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Exploring the visual world: The neural substrate of spatial orienting

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Inspecting the visual environment, humans typically direct their attention across space by means of voluntary saccadic eye movements. Neuroimaging studies in healthy subjects have identified the superior parietal cortex and intraparietal sulcus as important structures involved in visual search. However, in apparent contrast, spatial disturbance of free exploration typically is observed after damage of brain structures located far more ventrally. Lesion studies in such patients disclosed the inferior parietal lobule (IPL) and temporo-parietal junction (TPJ), the superior temporal gyrus (STG) and insula, as well as the inferior frontal gyrus (IFG) of the right hemisphere. Here we used functional magnetic resonance imaging to investigate the involvement of these areas in active visual exploration in the intact brain. We conducted a region of interest analysis comparing free visual exploration of a dense stimulus array with the execution of stepwise horizontal and vertical saccades. The comparison of BOLD responses revealed significant signal increases during exploration in TPJ, STG, and IFG. This result calls for a reappraisal of the previous thinking on the function of these areas in visual search processes. In agreement with lesion studies, the data suggest that these areas are part of the network involved in human spatial orienting and exploration. The IPL dorsally of TPJ seem to be of minor importance for free visual exploration as these areas appear to be equally involved in the execution of spatially predetermined saccades.

Keywords: Functional magnetic resonance imaging; Spatial representation; Spatial neglect; Visual exploration; Parietal cortex; Temporal cortex

Introduction

Efficient visual exploration is an indispensable skill for conscious perception of the environment. Scanning complex scenes and stimulus arrays for specific target stimuli (e.g. single objects which are relevant for ongoing activities) require prospective planning and execution of eye movements based on a stable representation of space. The outstanding importance of intact search behavior becomes evident in humans suffering from disorders of visual exploration after brain damage (Mort and Kennard, 2003). Among them, patients with spatial neglect after lesions of the right hemisphere demonstrate a remarkably strong and consistent bias of spontaneous activity towards the right, ipsilesional side of space. Recordings of visual and tactile exploration revealed the patients' center of active search to be shifted markedly towards the ipsilesional hemispace (Karnath, 2001). Interestingly, the manipulation of visual, vestibular, and proprioceptive information about the apparent orientation of the patient's body in space reduces this bias (Karnath et al., 1993; Pizzamiglio et al., 1990; Rubens, 1985). These findings suggested that the integration of multimodal sensory input into long-lasting egocentric representations of space relies crucially on those structures that are found damaged in stroke patients showing a horizontal bias of eye and head orientation (Karnath, 1997; Karnath and Dieterich, 2006).

Various lesion studies have identified a restricted number of cortical regions straddling the sylvian fissure in the right hemisphere that are associated with the occurrence of spatial neglect, namely the inferior parietal lobule (IPL) and temporo-parietal junction (TPJ) (Heilman et al., 1983; Mort et al., 2003a; Vallar and Perani, 1986), the superior temporal gyrus (STG) and adjacent insular cortex (Karnath et al., 2001, 2004), and – much less frequently – inferior frontal gyrus (IFG) (Husain and Kennard, 1996). Interestingly, several neuroimaging studies conducted with healthy subjects to investigate the neural substrates involved in processes of attentional orienting and visual search in the intact brain revealed activations that were essentially at odds with the anatomical findings in brain-damaged patients showing spatial neglect. Typically, they observed activations of the superior parietal lobule (SPL) and intraparietal sulcus (IPS) (Corbetta et al., 1995; Donner et al., 2000, 2002, 2003; Gitelman et al., 2002; Hopfinger et al., 2000; Leonards et al., 2000; Makino et al., 2004; Muller et al., 2003; Nobre et al., 2002; Olivers et al., 2004), i.e. activations that were far more dorsal to the typical lesion sites observed in patients with spatial neglect.

