Eye movements in patients with Neglect show space-centred attention when fixating rotating objects

Miriam K. Fuehr*† and Wolfgang H. Zangemeister*

*University of Hamburg, Neurology Clinic, Martinistrasse 52-S10, 20251 Hamburg, Germany
†Present address: Astley Ainslie Hospital, 133 Grange Loan, Edinburgh, Scotland, UK

Objectives and methods: *To determine whether attention operates in space-based or object-based coordinates, Neglect patients were confronted with a rotating object. After the object had undergone a 180° rotation a stimulus appeared on either side of the object and the reaction times were measured. The results of the present study showed that all patients performed worse on the contralateral side, both in the static as well as in the moving condition. This supports the theory that attention operates in space-centred reference frames. To bring some light into the discussion, the recording of eye movements was included.*
Results: *Our results showed three effects: (1) most eye movements started to the right of the mid-line; (2) some patients followed the moving object to the mid-line, before they returned to the ipsi-lesional side; (3) some patients followed the complete movement of the barbell.*
Conclusion: *It is argued that patients recovering from Neglect consciously make more eye movements to the left to compensate for the deficit, but attention remains in the ipsi-lesional field.* [Neurol Res 2005; **27**: 302–309]

Keywords: Overt-covert attention; reaction times; object-centred attention; hemianopia; body-centred attention; representational deficit

INTRODUCTION

Neglect is the inability to orient, respond or react to stimuli of the contralateral field. This includes personal as well as the extra-personal Neglect. Much debate has occurred concerning the mechanisms underlying the Neglect syndrome. One model attributes attentional deficits for the occurrence of Neglect: there are two opposing models postulated by Kinsbourne and Heilman. Kinsbourne's model[1–3], claims that the left hemisphere controls the attention of the right side of space and the right hemisphere guards over the left. If one hemisphere is damaged, the undamaged hemisphere is freed of the inhibition by the damaged hemisphere and takes over. Heilman's model[4,5] assumes that the right hemisphere controls attention in the left and right of space and the left hemisphere only on the right. This would also explain why Neglect rarely occurs after left hemisphere damage. When considering Neglect as a pathology of attention, there are three frames of reference in which attention operates: space-centered deficits become apparent when patients are asked to bisect a horizontal line[6]. When looking at an egocentric frame of reference one has to look at three different coordinate systems. Karnath[9] found an improvement in reaction times to targets in the contralateral field when rotating the trunk but not the head toward the left. A third explanation would be to see Neglect as a object-centred attentional deficit. For example, one patient with right-sided Neglect only made errors at the end of a word irrespective of its location in space[12]. Behrmann and Tipper[14] have conducted a study to de-tangle the object-based from the space-based frame of reference. Their patients were confronted with a barbell. In the static condition the barbell remained stationary before a stimulus appeared on one side. In the moving condition the barbell underwent a 180° rotation before the stimulus appeared. Now the left of space and the left of the object were de-coupled. The measurement of reaction times showed that the patients' performance in the static condition was better for the right side than for the left. In contrast, the results in the moving condition were reversed. Here the patients' performance was better for the left-end state of the barbell, where the favoured right side of the object lay.

In the present study this experiment was repeated, but this time monitoring the eye movements. This determined whether attention operates in object-centred or space-centred frames of reference.

Correspondence and reprint requests to: Wolfgang H. Zangemeister, Universitaetskrankenhaus Eppendorf, Neurologische Klinik, Martinistrasse 52-S10, 20251 Hamburg, Germany. [zangemei@uke.uni-hamburg.de]
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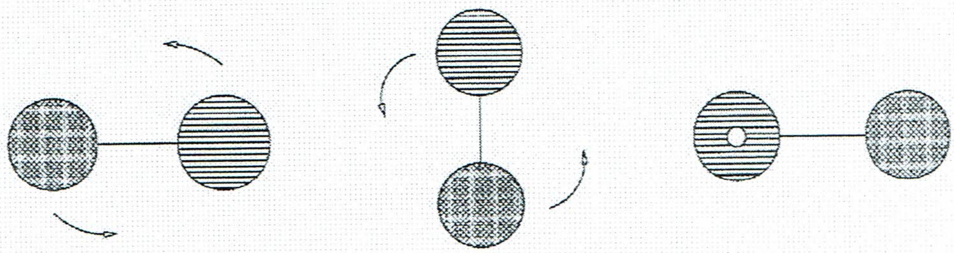

