Dissociation of egocentric and allocentric coding of space in visual search after right middle cerebral artery stroke

Cathleen Grimsen\textsuperscript{a,},*, Helmut Hildebrandt\textsuperscript{b,c}, Manfred Fahle\textsuperscript{a,d}

\textsuperscript{a} Department of Human Neurobiology, University of Bremen, Argenstr. 3, D-28211 Bremen, Germany
\textsuperscript{b} Hospital of Bremen-Ost, Neurology, Bremen, Germany
\textsuperscript{c} Institute of Psychology, University of Oldenburg, Germany
\textsuperscript{d} The Henry Welcome Laboratories for Vision Sciences, City University London, UK

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Abstract

Spatial representations rely on different frames of reference. Patients with unilateral neglect may behave as suffering from either egocentric or allocentric deficiency. The neural substrates representing these reference frames are still under discussion. Here we used a visual search paradigm to distinguish between egocentric and allocentric deficits in patients with right hemisphere cortical lesions. An attention demanding search task served to divide patients according to egocentric versus allocentric deficits. The results indicate that egocentric impairment was associated with damage in premotor cortex involving the frontal eye fields. Allocentric impairment on the other hand was linked to lesions in more ventral regions near the parahippocampal gyrus (PHG).

Keywords: Frame of reference; Neglect; Stroke; Parahippocampal region; Premotor cortex

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* Corresponding author. Tel.: +49 421 218 9523; fax: +49 421 218 9525.
E-mail address: cgrimsen@uni-bremen.de (C. Grimsen).

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1. Introduction

Patient studies have contributed many important insight on visual information processing and mechanisms underlying consciousness and awareness as impressively shown by Weiskrantz’s research on blindsight (for an overview see Weiskrantz, 2004). Another common syndrome affecting conscious perception is neglect, since neglect patients behave as if (usually the left) part of the environment were nonexistent. These patients may accomplish personal hygiene only on one body-side, eat only from half of their plate or do not turn to their left side. More specifically unilateral neglect is defined as “the failure (or slowness) to report, respond, or orient to novel or meaningful stimuli presented to the side opposite a brain lesion, when this failure cannot be attributed to either sensory or motor defect” (p. 296, Heilman, Watson, & Valenstein, 2003). Nelect might be caused by cerebral lesions involving temporal (Karnath, Ferber, & Himmelbach, 2001), parietal (Mort et al., 2003; Vallar & Perani, 1986), frontal (Heilman & Valenstein, 1972; Husain, Mattingley, Rorden, Kennard, & Driver, 2000) or subcortical areas (Karnath, Himmelbach, & Rorden, 2002), particularly of the right hemisphere.

The astonishing changes of behaviour in neglect brought forth a large number of investigations on the underlying mechanisms and on the nature of visuospatial attention in healthy subjects. One fertile proposal of visuospatial information processing is that it may rely on at least two different frames of reference: egocentric and allocentric (for a review see Landis, 2000). Egocentric spatial representations of an object depend on the object’s position relative to the viewer’s body, such as trunk, head or eyes. In this frame of reference the terms left and right refer to the observer, therefore it is viewer-centered. Allocentric spatial representation on the other hand is a concept that includes representations of space both in object-centered and in stimulus-centered coordinates. Strictly speaking an object-centered representation requires an intrinsic object orientation (Marr, 1982). In this case the terms left, right, top and bottom refer to the object itself and are independent of the observer. Typical examples for objects with well-defined intrinsic directions are words. The easiest way to investigate the distinction between viewer-centered and object-centered forms of neglect is reading. Patients may miss whole words on the contralesional side of space (viewer-centered) or they may miss the contralesional letters of a single word independent of where the word is presented and even if it is presented reversed or mirror-inverted (object-centered, Caramazza & Hillis, 1990; Hildebrandt & Ebke, 2003; Hillis, 2006). However, it is difficult to define strictly object-centered coordinates since most objects are not intrinsically orientated such as words are. Therefore a second concept of allocentric representation is the so-called stimulus-centered frame of reference, which is defined with respect to the observer’s viewing position. Stimulus-centered neglect presupposes that patients omit features appearing on the contralesional side of objects even though they are presented on the ipsilesional side of the body (Hillis, 2006; Walker, 1995). It is often difficult to distinguish stimulus-centred from egocentric neglect because in many tasks egocentric and stimulus-centred coordinates are overlapping, for example when the egocentric reference frame is retinotopic and the fixation of stimuli is central. Therefore there is still a controversy about the stimulus-centred frame of reference. Some authors suggest, that purely egocentric representation of space might account for phenomena that seem to be stimulus-centered in origin (Buxbaum, Coslett, Montgomery, & Farah, 1996; Driver & Pouget, 2000; Niemeier & Karnath, 2002).

