The role of the right dorsolateral prefrontal cortex in visual change awareness

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Received 25 August 2004; accepted 18 September 2004

Recently, the neural correlates of change detection *vs* change blindness have been investigated using fMRI. Results revealed that conscious perception of change is associated with enhanced activity in a neural network comprising the parietal (bilateral) and right dorsolateral prefrontal (DLPF) cortex. Here, by means of repetitive transcranial magnetic stimulation (rTMS), we unveil the causal role of the right DLPF cortex in perceiving changes. When rTMS was applied to this area, change perception was impaired as compared to left DLPF rTMS and sham stimulation. This result is important as it shows, for the first time, that conscious change perception is associated with normal activity in the right DLPF cortex. Our findings are in agreement with a recent view emphasizing the role of frontal areas, in addition to classical ventral and dorsal pathways, in visual awareness. *NeuroReport* 15:2549–2552 © 2004 Lippincott Williams & Wilkins.

Key words: Conscious perception; Change awareness; Prefrontal cortex; rTMS

INTRODUCTION

The ability to perceive changes in a visual scene is an important adaptive function, as correct change perception might be crucial in several everyday-life situations. However, recent studies have shown that large changes can remain unnoticed if they take place along with other, apparently innocuous, visual events [1]. For example, if visual continuity is briefly interrupted by events such as the sudden appearance of irrelevant spots [2], or a blank screen separating a pair of images [3], observers usually fail to notice even large changes in the image. This phenomenon, known as change blindness, is important for the issue of visual awareness, as it unambiguously demonstrates the role of focused attention in determining the contents of our conscious visual experience.

Neural correlates of change detection and change blindness have been recently investigated in an event-related fMRI study [4]. Neurologically intact observers performed a change detection task while the screen on which the stimuli were presented was flickering. Results revealed that conscious change perception, as compared to change blindness, was characterized by a pattern of neural activation comprising the bilateral parietal and the right DLPF cortex. In contrast to this differential activation pattern, activity in category-specific regions of the ventral pathway (e.g. parahippocampal place area and fusiform face area, for changing houses and faces, respectively) was observed regardless of whether the change was perceived or missed. These findings demonstrated that, in healthy participants, dorsal parietal activation correlated with visual awareness, a notion that complements the traditional view emphasizing the role of the ventral visual stream in the conscious perception of specific stimulus categories [5,6]. However, evidence that awareness of visual change is associated with enhanced activity in parietal areas is consistent with the fact that damage in this region (usually in the right hemisphere) causes a loss of awareness for stimuli in the contralesional visual field [7].

Recently, the causal role of parietal activation in awareness for visual change has been evaluated using rTMS [8]. In this study, the participants had to report any change between pairs of images separated by a brief blank. During the entire viewing period of 500 ms, rTMS was applied either to the left or to the right parietal cortex. As compared to the control condition (no TMS), accuracy in change perception was significantly reduced by rTMS. In the authors' view, rTMS caused a functional impairment of the parietal lobe, which affected the correct allocation of attention to the change location, thus increasing the degree of change blindness.

As already noted [9], the debate about the neural sites of visual awareness has largely overlooked the role of frontal regions; instead evidence and discussion has mainly focused on the contribution of either the dorsal-parietal areas (possibly by controlling attentional orienting) and the ventral-temporal areas (as neural sites for category-specific stimulus analysis). Evidence exists supporting the role of frontal regions in visual awareness [10], and visual neglect can also occur as a consequence of frontal brain damage [7]. Interestingly, conscious change perception seems to be associated not only with enhanced activity in parietal areas, but also with activation of the right DLPF cortex [4]. This is

in agreement with a recent event-related potentials (ERPs) study in which participants searched for a change between two images separated by a blank [11]. The ERP analysis revealed that change-detection trials, as compared to missed-change trials, were characterized by the presence of a positive wave peaked at about 300 ms, which originated in the frontal areas.