Figure 1: barbell in the moving condition

METHODS

Subjects

Ten right-handed patients with right hemisphere lesions documented by computerized tomography consented to participate in this experiment. All the patients suffered a right hemisphere infarct with the exception of patient 1, who had an intra-cranial bleed (*Table 2*). The mean age of the patients was 58.3±12.3 years. Neuropsychological testing revealed evidence of a unilateral left-sided Neglect for all patients. This included perimetric testing for field defects as well as various tests to detect visual, sensory and auditory Neglect. A group of patients with hemianopia only and without Neglect was not examined. We thought this to be of limited value for the present discussion, since hemianopic patients explore the blind hemifield more to compensate for their impairment (please refer to the Discussion for details). Just before the experiment, line cancellation, star cancellation and line bisection task (Behavioural Inattention test)[15] were performed as well as a computer program that tested for oculomotor disorders. As a cut-off criteria the Neglect patients needed to deviate 5% or more in the line bisection test. Twenty-two elderly volunteers consented to serve as control subjects. Their mean age was 60.4±9.8 years. All were right handed and none showed Neglect on any of the bedside tests (*Table 1*). All patients were from the inpatient wards of the Neuro-Orthopaedisches Rehabilitationszentrum Soltau and the Universitaetskrankenhaus Hamburg-Eppendorf.

The stimulus was a barbell consisting of two circles, each 2.5 cm in diameter, drawn with a black perimeter. One of the circles was coloured blue and the other red, and the side of the colour was counterbalanced across subjects. The circles were joined by an 8-cm-long black horizontal line. The full horizontal extent of the barbell was 13 cm, and the visual angle subtended by the barbell was 12° with the subject seated 56 cm from the screen with their head fixed. The target was a white circle, 0.75 cm in diameter (*Figure 1*). Before each trial a saccade program was performed to assure full motility of the eyes.

Procedure

Stimulus presentation and response recording were controlled by an IBM PC computer. The experimenter pressed a start key to initiate a trial. Immediately thereafter, the barbell appeared. In the static condition, the barbell remained static on the screen, and after 2.7 seconds, on half the trials, the white circular target appeared with equal probability in the centre of either the left or the right circle of the barbell. In these target-present trials, the barbell and target stayed on the screen together until a response key was pressed or for an additional 3 seconds if there was no response. In the remaining 48 target-absent trials, the barbell stayed on the screen alone for a further 3 seconds before the trial was terminated. The subject was required to press a single key on a joystick when a target was detected. All subjects used the index finger of their right hand for responding. Reaction time and accuracy of target detection as a function of side were recorded. In the moving condition, the barbell remained static on the screen for 1 second after which it began a 180° rotation

Table 1: Summary of the patients (n/a: patients non-compliant with testing instructions)

Patient	1	2	3	4	5	6	7	8	9	10
Age	53	42	61	77	66	67	43	48	50	76
Sex	Female	Male	Male	Female	Male	Male	Male	Male	Female	Male
Months since onset	2	2	1	0.5	8	6	2	10	30	2
Extinction	+	+	+	+	+	+	+	+	+	+
Hemianopia	+	+	−	+	−	−	+	−	+	+
Test results										
Line cancellation										
Omissions (l/r)	20/5	1/0	8/0	20/6	n/a	0/0	1/0	0/0	0/0	0/0
Star cancellation										
Omissions (l/c/r)	n/a	20/7/0	10/10/0	n/a	n/a	0/0/0	0/0/0	0/0/0	13/0/0	0/0/0
Line bisection										
(%)	12.5	25	7.5	45	5	7.5	2.5	5	5	5