Most clinical investigations focused on egocentric (that is viewer-centered) neglect, providing abundant evidence that information is neglected depending on its position relative to body coordinates, e.g. to the retina (Hillis, Rapp, Benzing, & Caramazza, 1998) or trunk (Bescin, Cubelli, Della Sala, & Spinazzola, 1997; Chokron, 2003; Farah, Brunn, Wong, Wallace, & Carpenter, 1990; Farne, Ponti, & Ládavas, 1998; Karnath, 1997; Mennemeier, Chatterjee, & Heilman, 1994). In the assessment of egocentric visuospatial behaviour after brain damage, visual search paradigms are widely used – particularly since visual search may involve processes with low (parallel feature search) or else high demands on visual attention (Chelazzi, 1999; serial conjunction search; for review see Wolfe & Horowitz, 2004). A recent study of a large patient group focussed on response slopes in parallel and serial search displays with increasing numbers of distractors (Behrmann, Ebert, & Black, 2004). The authors found generally impaired search in brain damaged patients for contralesional targets in both parallel feature and serial conjunction search compared to healthy controls. This impairment was stronger in patients with additional neglect and/or hemianopia.

In the majority of cases associations between egocentric and allocentric frames of reference have been reported. Patients may show viewer-centered or else stimulus-centered neglect depending on task instruction (Baylis, Baylis, & Gore, 2004), and both forms of neglect can occur in the same patient (Laeng, et al., 2001; Grimsen et al., 2008).
Neglect patients moreover show an egocentric gradient for target detection probability during visual feature search and defective stimulus-centered mechanisms during visual conjunction search (Pavlovskaya, Ring, Groszwater, & Hochstein, 2002). Egocentric as well as allocentric mechanisms obviously influence neglect, but little is known about the neuronal structures underlying the different frames of reference. Most lesion studies did not discriminate between viewer-centered and stimulus-centered neglect. One case study compared performance of two neglect patients during a cancellation task that allowed to distinguish between viewer- and stimulus-centered neglect. One case study compared performance of two neglect patients during a cancellation task that allowed to distinguish between viewer- and stimulus-centered neglect. One case study compared performance of two neglect patients during a cancellation task that allowed to distinguish between viewer- and stimulus-centered neglect. One case study compared performance of two neglect patients during a cancellation task that allowed to distinguish between viewer- and stimulus-centered neglect. One case study compared performance of two neglect patients during a cancellation task that allowed to distinguish between viewer- and stimulus-centered neglect.

In an earlier study of visual search behaviour of patients with middle cerebral artery stroke in the left hemisphere, lesions of three patients with an egocentric impairment overlapped in the precentral frontal area, involving the frontal eye fields (Hildebrandt, Schutze, Ebbe, Brunner-Beeg, & Eling, 2005). For patients, impaired in terms of stimulus-centered disturbance, no neuronal substrate could be defined. Hildebrandt and colleagues concluded that frontal eye fields and premotor cortex are involved in visual search and left hemisphere lesions of these areas may lead to severe impairments in shifting visuospatial attention.

The question which neuroanatomical regions are responsible for egocentric and allocentric coding of space is still controversial and comparable data from brain-damaged patients are lacking. On this background the aim of the present study was to analyse cortical regions involved in egocentric and allocentric neglect respectively. We investigated a group of patients with right hemisphere (RH) stroke using visual search paradigms and correlated their behavioural data with the site of lesion. To evaluate different frames of reference we systematically varied both the allocentric features (centered on target-item) and the egocentric positions (centered on search-array) of targets in both a parallel and a serial visual search task (see methods, Fig. 1).

If the array-centered position of targets is crucial, one would expect a spatial gradient for target detection independent of item-centered features to indicate egocentric neglect. For allocentric neglect on the other hand, the item-centered feature position is crucial, and we should find a pronounced decrease of detection independent of absolute position within the search array. If different brain lesions produce array-centered or else item-centered neglect, we should be able to dissociate these types of patients with our search paradigms. Comparison of the topology of patient’s brain lesions should inform us about the neuronal structures responsible for these different kinds of representations.

2. Materials and methods

2.1. Subjects

Twenty-one right-handed patients with right hemisphere unilateral first ever stroke of the middle cerebral artery were studied (RBD = right brain damage, see Table 1 for demographical and clinical data). Patients with bilateral lesions, second stroke or additional psychiatric diagnosis were excluded. Twelve right-handed, age-matched subjects without neurological or psychiatric disorders served as control group. All participants gave informed consent for inclusion in the study, which was approved by the local ethics committee of the hospital.

2.2. Clinical Investigation

All patients underwent a series of neuropsychological tests, including line bisection and star cancellation from the Behavioural Inattention Test (BIT) for neglect examination (Wilson, Cockburn, & Halligan, 1987), the neglect test from the Testbattery of Attentional Performance (TAP, Zimmermann & Finn, 1992) for assessment of visual field deficits and visual extinction (Hildebrandt, 2006) and the block-design from the WAIS-R to evaluate visuo-constructive functions. All patients were tested for eye movements (tracking and saccades) and extinction (visual, tactile and auditory) through clinical confrontation.