Hence, what remains to be explored is whether activity in frontal regions is also crucial for conscious change perception. Specifically, the present experiment was aimed at establishing the causal role of the right DLPF cortex in consciously perceiving a change. To this purpose we applied rTMS to both the left and right DLPF cortex while participants were engaged in a change-perception task. Awareness of change was addressed by presenting a pair of images, each consisting of 4 black and white male faces, separated by a blank. Any effect of rTMS on the participants' ability to perceive changes in the images would provide critical support to the hypothesis that frontal regions are involved in visual change awareness. Moreover, on the basis of previous fMRI findings showing that conscious change detection was associated with activation in the right DLPF cortex but not in the left DLPF cortex [4], we expected change perception for faces to be more severely disrupted when functioning of the right rather than left DLPF cortex was disrupted by rTMS application.

MATERIALS AND METHODS

Twelve healthy participants (8 male) aged 24–42 years (mean 29), gave their written informed consent prior to the experiment. The local Human Ethics Committee approved the protocol. All were right-handed (mean score on Edinburgh handedness inventory 84) and had normal or corrected-to-normal vision. Participants viewed a screen in which a fixation point was always present in the centre. Two displays consisting of four faces each, appeared briefly (200 ms), separated by a 300 ms blank interval. The faces were carefully matched both in terms of luminance and area covered by the image, and were arranged in a 2×2 matrix centred on the fixation point. This criterion was adopted to avoid the possibility that change perception could be performed on the basis of low-level differences in the physical properties of the faces across the two images, rather than by comparing the identity of the faces. rTMS was delivered at the onset of the first display ensuring that stimulation was delivered during the entire display time (700 ms).

Participants kept their forearms resting on the arms of the chair, with left and right index fingers resting on two response keys on the computer keyboard. They were instructed to press, following onset of the second display, the left or right key according to whether or not one of the faces changed. The allocation of response to left-*vs*-right hands was counterbalanced between participants. Change was present in 50% of trials, and the four locations were equally likely to contain the change. On each trial, the four faces were randomly chosen from a set of nine different black-and-white pictures of male faces ($2.5 \times 3.0^\circ$ of visual angle). Stimuli subtended a visual angle of $\sim 5.6 \times 6.6^\circ$. The inter-trial interval after the response was 3000 ms, and overall the experimental session lasted ~ 20 min.

Before the experiment began, participants completed a block of 20 practice trials. The experiment included six blocks, counterbalanced between participants as to order of presentation (rTMS to the right, or to the left DLPF cortex or sham stimulation). Each block consisted of 40 sets of displays.

rTMS was applied using a Magstim Rapid with a figure-of-eight (double 70 mm) coil. Before the experiment, individual resting excitability thresholds of stimulation were determined by stimulating the left motor cortex. The threshold was defined as the minimum intensity which induced a visible contraction in the first interosseus dorsalis muscle, as agreed by two experimenters on at least three out of six trials. The stimulation intensity used during the experiment was set at 100% of each participant's threshold. During the experiment, rTMS was delivered using a train of eight pulses with a frequency of 10 Hz (i.e., lasting a total of 700 ms).

The participants wore a close-fitting skullcap on which the positions of all the electrodes from the International 10/20 EEG system were reproduced. Two additional points were marked on the cap, corresponding to the stimulation sites used in the study. Thus, two sites, which were estimated to overlie the left and right DLPF cortices were stimulated, when required, by placing the anterior end of the junction of the coil wings on one of two points marked. The stimulation site for the sham condition was on the midline at the same horizontal level as the frontal sites but the coil being perpendicular to the scalp. This ensured that no magnetic stimulation reached the brain during the sham condition. These positions on the paricipant's scalp were automatically identified using the SofTaxic Evolution navigator system that works in the absence of individual radiological images on the basis of digitized skull landmarks (nasion, inion and two pre-auricular points) from which 40 uniformly-distributed points can be mapped out on the scalp (3D Fastrak Polhemus digitizer) and related to cerebral anatomy [12].

Although individual magnetic resonance images were not available, Talairach coordinates of cortical sites underlying coil locations (Fig. 1) were automatically estimated for the participants by the navigator system, on the basis of an MRI-constructed stereotaxic template (location estimate has an error <1 cm, Talairach space). This method represents a good compromise among the localization accuracy and the availability of the single participant MRI. It should be noted that we can compute with very high precision the location of the coil but this does not strictly imply that we know with such a high precision the width of brain areas that are directly or even indirectly influenced by the magnetic field, independently of the presence of single participant MRI. Therefore we can only assume that we were stimulating the estimated cortex site underling the coil. We chose to stimulate dorsolateral prefrontal cortex on the basis of previous results by Beck *et al.* [4], and the site of stimulation based on Tailarach coordinates are within these values. The location of these points was on average centred on Talairach coordinates $X = \pm 50$ (range 41–56; s.d. 4,3), $Y = 22$ (range 16–34; s.d. 5,2), $Z = 34$ (range 26–43; s.d. 4,6).