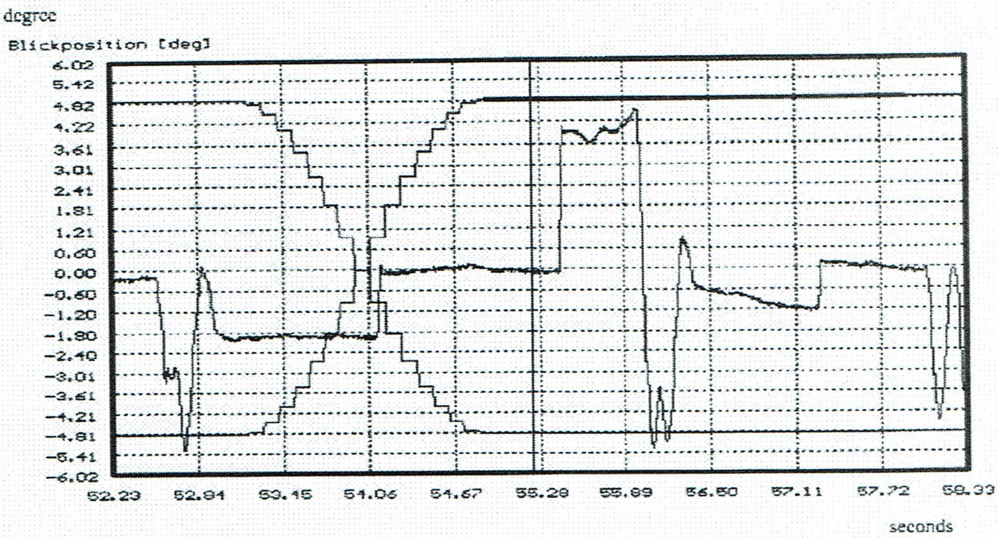

Figure 2: Control group: moving condition with right-sided stimulus. The blue line represents the right side of the barbell rotating to the left. The broad red line reflects the stimulus presentation. The green line shows the eye movements. The black line indicates when the button was pressed

(pivoting on the centre of the bar) until it reached its final position, or end state, rotation time 1.7 seconds. The barbell rotated with equal frequency in a clockwise and an anticlockwise direction (target on and target off trials were each n=48). Reaction time and accuracy were obtained for target detection. These reflect not only the direction of the movement but also the side of the target end state.

Eye movements were monitored using an Eye-Track Program designed to monitor and evaluate eye movements (Ober 2, Permobil Meditech, Box 120, S-86123, Sweden) using infra-red oculography (Bandwidth 100 Hz).

Statistics

The eye movements were analysed in two different aspects. The qualitative analysis looked at the eye movement patterns with a view to the initial fixation point, the eye position during the movement of the barbell, as well as during and after the appearance of the target. For quantitative analysis we looked at the