For line bisection, patients marked subjective midpoints of three lines (21 cm long). Deviations from the objective middle to the right were counted as positive.
2.3. Search paradigms

Following classical search paradigms (Treisman & Gelade, 1980) we used target features that induce either parallel or serial visual search. In the first condition (parallel search) the target differed from the standard stimulus in one feature consisting of a thick vertical bar on the left or right side of one item (see Fig. 1B). In the second condition (serial search) the target was categorized to either left or right target side after the midpoint of the screen (fixation was controlled by the examiner). The stimulus display extended over approximately 32° horizontally and 24° vertically. Omissions (maximum 22 in each hemifield) and response times for both hemifields were measured. ‘Block design’ is a sub-test of the W AIS-R, where subjects have to put together nine cubes to match a visual pattern, for which reference values are available. Age-corrected scores below seven are defined as visuo-constructive impairment.

2.4. Procedure

Subjects were seated 60 cm in front of a 17 in. monitor, where the search array (18.2° wide and 2.3° high) appeared bright on a dark background. Individual items were approximately 2.3° wide and 0.9° high. During the whole experiment one example with a right- and one example with a left-sided target feature were shown at the top of the screen. Subjects had to indicate whether or not the search array contained a target and entered their responses by pressing the appropriate button on a standard keyboard. Each condition was free-viewing and started with eight practice trials to ensure that subjects understood the task and knew which kind of stimuli were presented. Experimental trials were not time limited, but subjects were instructed to answer as accurate and fast as possible. The first condition was always parallel search. Correct responses and response times were recorded separately for item-centered (left vs. right) and array-centered (column 1 to 5) target position. Additionally, response times for target absent trials were measured.

2.5. Lesion reconstruction

We used T1 weighted MRI and additionally diffusion weighted MRI scans (Roberts & Rowley, 2003) to trace the lesions. For one patient only CT scans were available. Mapping of lesion was carried out by inspecting digitized images (Roberts & Rowley, 2003) to trace the lesions. For one patient only CT scans were available. Mapping of lesion was carried out by inspecting digitized images 

Table 1

Demographical and clinical data for patient groups

<table>
<thead>
<tr>
<th>Subject</th>
<th>Age (in years)</th>
<th>Gender (M, male; F, female)</th>
<th>Time since onset (in days)</th>
<th>Star cancellation (omissions left/right)</th>
<th>Line bisection (deviation (mm))</th>
<th>WAIS (age-corrected)</th>
<th>Neglect-test TAP (omissions left/right)</th>
<th>Response-time in ms left/right</th>
</tr>
</thead>
<tbody>
<tr>
<td>H.R.</td>
<td>46</td>
<td>F</td>
<td>44</td>
<td>21/5</td>
<td>15.3</td>
<td>1</td>
<td>22/7</td>
<td>−4/94</td>
</tr>
<tr>
<td>EGO</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pat 01</td>
<td>65</td>
<td>M</td>
<td>6</td>
<td>2/2</td>
<td>−6.7</td>
<td>7</td>
<td>5/4</td>
<td>976/611</td>
</tr>
<tr>
<td>Pat 02</td>
<td>45</td>
<td>F</td>
<td>5</td>
<td>2/5</td>
<td>−1.3</td>
<td>2</td>
<td>0/0</td>
<td>563/481</td>
</tr>
<tr>
<td>Pat 03</td>
<td>34</td>
<td>F</td>
<td>71</td>
<td>3/2</td>
<td>8.0</td>
<td>–</td>
<td>5/3</td>
<td>1355/1898</td>
</tr>
<tr>
<td>Pat 04</td>
<td>59</td>
<td>M</td>
<td>3</td>
<td>6/2</td>
<td>−0.7</td>
<td>3</td>
<td>1/0</td>
<td>437/327</td>
</tr>
<tr>
<td>ALLO</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pat 01</td>
<td>75</td>
<td>M</td>
<td>5</td>
<td>3/1</td>
<td>−1.7</td>
<td>3</td>
<td>3/0</td>
<td>1047/537</td>
</tr>
<tr>
<td>Pat 02</td>
<td>63</td>
<td>M</td>
<td>6.7 years</td>
<td>3/4</td>
<td>42.0</td>
<td>8</td>
<td>17/0</td>
<td>1363/424</td>
</tr>
<tr>
<td>Pat 03</td>
<td>68</td>
<td>M</td>
<td>3</td>
<td>6/5</td>
<td>11.3</td>
<td>7</td>
<td>7/11</td>
<td>1160/2022</td>
</tr>
<tr>
<td>Pat 04</td>
<td>29</td>
<td>M</td>
<td>64</td>
<td>2/1</td>
<td>36.7</td>
<td>6</td>
<td>2/0</td>
<td>1511/446</td>
</tr>
<tr>
<td>RBD-C</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pat01</td>
<td>39</td>
<td>M</td>
<td>3</td>
<td>0/0</td>
<td>−1.3</td>
<td>16</td>
<td>0/0</td>
<td>326/331</td>
</tr>
<tr>
<td>Pat02</td>
<td>61</td>
<td>F</td>
<td>2</td>
<td>0/0</td>
<td>−2.0</td>
<td>5</td>
<td>1/0</td>
<td>645/670</td>
</tr>
<tr>
<td>Pat03</td>
<td>71</td>
<td>M</td>
<td>5</td>
<td>0/0</td>
<td>−5.0</td>
<td>10</td>
<td>2/3</td>
<td>549/494</td>
</tr>
<tr>
<td>Pat04</td>
<td>18</td>
<td>F</td>
<td>7</td>
<td>0/0</td>
<td>−1.0</td>
<td>8</td>
<td>0/0</td>
<td>472/390</td>
</tr>
<tr>
<td>Pat05</td>
<td>51</td>
<td>M</td>
<td>165</td>
<td>0/0</td>
<td>−0.3</td>
<td>9</td>
<td>0/0</td>
<td>477/344</td>
</tr>
<tr>
<td>Pat06</td>
<td>69</td>
<td>M</td>
<td>4</td>
<td>1/2</td>
<td>−4.7</td>
<td>7</td>
<td>3/3</td>
<td>682/480</td>
</tr>
<tr>
<td>Pat07</td>
<td>47</td>
<td>M</td>
<td>2</td>
<td>3/0</td>
<td>2.7</td>
<td>4</td>
<td>0/0</td>
<td>366/296</td>
</tr>
<tr>
<td>Pat08</td>
<td>43</td>
<td>M</td>
<td>11</td>
<td>0/1</td>
<td>2.0</td>
<td>2</td>
<td>1/0</td>
<td>930/751</td>
</tr>
<tr>
<td>Pat09</td>
<td>66</td>
<td>F</td>
<td>2</td>
<td>13/4</td>
<td>0</td>
<td>4</td>
<td>11/3</td>
<td>2102/1236</td>
</tr>
<tr>
<td>Pat10</td>
<td>39</td>
<td>F</td>
<td>17</td>
<td>1/0</td>
<td>10.7</td>
<td>5</td>
<td>1/0</td>
<td>932/699</td>
</tr>
<tr>
<td>Pat11</td>
<td>72</td>
<td>F</td>
<td>3</td>
<td>0/0</td>
<td>3.3</td>
<td>11</td>
<td>8/2</td>
<td>772/664</td>
</tr>
<tr>
<td>Pat12</td>
<td>70</td>
<td>F</td>
<td>24</td>
<td>18/5</td>
<td>14.7</td>
<td>1</td>
<td>19/4</td>
<td>2390/1728</td>
</tr>
</tbody>
</table>