RESULTS

Percentages of correct change detection and response times were analyzed by repeated measures ANOVA, in which the factors were condition (change present *vs* change absent) and site of stimulation (left DLPF cortex, right DLPF cortex,

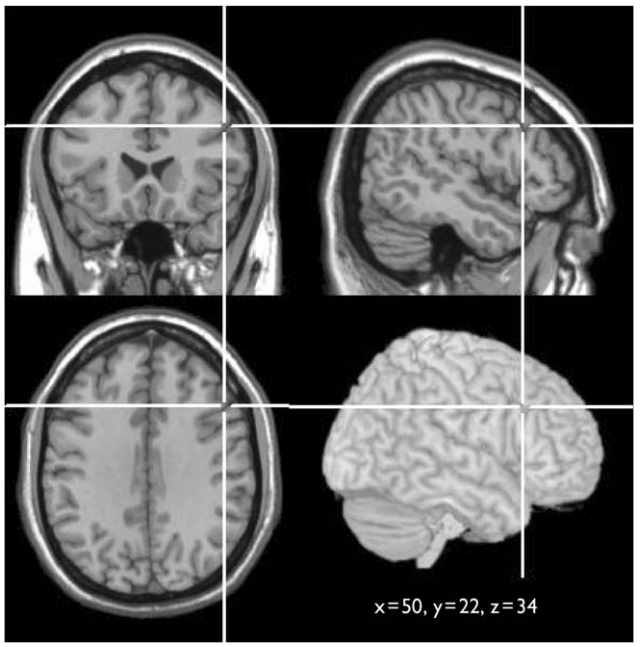

Fig. 1. Coronal, axial, sagittal and brain surface views of the stimulated site depicted on a standard template from MRIcro software (v.1.37). The cross hairs indicate the estimated site under the coil location. The average Talairach coordinates of this site, calculated with the SofTaxic Evolution navigator software, are x= 50, y=22, z=34, corresponding to right DLPF cortex.

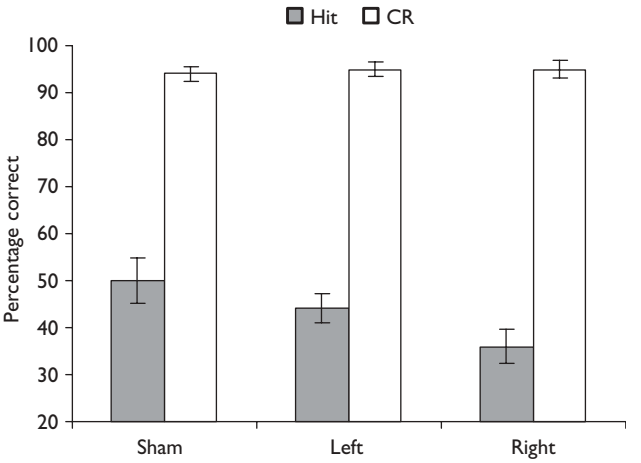

Fig. 2. Behavioural results of the experiment. The graph shows percentage errors in detecting changes, for the three stimulation conditions (sham, left and right rTMS). Hit correspond to correct detection on change-present trials, while CR correspond to correct rejection on change-absent trials. The error rate is higher after right rTMS, suggesting a direct involvement of the DLPF cortex in conscious change perception. Verticals bars represent s.e.m.

and sham rTMS), followed by planned comparisons where appropriate. Accuracy data showed a significant condition $\times$ site of stimulation interaction ($F(2,22)=6.190$; $p=0.007$), arising from a different effect exerted by rTMS on change-present *vs* change-absent trials. Indeed, errors on change-absent trials were very low, 5% in all conditions and did not differ as a function of site of stimulation (all $p<0.66$). By contrast, rTMS clearly affected participants' performance on change-present trials ($F(1,11)=8.547$; $p=0.002$). Planned comparisons showed that, after right DLPF cortex rTMS, participants were less accurate (36%) than after either sham (50%; $p=0.004$) or left (44%; $p=0.027$) stimulation, in perceiving changes. This suggests a specific role of the right DLPF cortex in the awareness of change. No significant differences were present between left and sham stimulation (Fig. 2). Analysis of reaction times showed no differences between conditions ($F(2,22)=0.66$; $p=0.526$) despite the fact that participants' reaction times to both sham (560 ms) and left (553 ms) rTMS were faster than those to right (581ms) rTMS.