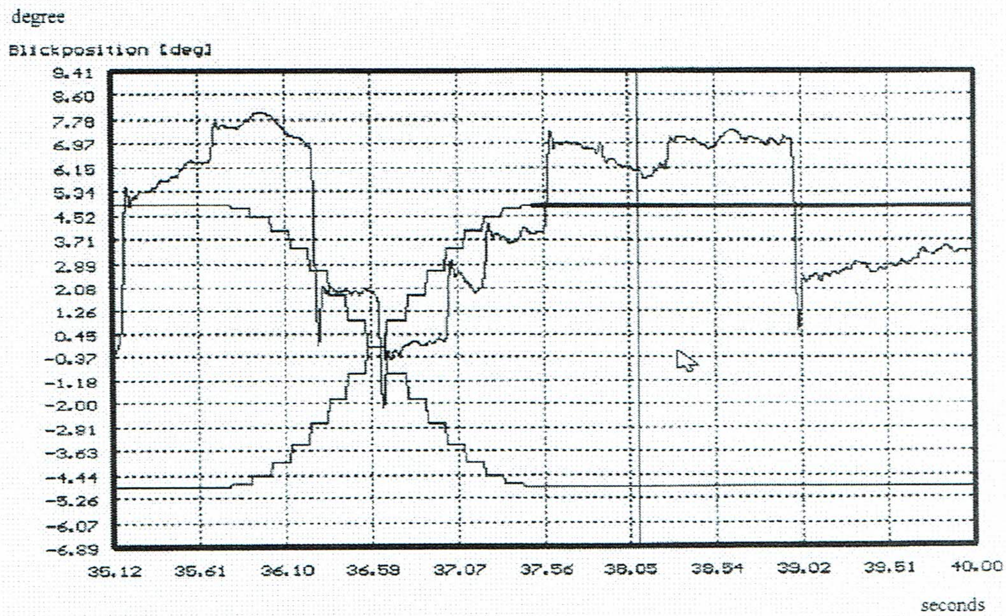

Figure 3: Neglect patient 5: moving condition with right-sided stimulus. The blue line represents the right side of the barbell rotating to the left. The broad red line reflects the stimulus presentation. The green line shows the eye movements. The black line indicates when the button was pressed

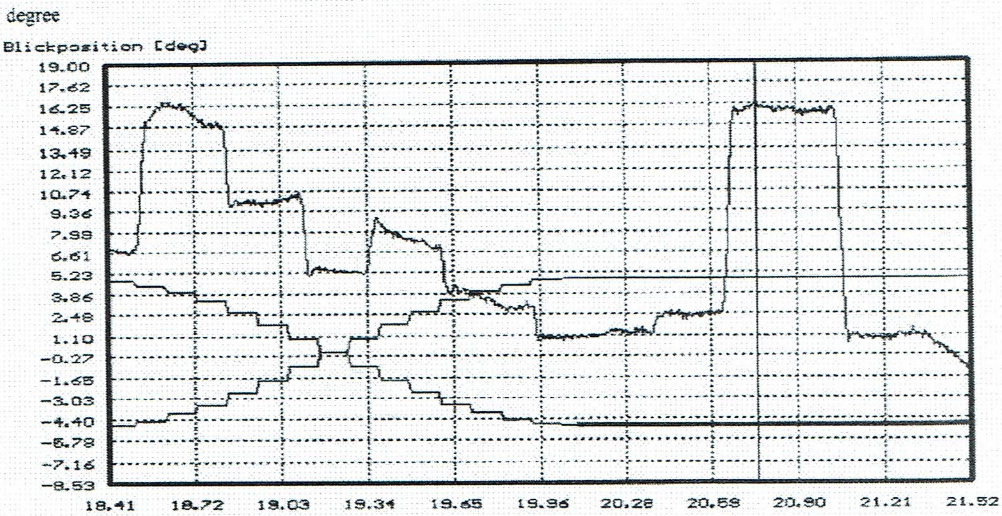

Figure 4: Neglect patient 3: moving condition with left-sided stimulus. The blue line represents the right side of the barbell rotating to the left. The broad blue line reflects the stimulus presentation. The green line shows the eye movements. The black line indicates when the button was pressed

Table 2: Computer tomography reports

Patient	CT findings
1	-Small right temporal haemorrhage.
2	-New right frontal infarct of the medulary layer and cortex. -Old right parietal cortical infarct. -Old right frontal cortical infarct.
3	-Old infarct lateral to the anterior horn of the right lateral ventricle. -New infarct of the right media territory extending to the basal ganglia.
4	-Right occipital haemorrhage with narrowing of the posterior horn of the right lateral ventricle.
5	-Infarct in the territory of the right medial cerebral artery.
6	-Extensive infarct of the right medial cerebral artery.
7	-Infarct in the right temporal and occipital territories of the medial cerebral artery. -1.5-cm-lesion next to the Cisterna magna.
8	-Right middle artery infarct affecting the temporal and basal territories including the lentiform nucleus.
9	-Multilocular ischaemias at multiple times. Picture consistent with septic emboli.
10	-Extensive infarct of the posterior cerebral artery.

amount of time that each patient spent looking either to the right or left of the mid-line. A normal individual spending the same amount of time on the right as on the left would get 50% for each side. A mixed-effect ANOVA analysis was carried out for these values, comparing it with the control group.