Patients with neglect are labelled with N+ and those without neglect with N−. Patients were considered to have neglect if they omitted four or more elements during star cancellation on the left compared to the right side; or if they deviated by more than five mm to the right in line bisection, or if they omitted five or more elements in the neglect-test of the TAP on the left side compared to the right side.

values, deviations to the left as negatives. Deviations from the midpoint of more than 0.5 cm are considered as impaired performance. During star cancellation patients had to cross out a number of small stars among a variety of distractors, like big stars, letters and words. Each side of the sheet contained 27 targets; a difference of more than four omissions between left and right side was defined as cut-off score to determine impairment. In the neglect test of the TAP distractors are presented scattered over the whole screen and patients have to detect one flickering target, while fixating the midpoint of the screen (fixation was controlled by the examiner). The stimulus display extended over approximately 32° horizontally and 24° vertically. Omissions (maximum 22 in each hemifield) and response times for both hemifields were measured. ‘Block design’ is a sub-test of the W AIS-R, where subjects have to put together nine cubes to match a visual pattern, for which reference values are available. Age-corrected scores below seven are defined as visuo-constructive impairment.

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pole and posteriorly most of the inferior parts of the occipital lobe posterior to the cerebellum. The last slice was located at the most rostral part of the brain. The lesioned areas of each patient can be superimposed on the standard template using the Region of Interest (ROI) function of MRICro. The resulting images are color coded, where each color represents the absolute number of patients with a lesion in this area. Subsequent analysis of lesions (ROI subtraction method) allows to compare lesioned areas associated with specific and non-specific performance in visual search. We used absolute numbers for comparisons, because sample sizes differed between patient groups. The subtraction procedure used follows the description by Karnath et al. (2002). This method creates an image where the superimposed lesions of a defined group are reduced by the superimposed lesions of another group. Basically, for each particular area (voxel) each patient of the first (minuend) group who has a lesion in this particular area is coded as +1. Each patient of the second (subtrahend) group with a lesion in this area is coded as −1. The resulting colours reflect the difference of scores in this area. The hot colors in Fig. 4E are therefore to be interpreted as follows: Yellow indicates that these areas (voxels) are damaged in all of the five patients with egocentric impairment (including H.R.), but not in any of the other 16 patients. Orange colour may result either from only four of the five patients and none of the other 16 patients or from all five patients but also one from the other 16. Data are best interpreted in comparison with the traditional overlap method.

### 2.6. Group classification of patients

Impairment of array- or item-centered visuo-spatial processing in patients was identified on the basis of their results in target present trials during serial search, because this type of search is more sensitive, being more attention demanding. First, we determined the difference between correct responses to the leftmost versus the rightmost column. Patients within the worst quartile of this difference were treated as impaired in egocentric coding of space (RBD-EGO). To estimate item-centered impairment, we calculated the mean difference between correct responses to target features on the right versus on the left side. Patients within the worst quartile were considered as impaired in allocentric coding of space (RBD-ALLO). Because item- and array-centred positions are within subject factors in our paradigm, it was possible that a patient could be assigned to both groups. In this case this patient was excluded from statistical analysis. Patients that did not fall in any of these groups were treated as right brain damage control group (RBD-controls).

