancement or recovery observed after various brain lesions [17]. Future studies will have to describe systematically the specific contributions the different neural components make in the widely distributed network for spatial attention, and should explore their functional interactions.

Acknowledgement: Supported in part by the Wellcome Trust.

References

- [1] A. W. Toga, F. S. J. Frackowiak, J. C. Mazziotta (eds.), Special issue (issue 1, part 2): Action and visio-spatial attention: Neurobiological bases and disorders, in *Neuroimage*, Vol. 14, pp. 1-146 (2001).
- [2] G. Vallar, Spatial hemineglect in humans, *TICS* 2 (1998) 87-97.
- [3] N. Smania, M. C. Martini, G. Gambina, G. Tomelleri, A. Palamara, E. Natale, C. A. Marzi, The spatial distribution of visual attention in hemineglect and extinction patients, *Brain* 121 (1998) 1759-1770.
- [4] A. Pascual-Leone, D. Bartres-Faz, J. P. Keenan, Transcranial magnetic stimulation: studying the brain-behaviour relationship by induction of 'virtual lesions', *Philos Trans R Soc Lond B Biol Sci* 354 (1999) 1229-1238.
- [5] R. Rafal, Virtual neurology, *Nat Neurosci* 4 (2001) 862-864.
- [6] C. C. Hilgetag, R. Kötter, M. P. Young, Inter-hemispheric competition of sub-cortical structures is a crucial mechanism in paradoxical lesion effects and spatial neglect, *Prog Brain Res* 121 (1999) 121-141.
- [7] C. C. Hilgetag, Spatial neglect and paradoxical lesion effects in the cat - A model based on midbrain connectivity, *NeuroComputing* 32-33 (2000) 793-799.
- [8] C. C. Hilgetag, S. G. Lomber, B. R. Payne, Neural mechanisms of spatial attention in the cat, *NeuroComputing* 38-40 (2001) 1281-1287.
- [9] C. C. Hilgetag, H. Theoret, A. Pascual-Leone, Enhanced visual spatial attention ipsilateral to rTMS-induced 'virtual lesions' of human parietal cortex, *Nat Neurosci* 4 (2001) 953-957.
- [10] R. Chen, J. Classen, C. Gerloff, P. Celnik, E. M. Wassermann, M. Hallett, L. G. Cohen, Depression of motor cortex excitability by low-frequency transcranial magnetic stimulation, *Neurology* 48 (1997) 1398-1403.
- [11] F. Maeda, J.P. Keenan, J. M. Tormos, H. Topka, A. Pascual-Leone, Interindividual variability of the modulatory effects of repetitive transcranial magnetic stimulation on cortical excitability, *Exp Brain Res* 133 (2000) 425-430.

No presentation preference.

- [12] S. M. Kosslyn, A. Pascual-Leone, O. Felician, S. Camposano, J. P. Keenan, W. L. Thompson, G. Ganis, K. E. Sukel, N. M. Alpert, The role of area 17 in visual imagery: convergent evidence from PET and rTMS, *Science* 284 (1999) 167-170.
- [13] H. Theoret, J. Haque, A. Pascual-Leone, Increased variability of paced finger tapping accuracy following repetitive magnetic stimulation of the cerebellum in humans, *Neurosci Lett* 306 (2001) 29-32.
- [14] M. Oliveri, P. M. Rossini, R. Traversa, P. Cicinelli, M. M. Filippi, P. Pasqualetti, F. Tomaiuolo, C. Caltagirone, Left frontal transcranial magnetic stimulation reduces contralesional extinction in patients with unilateral right brain damage, *Brain* 122 (1999) 1731-1739.
- [15] J. M. Sprague, Interaction of cortex and superior colliculus in mediation of visually guided behavior in the cat, *Science* 153 (1966) 1544-1547.
- [16] V. Walsh, A. Ellison, L. Battelli, A. Cowey, Task-specific impairments and enhancements induced by magnetic stimulation of human visual area V5, *Proc R Soc Lond B Biol Sci* 265 (1998) 537-543.
- [17] N. Kapur, Paradoxical functional facilitation in brain-behaviour research. A critical review, *Brain* 119 (1996) 1775-1790.