RESULTS

The reaction times were analysed for the right and left side only, independent of the eye movements. No difference in reaction times was seen if patients fixated the object to the left, right or centre. Patients explored the contralateral field more towards the end of the experiment, but this had no impact on the reaction times. The analyses of the control data revealed no significant differences (p=0.37) between the left and the right side of stimulus presentation, neither in the moving nor in the static condition. The mean reaction times in the moving condition were 0.420 seconds (±0.007) for the left and 0.408 seconds (±0.006) for the right side. The mean reaction time for the left side was 0.442 seconds (±0.007) and for the right side 0.440 seconds (±0.007) in the static condition. The data of the Neglect patients revealed a different picture. For the moving condition the patient group favoured the right side (p<0.001). The results are as follows: the Neglect patients' reaction times in the moving condition for the left was 0.698 seconds (±0.026) and for the right 0.545 seconds (±0.014). All patient showed a

Table 3: Reaction times in seconds

	Neglect			Control			Neglect with hemianopia			Neglect without hemianopia		
	Left	Right	p	Left	Right	p	Left	Right	P	Left	Right	p
Moving	0.698 (±0.026)	0.545 (±0.014)	<0.001	0.420 (±0.007)	0.408 (±0.006)	0.37	0.78 (±0.039)	0.61 (±0.02)	0.0009	0.59 (±0.024)	0.49 (±0.017)	0.0009
Static	0.750 (±0.030)	0.589 (±0.016)	<0.001	0.442 (±0.007)	0.440 (±0.007)	0.37	0.88 (±0.058)	0.604 (±0.021)	0.0009	0.628 (±0.024)	0.548 (±0.021)	0.0009

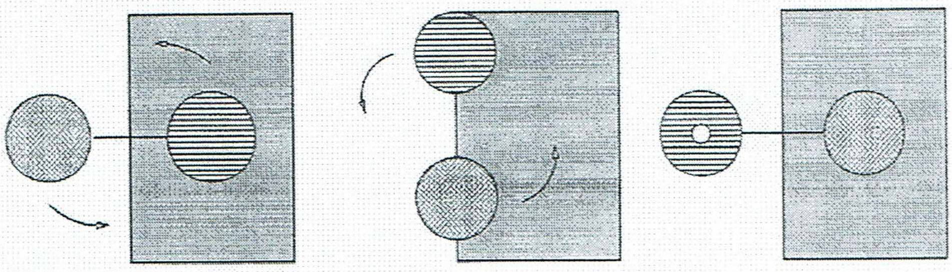

Figure 5: Object-centred attention

significantly ($p<0.001$) slower detection of left-sided stimuli in the static condition with a mean reaction time of 0.750 seconds (± 0.030) for the left and 0.589 seconds (± 0.016) for the right. The reaction times of the left are increased by 1.42 times compared with the right with a confidence interval of 1.34–1.50. The difference between the Neglect patients and the control group was significant with $p<0.05$ ($p=0.0114$) in the moving condition and highly significant with $p<0.01$ ($p=0.0021$) in the static condition (*Table 3*).

The results of the quantitative eye movement analysis showed that there was no statistical significance between the amount of time the Neglect patients spent looking to the right and to the left of the mid-line. The p-values of the ANOVA lie between 0.07 and 0.8. However, the findings of the qualitative analysis were significantly different:

The recordings of the control group in the moving condition revealed two results: (1) a saccade towards the stimulus after the button has been pressed and (2) central fixation of the barbell with only a few searching saccades to the sides of the object (*Figure 2*).