Demographical and clinical data for all patient groups are summarized in Table 1. In the RBD-EGO group two of the patients suffered from neglect, in the RBD-ALLO group three patients, and in the RBD-control group four patients, as defined through classical neglect tests.

### 2.7. Statistical analysis

Analyses of variance for repeated measurements were carried out for all groups with two factors [item (left vs. right) and position within the array (columns 1 to 5)] for both hits and reaction times in each task.

### 3. Results

Statistics and results for all groups are summarized in Table 2 and Fig. 2 for parallel search and in Table 3 and Fig. 3 for serial search. Because we classified patients depending on either item- or array-centred behaviour there must be a significant effect for the accordant factor in the statistical analysis. However the question we statistically analysed was whether one or both groups show an interaction between item- and array-centred search performance. Furthermore, we wanted to explore if the specific impairment of the groups is reflected by similar results in reaction time analyses and in parallel search. If the impairment would be present in parallel search the cognitive processes involved should be more basal than visuo-spatial selective attention.

### 3.1. Parallel and serial search tasks in healthy subjects

To make sure that the two tasks induce parallel and serial visual search respectively, we calculated response time quotients of correct responses to target present versus target absent trials in healthy subjects. In parallel search the mean quotient was 0.73 (±0.1; range 0.59–0.84) and in serial search it was 0.57 (±0.2; range 0.32–0.80). This is to say that reaction times for target absent trials were almost doubled compared to target present trials in serial search, while the difference was much smaller in parallel search. This difference between search types was significant in controls ($T = 3.3, p < 0.01$). We concluded that our paradigm complied with requirements for visual search types, because models predict a higher ratio for parallel than for serial search strategies (Treisman & Gelade, 1980; Treisman & Sato, 1990). Analysis of variance for repeated measurement with factors item (left vs. right) and array (columns 1 to 5) for hits showed no significant main or interaction effects neither in the parallel nor in the serial task, but ceiling effects may have impeded any influence of feature and target positions due to task simplicity for healthy subjects. Reaction time analysis showed significant main effects for both search types (see Tables 2 and 3 and Fig. 2E and 3E).

### 3.2. Egocentric impairment of visuo-spatial processing after right hemisphere brain damage

Four out of 21 patients omitted primarily targets in the first column of the array while rarely in the last column (independent of item-centered feature). For these patients detection probability increased from the leftmost (3%) to the rightmost (81%) column indicating impaired egocentric visuo-spatial processing (RBD-EGO group). In this group array-centered position revealed a significant main effect for hits and reaction times in serial search while item-centered position did not (Table 3, Fig. 3B). In parallel visual search no significant differences were observed, except for a significant main effect for array on reaction times (Table 2, Fig. 2B). The amount of overlap of lesions in these patients is shown in Fig. 4B.

### 3.3. Allocentric impairment of visuo-spatial processing after right hemisphere brain damage

Another group of 4 out of 21 patients missed primarily those targets which were defined by item-centered target features on the left side of the stimulus (independent of array-centered position). These patients show clear signs of impaired allocentric visuo-spatial processing. On average they made 35% correct responses to left-defined targets and to 91% of right-defined targets. We will refer to this group as RBD-ALLO group. Analysis of variance for repeated measurements confirmed a significant main effect of item and no significant main effect of array in serial search. Reaction time analysis showed a significant effect of array-centered target position (Table 3, Fig. 3C). Corresponding results of this group in parallel search revealed no significant differences (Table 2, Fig. 2C). Lesion overlap of these four patients is shown in Fig. 4C.
Table 2
Statistics of parallel search tasks for all groups

<table>
<thead>
<tr>
<th>Group</th>
<th>Factor</th>
<th>Hits</th>
<th>Reaction times</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Item</td>
<td>Array</td>
</tr>
<tr>
<td>RBD-EGO</td>
<td>p&lt;</td>
<td>$F(1,3) = 1.0$</td>
<td>$F(4,12) = 2.5$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>n.s.</td>
<td>n.s.</td>
</tr>
<tr>
<td>RBD-ALLO</td>
<td>p&lt;</td>
<td>$F(1,3) = 3.0$</td>
<td>$F(4,12) = 1.9$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>n.s.</td>
<td>n.s.</td>
</tr>
<tr>
<td>RBD-CON</td>
<td>p&lt;</td>
<td>$F(1,11) = 2.2$</td>
<td>$F(4,44) = 1.7$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>n.s.</td>
<td>n.s.</td>
</tr>
<tr>
<td>Controls</td>
<td>p&lt;</td>
<td>$F(1,11) = 0.1$</td>
<td>$F(4,44) = 2.3$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>n.s.</td>
<td>n.s.</td>
</tr>
</tbody>
</table>

$F$-values, degrees of freedom (Greenhouse–Geisser correction was applied when necessary) and level of significance are indicated.