DISCUSSION

The present study provides the first evidence that activity in the right DLPF cortex is causally related to conscious change perception. rTMS was applied either to the right or left DLPF cortex of neurologically healthy participants while they looked for a change between pairs of images separated by a blank. Compared to the sham-stimulation condition, accuracy in change perception decreased significantly when activity of the right DLPF cortex was transiently disrupted. This finding is in agreement with and extends those from a previous fMRI study [4], in which enhanced activity in parietal and right DLPF cortex was associated with correct conscious change perception. Importantly, here we documented a causal relation between intact neural activity in the right DLPF cortex and visual change awareness.

Previous findings have already documented an increased degree of change blindness when rTMS was applied to the parietal cortex [8]. Disrupting the parietal lobe activity might have led to a lack of awareness for visual change as this area controls the orienting of attention. Because the orienting of attention is controlled also by the frontal eye fields (FEF) [13], one might conclude that, by applying rTMS to these areas, we interfered with the corresponding neural mechanism. However, the FEF are located posterior and superior to the cortical area stimulated in the present study [14], and given the relatively high spatial resolution of the TMS [15], we can reasonably exclude the possibility that we might have affected activity in the FEF in a significant manner.

An alternative explanation of the present findings points to the role of the DLPF cortex as the neural substrate of working memory (WM), a system for the temporary storage and manipulation of information [16], which is crucial in change perception [3]. Indeed, to perceive a change in the present experiment, the participants needed to select some information from the first image and to maintain it in WM across the blank interval for comparison with the second image. Accordingly, neuroimaging studies show that the DLPF cortex is routinely activated in task that require the processing of information stored in WM (for review see [17,18]).

Our results might specifically be concerned with the crucial involvement of the right DLPF cortex in visual change awareness. With this regard, results from neuroimaging studies seem to indicate that awareness of visual stimuli is characterized by activity in a cortical network comprising, beside the primary visual cortex, parietal and frontal regions [19,20]. In particular, studies using either a

binocular rivalry paradigm or bistable figures (e.g. the Necker cube) showed that activity in prefrontal cortex was time-locked to changes in conscious perception rather than with the stable viewing phase [21,22]. What all these observations suggest is the existence of a frontoparietal neural network which is particularly active concomitant with either exogenously- or endogenously-driven change in visual perception.

In a similar manner, the frontoparietal activity revealed by the fMRI study on change blindness [4] could be interpreted as being more related to awareness of change rather than reflecting specific involvement of attention and WM in change perception. Note that, indeed, activity in parietal and prefrontal cortex related to awareness resulted from the subtraction of activation on change detected trials *vs* change missed trials. These two types of trials were exactly the same except that in the former the change was correctly perceived, whereas in the latter it remained unnoticed. Importantly, the two types of trials were the same also with regard to the orienting of attention and WM. As a matter of fact, the only difference between these two conditions is that attention was correctly directed to the changing face when the change was perceived, whereas it was likely oriented to the wrong place (i.e., the non-changing face) when the change was missed. Likewise, WM encoded the correct information, or incorrect information, respectively. The important point we want to stress is that both orienting of attention and WM processes were active in the same manner regardless of whether the change was reported or missed, leaving open the possibility that parietal and right DLPF involvement might reflect genuine brain activity related to conscious change perception. Consequently, in the present study application of rTMS to the right DLPF cortex might have interrupted the neural circuit responsible for visual change awareness, in addition to possibly interfering with WM processes [23].

CONCLUSION

While future fMRI and TMS studies will help in distinguishing between these two alternatives, at the moment the present results are important as they demonstrate that when the anterior component of the frontoparietal network related to visual awareness is disrupted, change blindness is increased. In particular our study seems to indicate right rather than left DLPF cortex to be specifically and causally involved in visual change awareness, thus supporting recent views emphasizing the contribution of frontal regions to conscious perception [9].

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