The Neglect patients showed a much more heterogenic picture in the moving condition: (1) most patients started fixating the right side of the barbell, (2) some patients followed the right side of the barbell up to the mid-line and returned to the ipsi-lesional field with the other side of the rotating barbell, (3) some patients followed the barbell completely into the contra-lesional field (*Figures 3* and *4*). The recordings during the static condition for the control group again show a central fixation of the barbell.

The Neglect patients fixated the right side of the barbell and performed a small saccade towards the stimulus before they pressed the button. After that their eyes returned to the ipsi-lesional side immediately. *Table 4* shows the time they spent with horizontal eye movements on the left versus right side in per cent of the total time.

So, the Neglect group shows significantly different behaviour from the control group in terms of the reaction times of eye movements to the left versus right, and in terms of the time spent on the left versus right as demonstrated in *Table 4*.

DISCUSSION

To determine whether attention operates in space-based[7,8] or object-based[13] coordinates, we confronted Neglect patients with a rotating object and found that all patients performed worse on the contralateral side, both in the static as well as in the moving condition, which supports the theory that attention operates in space-centred reference frames.

As far as the analysis of the reaction times is concerned, the patients in the present study show a clear preference of the right over the left side of space, independent of whether the right side or the previous left side of the object is shown. This is in contrast to the results of Behrmann and Tipper[14] where the patients preferred the right side in the static condition and showed better performance on the left side in the moving condition. This result was seen as being due to object-centred representation (*Figure 5*): the former preferred the right side of the object moved to the left side of space and enabled the patient to detect the stimulus faster than on the right side of space where the ignored left of the object now lies.

Driver and Halligan[16] performed a similar experiment where they rotated a nonsense shape by 45° to the left and to the right. After rotating, the left side of the object fell into the right side of space. The patient still was not able to detect differences on the left side of the object. This was claimed to be due to object-centred frames of reference, even though the patient also failed to detect differences on the right of the object if it fell into the left side of space in a few trials. In these few cases it is argued that the page functioned as a larger scale object.

Table 4: Time spent of horizontal eye movements on the left versus right side in per cent of the total time

	Neglect			Control			Neglect with hemianopia		Neglect without hemianopia	
	Left	Right	*P*	Left	Right	*p*	Left	Right	Left	Right
Moving	27.85 (±5.08)	42.31 (±4.98)	0.8	61.13 (±4.07)	33.65 (±3.66)	0.07	26.36 (±6.0)	29.54 (±6.0)	26.68 (±4.01)	60.49 (±10.04)
Static	22.23 (±4.71)	47.21 (±5.88)	0.8	48.64 (±6.07)	31.81 (±4.67)	0.07	17.49 (±3.98)	30.83 (±5.99)	29.84 (±9.13)	62.09 (±9.45)

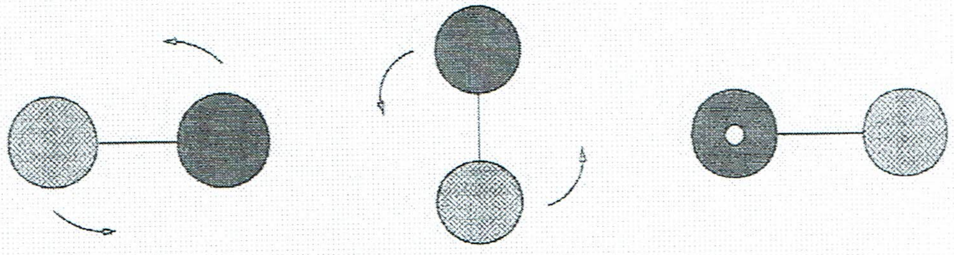

Figure 6: Space-centred attention

Rotating an object by 90°[17], showed that Neglect is also tied to the top–bottom axis of an object. The patient still identified the left of a chimeric object poorly after a 90° rotation where the left of the object fell on the patients' egocentric up or down.