3.4. Association of egocentric and allocentric impairment after RBD

One patient (H.R.) falls within the worst quartile of both item- and array-centered hits in serial search. Performance results for patient H.R. are shown in Fig. 2A for parallel search and in Fig. 3A for serial search. The lesion of H.R. is shown in Fig. 4A.

3.5. Visual search after right hemisphere brain damage

The 12 remaining patients did not show a specific spatial performance pattern during serial visual search (Table 3) and served as RBD-control group. Performance in this group was generally inferior to that of healthy controls as shown by an analysis of variance for repeated measurements with the additional between-subject factor group (RBD-control vs. healthy-controls). This was true for hits [F(1,22) = 6.6; p < 0.05] and reaction times [F(1,22) = 13.7; p < 0.01] in serial search as well as for reaction times in parallel search [F(1,22) = 6.7; p < 0.05]. On the other hand regarding hits these patients performed as well as healthy controls in parallel visual search [F(1,22) = 0.05; p > 0.05; see Fig. 2D and Fig. 3D].

4. Lesion location for different impairments in visuo-spatial processing

Subtracting the lesions of the RBD-controls and the patients with allocentric neglect from the overlap of both four patients with egocentric neglect and H.R. yields critical areas in the precentral gyrus (Brodmann area 4) and in the superior frontal gyrus (BA 6, see Fig. 4E). Subtracting lesions of RBD-controls and patients with egocentric neglect from the overlap of four patients with allocentric neglect and H.R. revealed a region in the ventromedial temporal lobe (parahippocampal cortex, see Fig. 4F).

4.1. Lesion reconstruction for patients with and without neglect in standard procedures

For a better comparison of our results with the classical areas found in neglect patients, we post hoc subtracted the lesions of

Table 3
Statistics of serial search task for all groups

<table>
<thead>
<tr>
<th>Group</th>
<th>Factor</th>
<th>Hits</th>
<th>Reaction times</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Item</td>
<td>Array</td>
</tr>
<tr>
<td>RBD-EGO</td>
<td>p&lt;</td>
<td>$F(1,3) = 2.5$</td>
<td>$F(4,12) = 9.9$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>n.s.</td>
<td>n.s.</td>
</tr>
<tr>
<td>RBD-ALLO</td>
<td>p&lt;</td>
<td>$F(1,3) = 173.5$</td>
<td>$F(4,12) = 2.4$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.001*</td>
<td>n.s.</td>
</tr>
<tr>
<td>RBD-CON</td>
<td>p&lt;</td>
<td>$F(1,11) = 1.5$</td>
<td>$F(4,44) = 0.7$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>n.s.</td>
<td>n.s.</td>
</tr>
<tr>
<td>Controls</td>
<td>p&lt;</td>
<td>$F(1,11) = 3.7$</td>
<td>$F(4,44) = 1.4$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>n.s.</td>
<td>n.s.</td>
</tr>
</tbody>
</table>

$F$-values, degrees of freedom (Greenhouse-Geisser correction was applied when necessary) and level of significance are indicated.

* These effects are explained by procedure of group classification.

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5. Discussion

The aim of the present study was to analyse cortical regions involved in egocentric versus allocentric visuo-spatial processing after right hemisphere brain damage. We developed a search paradigm, allowing to distinguish between impairment related to two different reference frames. In the following the behavioural data are discussed first referring to the subgroups of patients and thereafter regarding the neuroanatomical results.

The behavioural results indicate that our paradigm differentiates between ego- and allocentric impairment, since in a subgroup of patients variation of position parameters led to the expected behaviour during serial search. Four patients showed an egocentric deficit while four others suffered from an allocentric deficit. This dissociation suggests that at least two distinct

patients without neglect from patients with neglect. Although there was no exclusively damaged area in neglect patients the highest overlap was found in regions described in previous studies, such as white matter and putamen (Karnath et al., 2002), temporal structures (Karnath et al., 2001) and both right angular and supramarginal gyri (Mort et al., 2003; Fig. 5C).
frames of reference are involved in visuo-spatial processing during visual search. Egocentric impairment may be attributed to a deficit of shifting attention to the contralesional side of space with respect to the observer, whereas allocentric impairment mirrors deficient representations of individual objects.

5.1. Shifting attention to the contralesional side of egocentric space

Patients with egocentric impairment increased their number of correct responses and decreased their reaction times from left to right in serial search irrespective of the item-centered feature. This result is consistent with previous studies in neglect patients which have shown detection to improve in a graded way from left to right in cancellation tasks (Chatterjee, Thompson, & Ricci, 1999), visual scanning tasks (Butler, Eskes, & Vandorpe, 2004; Karnath, Niemeier, & Dichgans, 1998), and in visual search when studied through eye movements (Behrmann, Watt, Black, & Barton, 1997).

None of these patients suffered from hemianopia, only one deviated slightly ipsilesionally in line bisection, and another one made four more omissions on the left side in the cancellation

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Fig. 3. Results for serial search. Abscissa shows array-centered target position. White bars indicate left item-centered targets and grey bars right item-centered targets, error bars indicate standard errors (A) Patient H.R., (B) RBD-EGO, (C) RBD-ALLO, (D) RBD-controls and (E) healthy controls.
task (Table 1). On the basis of standard clinical tests only two of these patients would have been classified as suffering from neglect. Obviously, these patients should not miss targets due to a visual field loss or due to incomplete sensory perception of the environment.