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Among the large body of investigations on visual search behavior (Corbetta et al., 1995; Donner et al., 2000, 2002, 2003; Gitelman et al., 2002; Hopfinger et al., 2000; Leonards et al., 2000; Makino et al., 2004; Muller et al., 2003; Nobre et al., 2002; Olivers et al., 2004), those studies stand out which investigated visual search of target stimuli among numerous similar distracters (Gitelman et al., 2002; Nobre et al., 2002), i.e. tasks that are very similar to the typical exploration tasks used in the clinical diagnosis of patients with neglect (Gauthier et al., 1989; Ota et al., 2001; Weintraub and Mesulam, 1985). Gitelman et al. (2002) have compared free exploratory eye movements across a digit array with the instructed execution of horizontal saccades directed to predetermined targets. With respect to the cortical surface, the analysis revealed increased activation of the posterior parietal cortex (PPC) surrounding the intraparietal sulcus (IPS) and extending to visual association areas, the anterior insula and frontal eye fields (FEF). No significant signal differences were found in those areas typically lesioned in patients with spatial neglect (Heilman et al., 1983; Husain and Kennard, 1996; Karnath et al., 2001, 2004; Mort et al., 2003a; Vallar and Perani, 1986). However, it must be pointed out that the authors focused their analysis on a certain number of regions (FEF, PPC, supplementary eye fields, anterior cingulate cortex, anterior insula, posterior temporal-occipital junction, basal ganglia, superior colliculi, and posterior thalami) by decreasing the statistical thresholds used for the detection of significant signal increases within these ROIs. This is a widely accepted procedure introduced by Worsley et al. (1996) allowing for a specific examination of the potential involvement of selected brain regions at the expense of valid and reliable findings in other areas (Turkheimer et al., 2004). Yet, most of those regions which have been reported as typical lesion sites in patients with spatial neglect (Heilman et al., 1983; Husain and Kennard, 1996; Karnath et al., 2001, 2004; Mort et al., 2003a; Vallar and Perani, 1986) were not included as ROIs and thus were 'disadvantaged' in this analysis. A PET study by Nobre et al. (2002) employed a very similar behavioral paradigm but analyzed the data without any a priory assumptions of critical ROIs. This work found significant differences between free exploration and exogenously determined saccades being essentially confined to the superior parietal and occipital cortex (Nobre et al., 2002). Again, these results were inconsistent with the findings from numerous lesion studies in patients with exploratory disorders (Heilman et al., 1983; Husain and Kennard, 1996; Karnath et al., 2001, 2004; Mort et al., 2003a; Vallar and Perani, 1986). Nobre et al. (2002) could not find evidence for a differential involvement of these latter areas in exploration tasks in comparison to the execution of predetermined saccades.

Up to now, a direct examination – i.e. a region of interest analysis (Turkheimer et al., 2004; Worsley et al., 1996) – of the contribution of those areas to active visual search which have been reported to be typically lesioned in patients showing a bias in spatial exploration, namely IPL, TPJ, STG, and IFG (Heilman et al., 1983; Husain and Kennard, 1996; Karnath et al., 2001, 2004; Mort et al., 2003a; Vallar and Perani, 1986), is still missing. Thus, we conducted an fMRI experiment which was supposed to closely resemble the clinical tasks known to be sensitive to the patients' behavioral bias. We investigated visual exploration of a letter array similar to the cancellation task of Weintraub and Mesulam (1985). Brain activity has been compared in a search volume consisting of the bilateral IPL, TPJ, STG, and IFG during the execution of free exploratory eye movements with the activity during the execution of stepwise horizontal and vertical saccades to predetermined target positions.

Materials and methods

Procedures

Thirteen right handed healthy subjects (8m/5f, mean age: 29 years, range: 20–47 years) participated in the experiment. All subjects gave their informed consent to participate in the study which has been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. All subjects underwent 3 measurements of 750 s duration each. Visual exploration (VE) and two control tasks were applied in a block design (Fig. 1). The visual exploration control task (VEC) included the spontaneous execution of stepwise horizontal and vertical saccades on the same visual background as presented in the experimental condition. During a second saccade control task (SC), subjects conducted stepwise saccades on a blank screen. This additional control task obviously lacks the prominent visual background of the other two conditions but was included for the purpose of comparison with previous experiments using similar control conditions (Gitelman et al., 2002). All tasks were applied in a block design with a baseline consisting of central fixation between each block. Each block and the baseline periods lasted 25 s (Fig. 1). During visual exploration (VE) a letter array of 24 × 35 cm^2 (~9° × 13°) was presented consisting of about 370 letters set in Arial font with a vertical size of 0.95 cm (~0.36°) per letter at a viewing distance of 150 cm. Parallel to the procedure used in brain-damaged patients with spatial neglect (Karnath et al., 1998), the subjects were instructed to search for the target letter 'A'. They had to indicate finding of target letters by pressing a button with their right hand. In fact in all but one block, the target was not part of the letter array. The block with the target – and thus with a button press – was not included in the final data analysis. It was used to hold up the motivation of the subjects.

In the visual exploration control (VEC) and the saccade control (SC) conditions, subjects were instructed to perform stepwise voluntary, self-triggered horizontal and vertical saccades, at a speed comparable to their behavior during exploration. The saccades should be performed on a cross of dots from the left to the right, up and down, alternating between direction and orientation. Each line consisted of 9 dots of a size of 0.5 cm (0.2°) at a distance of 2.75 cm (1°) from each other, resulting in a covered angle of about 8.3° horizontally and vertically for the whole cross (Fig. 1). Eye movements were recorded throughout the whole measurement with an infrared eye tracker (Cambridge Research Systems) digitized at a rate of 1000 Hz for offline analysis. We computed the number of saccades per condition using the first derivative of the horizontal eye movement data applying a threshold of 30 cm/s (~11.3°/s). Horizontal eye movements and oblique saccades up to ±45° were analyzed.

Data acquisition

The experiment was conducted using a 1.5 T whole body MRI scanner (Siemens Magnetom Vision, Erlangen, Germany) using a standard head coil system. T2*-weighted echo-planar images were acquired in axial orientation (TR = 5 s, TE = 40 ms, flip angle = 90°, FOV = 192 × 192 mm, 64 × 64 matrix, 44 slices, slice thickness 3 mm) for blood oxygen level-dependent (BOLD) based imaging. The planes were individually oriented in parallel to the AC–PC line and covered the whole cerebral volume including the