To explain the results of the present study it has to be considered that attention operates in space-centred coordinates (*Figure 6*). Attention is drawn to the ipsi-lesional side of the lesion. Stimuli on the left of the egocentric mid-line are attended to with great delay. If patients are asked to recall images from memory[18], objects that are located on the left of a scene are ignored. Space representation seems to be dependent on the saggital mid-line. Calvanio *et al.*[19] confronted patients with objects while sitting and reclining on their sides. In both cases patients reported less from the left. Farah *et al.*[20] rotated the patient and the object to decouple the space-centred from the object-centred coordinate system. These results showed that attention operated in space-centred coordinates. Another coordinate system has to be mentioned as well. Karnath *et al.*[21] exposed patients to complete darkness before he tilted their bodies 30° to the left and right, to the front and back. The results showed that the performance is dependent on body axis, not gravitation[10,11].

A possible way to combine the space-centred and the object-centred frame of reference was suggested by Buxbaum *et al*[22]. Buxbaum noted object-based Neglect only when patients were asked to mentally rotate the object into an upright position. If the mental and the visual image were equal Neglect operated in space-centred coordinates. Alternatively Neglect might be caused by the inability to mentally rotate objects. Patients with right parietal lesion had greater difficulty in recognizing rotated Bender Gestalt images than patients with left hemispheric lesions[23].

When the eye movements of hemianopic patients and Neglect patients are compared[24–26] the hemianopic patients show much more searching saccades into the blind hemi-field to compensate for the impairment. Neglect patients on the contrary make no or few saccades to the contralateral field. Therefore, we presented the barbell centrally to all the patients, since the patients were allowed to move their eyes freely and the field defect should not inhibit the search for the stimulus. In addition hemianopic patients show a training effect. After a short time patients are able to compensate for their field defect (Zangemeister und Oechsner[27]). Different strategies used by hemianopic patients include a staircase pattern of eye movements toward the blind hemi-field, as well as over and undershooting eye movements[28]. These compensating mechanisms are mainly restricted to eye movements. Head movements are restricted in favour of eye movements[29].

For patients with Neglect the recording of the eye movements show a similar picture for all patients whether they had a field defect or not. Actually the severity of the Neglect was the determining factor for the way the eyes moved. The less severe the Neglect the more the patient was able to fixate centrally, although most of the patients remained in the ipsi-lesional field and only followed the rotating barbell to the centre of the screen before returning with the other half of the barbell into the right field again. Even though the qualitative analysis of the eye movements shows a preference for the ipsi-lesional side, a statistical analysis reveals no significant difference in either side. This might be due to the fact that the analysis was based on a comparison between the whole of the right versus the whole of the left screen. It may be that if the comparison was restricted to the outer portion of the screen, significant differences could have been noted. Walker and Young[30] confronted Neglect patients with whole, half and chimeric objects. Eye movements to the left were only present for left half objects. For the whole and the chimeric objects the eye movements remained in the ipsi-lesional field. Also, the patients reported seeing the right half-objects as whole ones more often than left half objects. This is claimed to be the consequence of object-centred Neglect. In our study we were able to show that some patients were able to follow the right of the barbell into the left of space. But most of the patients remained in the ipsi-lesional field.

This study demonstrated a similar pattern of eye-movements as that during reading reported by Karnath and Huber[31]. Patients were able to follow the text line to the right end but the return sweep to the beginning of the next line was left incomplete. The patients were unable to cross the saggital mid-line with their eyes and started backward reading from there. The line bisection test with healthy subjects showed eye movements similar to those found in reading[32]. They started on the left of the line then scanned to the right and returned to the middle before bisecting the line. Neglect patients remained on the right half of the line and bisected from there. If a patient was asked to move their eyes freely on a complex display, the eye movements showed a gradient in fixation from the left to the right[33]. But the maximum of fixation did not lie in the extreme right, instead it suggests a pattern of saggital mid-line shift to the right. The same was seen with patients in complete darkness[34]. This suggests an association between Neglect and cortical inability to determine our position in space. In contrast to these results Egner *et al.*[35] found no advantage for left-sided saccades if the patient is rotated 30° instead of the 0° alignment.