Overt shifts of attention within egocentric space are coupled with (saccadic) eye movements. Not surprisingly two of the patients experienced problems with executing saccades during clinical confrontation, while the other two had no such problems. This result impedes an explanation of the egocentric impairment based purely on defective execution of eye movements. Rather these patients must have difficulties to shift attention to their egocentric left side prior to the eye movement. Actually, the impairment in shifting attention to the left was also found for
parallel search – these patients were slower in target detection on the left and missed more items at the outmost left positions.

5.2. Detailed representations of individual objects

Patients with allocentric impairment missed more left-sided features in serial search independently of absolute target position. These patients were more impaired in clinical tests than the other patient groups (Table 1). Two patients suffered from left-sided visual field loss, three showed a strong ipsilesional deviation of the subjective midline during line bisection, and all needed more than 1 s to respond to targets on the left side during the neglect test (TAP). Execution of saccades was restricted in three of the patients. One possibility to account for the specific behaviour of this group is visual field loss, but only one patient had nearly complete hemianopia, and each target stimulus extended only 1.2° in both directions from the center and thus should be entirely analysed due to macula sparing after brain damage (Kötler, 1988). More importantly, these patients explored the egocentric space in terms of array-centered target position without difficulty. Hence this allocentric impairment is probably caused by incomplete stimulus representation or else a deficit in attentional allocation on an object-based level. But these patients had no problems with item-centered features in parallel search. Two possible explanations come to mind. First, their deficit in serial search involves attentional mechanisms, so that as a result of the (pre-attentive) pop-out character of parallel search no deficit can be observed (since focusing and attentional inspection of stimuli is not necessary). Secondly, the pop-out character of the parallel search task used in this study brought forth that the whole array is perceived as a single object. This interpretation would cause a specific low hit rate in the left columns during parallel search. Such a tendency might be present in Fig. 2C, but not in the statistical analysis (Table 2).

Reaction time analysis of serial search shows that RBD-ALLO patients perform significantly slower for targets presented on left side of the array despite patients being able to find targets on these positions of the search array. This finding might suggests that there is also an egocentric component in these patients, because visual shifts to the egocentric left are obviously time-demanding in this group. Hits and response times seem to account for different processes. In healthy controls there is also an array-centred effect with increasing response times from left to right array reflecting the scanning direction. The array-centred effect for response time of the RBD-ALLO group may therefore reflect a modified scanning direction in these patients from right to left.

5.3. Neuroanatomical correlates of reference frames

Locations of lesions in patients with egocentric impairment differ clearly from those in patients with allocentric impairment (Fig. 4E and F). Egocentric deficits are associated with damage to frontal regions especially premotor cortex (BA 6), whereas allocentric deficits seem to be linked to ventromedial temporal cortical structures.

Our result is similar to the study of Hillis et al. (2005), who have shown that egocentric neglect is associated with hypoperfusion of the right angular and inferior frontal gyrus while allocentric neglect correlates with hypoperfusion of the superior temporal gyrus. Here we show that also after persistent structural damage to cerebral cortex different forms of neglect are associated with different lesion sites. In our sample the premotor cortex was involved in all patients with egocentric deficit. This corresponds to the study of Hillis and colleagues, which
also found hypoperfusion in frontal areas. Nevertheless, there are some differences regarding the classification of egocentric neglect. The task used by Hillis and colleagues requires a motor response to the contralesional space. So they could not distinguish between decreased limb movements and reduced attention to the contralesional side. Our task did not require contralesional movements — therefore egocentric neglect in our study depends rather on attentional mechanisms. This supports the findings of Husain et al. (2000) whose patients with frontal damage and neglect showed no directional motor biases whereas patients with parietal brain damage did.

The areas of overlap between patients do not unambiguously allow a definitive allocation of function but they show a clear dissociation between both types of visuo-spatial mechanisms. The assumption of a (coarse) division into a dorsal and a ventral path fits well with this dissociation (Goodale & Milner, 1992; Mishkin, Ungerleider, & Macko, 1983) and the associated behavior. Disturbances of ventral (temporal) information processing — concerning detailed object representations — lead to allocentric impairment. Disorders of the fronto-(parietal) processing stream — dealing with spatial information — cause egocentric deficits. This finding is confirmed by earlier studies, which shed light on the dissociation between dorsal and ventral processing by emphasising the functional part of the ventral stream in allocentric processing (Carey, Dijkerman, Murphy, Goodale, & Milner, 2006; Murphy, Carey, & Goodale, 1998; Schenk, 2006).