Instead of viewing Neglect as a deficit of attention, another alternative would be to view it as a representational deficit. Objects and scenes are either stored insufficiently or cannot be accessed completely. Bisiach *et al.*[36] confronted patients with pictures that could not be seen completely and asked the patients to reconstruct the images mentally. Differences on the left of the pictures were not detected as well, if at all. The attentional disorder underlying the Neglect symptoms seems to be secondary[37]. The attentional filtering occurs at a cortical level involving internalized representation rather than at a peripheral sensory input level. Mesulam proposed that the unilateral Neglect syndrome is caused by a dysfunction of a large-scale neuro-cognitive network, the cortical epicentres of which are located in the posterior parietal cortex, the frontal eye fields and cingulate gyrus[38]. The recordings of eye movements in complete darkness[39] as well as the analysis of REMs[40] showed that the patients' eye movements remain in the ipsi-lesional field.

Comparison and conclusion

Behrmann and Tipper[14] concluded that their results were due to an object-centred representational deficit, since their patients performed better on the left in the moving condition than on the right. Our results showed the opposite. All patients reacted faster to the appearance of the target on the right. The recording of the eye movements showed longer fixation on the right of the object. Only in the moving condition was the right side of the object tracked while moving into the left side of space. This explains the faster performance in the moving condition rather than in the static condition for left-sided targets. One explanation for the discrepancy between their results and our results might be found by looking at the duration since the onset of the disease. This was about 6 years for the patients in their study. In our study the patients suffered a cerebrovascular accident <6 months previously. Butter *et al.*[41] examined the time course of Neglect symptoms and found more eye movements to the left with a decline of Neglect symptoms. Patient 9 in this study showed the most frequent eye movements to the left. Her duration of the disease was 10 months. Another explanation for the difference of the two studies might be the severity of Neglect: Johnston and Diller[42] compared the 'Neglect-Index' and eye movements in the contralateral field. They found a negative correlation between the two. The more severe the Neglect the less eye movements to the left would occur. The Neglect Index was determined by subtracting the results of the left side from the ones on the right side in different cancellation tasks. Therefore, the higher the score the more severe the Neglect symptoms. It would be very interesting to follow-up the patients of this study in 5 years and see if the same patients demonstrate object-centred Neglect when tested again. Should each patient's Neglect undergo different phases? How does the training effect fit into this. Even though patients seem to be able to consciously orient attention to the left, they still prefer the right side, even after longer periods of training[43].

Even though the present results favour space-centred attentional mechanisms, we have to take a closer look at the set-up of the experiment as a source for errors. The line that connected the two sides of the barbell might have been too weak to recognize the barbell as a whole object. Karnath[44] has shown that only objects with a strong connective element in the middle were recognized as whole objects by the patients. This would mean that the patients here saw two separate objects and favoured the right one until it exited the right of space and a second object came into view—the left half of the barbell.

Tipper and Behrmann[45] conducted a second experiment where the two sides of the barbell were disconnected and functioned as separate objects. There the results showed a better performance for all patients on the right for the static and the moving condition. This is consistent with the present results. We included the eye movements into the experiment assuming that the patients have to fixate centrally to recognize the whole object. This would support the role of object-centred mechanisms. We were able to show that most patients fixate on the right half of the objects and then simply follow the movement of the barbell. Does this suggest that only the right circle has been recognized and not the entire barbell?

Another point that has to be considered is that eye movements do not always represent the movement of attention[46]. Attention consists of an overt and a covert component. Ladavas *et al.*[47] have shown eye movements without a shift of attention in patients with fronto-parietal lesions. Maybe eye movements are not as helpful in determining between object-centred and space-centred attention.

For future research it would be interesting to decouple body-centred from space-centred reference frames. At the moment it appears that different reference frames are affected in different patients. Other research could be conducted by letting patients either mentally or physically rotate an object. This could explain why some patients detect differences better on the left side, if they mentally rotated the object into an upright position.

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