5.4. A fronto-parietal network for shifting attention in egocentric space

The frontal lesions of the RBD-EGO group correspond to areas activated in imaging studies by spatial shifts of attention in healthy subjects. In these functional imaging studies both covert and overt shifts of attention to peripheral stimuli activate an overlapping network of frontal, parietal and temporal regions (Corbetta & Shulman, 1998). Lesions of the frontal cortex may therefore disrupt this fronto-parietal network, which is involved in attentional mechanisms. In frontal regions the right precentral sulcus and the superior frontal sulcus are involved in spatial shifts of attention. Frontal eye fields are activated both during saccades and in covert shifts of attention without eye movements (Donner et al., 2000; Muller et al., 2003; O’Shea, Muggleton, Cowey, & Walsh, 2006).

It is certainly plausible that the frontal areas influence spatial behaviour, but so far only few patients were described who prove this assumption (Husain & Kennard, 1996). Analysis of eye movement patterns in neglect patients shows that these patients make more and longer fixations on the ipsilesional side of space and explore the contralesional side to a lesser extent (Behrmann et al., 1997; Walker, 1995). These findings support the assumption that spatial attention in these patients is distributed following a gradient from left to right and cannot be explained by an oculomotor deficit alone. But not all authors follow this hypothesis. Karnath et al. (1998), finding similar results in exploratory behaviour of patients, assume that the egocentric frame of reference is shifted toward the ipsilesional side of space. Zihl and Hebel (1997) concluded, based on oculomotor scanning patterns of brain damaged patients, that frontal regions are involved in scan path planning and parietal regions in visuo-spatial guidance of the scan path, both being parts of a distributed neural network for visually-guided scanning behaviour. Since close co-operation between these cortical areas is necessary, brain damage must lead to impaired spatial exploration.

Lesion overlap of four patients (and H.R.) with difficulty to execute spatial shifts of attention support the notion of frontal involvement in egocentric attentional shifts. This is consistent with our results for patients with left hemispheric damage, where the overlap of lesions for patients with egocentric deficit lies in the anterior precentral gyrus (Hildebrandt et al., 2005).

5.5. Processing of detailed stimulus features in the temporal lobe

Lesions of the RBD-ALLO group correspond to areas which are described in patients with neglect after posterior cerebral artery stroke (Mort et al., 2003). These authors could not ascertain a characteristic relation between parahippocampal damage and neglect and concluded that neglect after parahippocampal damage may be explained by remote effects on parietal cortex (diaschisis) or alternatively through disruption of white matter tracts.

The question after the involvement of ventromedial temporal lobe in visual perception became more prominent with the discovery of the parahippocampal place area (PPA), which is thought to encode the geometry of the local environment (Epstein & Kanwisher, 1998). Lepsien and Nobre (2006) showed increasing parahippocampal activity when attention was shifted to a mental scene representation, indicating a close relationship with working memory processes. Moreover, in healthy subjects recognizing objects bilaterally activates the parahippocampal gyrus (PHG), occipito-temporal sulcus, fusiform gyrus and V4v (Bar et al., 2001). The authors conclude that posterior areas are involved more in pre-recognition analysis while PHG and prefrontal cortex are more concerned with post-recognition. Other imaging studies found activation in anterior collateral sulcus, when subjects looked at objects (buildings) irrespective of attentional allocation (Avidan, Levy, Hendler, Zohary, & Malach, 2003). Most of the areas reported to be involved in object-based attention and object recognition are located posteriorly to the most pronounced lesion overlap in our allocentric impaired patients (Serences, Schwarzbach, Courtney, Golay, & Yantis, 2004).

In patients with damage to the left middle cerebral artery no specific area was found for item-centered omissions (Hildebrandt et al., 2005). This may be due to the fact that after left hemisphere damage patients had no absolute item-centered impairment, but there was an interaction between item- and array-centered omissions in visual search. Patients omitted increasingly more item-centred right targets when these were located more and more on the right side of the search array.

The cortical representation of an allocentric reference frame then seems to be more diffuse than that of the egocentric reference frame, maybe due to elaborated and less local-
ized object-representations on higher processing stages. Hence despite a more blurred location of lesion overlap in the RBD-ALLO group, ventromedial temporal structures seem to be crucial for processing of detailed stimulus features.

5.6. Neuroanatomy of neglect

Which neuroanatomical regions are responsible for the manifestation of clinical neglect is still controversial. In our opinion this fact reflects that ‘neglect’ subsumes different kinds of defective spatial behaviour becoming evident under different task requirements. For instance our paradigm does not require limb movements to the contralesional egocentric space, as is the case in cancellation tasks. The serial search task used requires primarily attentional shifts over space (in other words, voluntary visual exploratory behaviour) and a mental representation of the stimulus to search for. In classical procedures neglect is diagnosed based on disturbed behaviour in different tasks. Interestingly, if we compare the lesions of neglect patients with those of non-neglect patients as revealed by classical procedures, the highest overlap tends to result in the areas typically described as associated with neglect.

5.7. Conclusions

Visuo-spatial impairments, like neglect, are multi-faceted syndromes that require differentiation between disturbed versus preserved functions. In this study we show that egocentric and allocentric omissions in serial visual search are associated with lesions in frontoparietal versus ventromedial regions, respectively. The critical regions we found for specific visuo-spatial impairment confirm the hypothesis that the dorsal path is linked with egocentric information processing (required for spatial behaviour) and the ventral path is linked with allocentric processing (required for object perception and recognition).

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References


