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A non-spatial bias favouring fixated stimuli revealed in patients with spatial neglect

Radek Ptak,[1] Armin Schnider,[1] Laetitia Golay[1] and René Müri[2]

[1]Division of Neurorehabilitation, University Hospital Geneva, 1211 Geneva 14 and [2]Department of Neurology, University Hospital Bern, 3000 Bern, Switzerland

Correspondence to: Dr Radek Ptak, Division of Neurorehabilitation, University Hospital Geneva, 26, Av. de Beau-Séjour, 1211 Geneva 14, Switzerland
E-mail: radek.ptak@hcuge.ch

The cardinal feature of spatial neglect is severely impaired exploration of the contralesional space, a failure resulting in unawareness of many contralesional stimuli. This deficit is exacerbated by a reflexive attentional bias toward ipsilesional items. Here we show that, in addition to these spatially lateralized failures, neglect patients also exhibit a severe bias favouring stimuli presented at fixation. We tested neglect patients and matched healthy and right-hemisphere damaged patients without neglect in a task requiring saccade execution to targets in the left or right hemifield. Targets were presented alone or simultaneously with a distracter that appeared in the same hemifield, in the opposite hemifield, or at fixation. We found two fundamental biases in saccade initiation of neglect patients: irrelevant distracters presented in the preserved hemifield tended to capture gaze reflexively, resulting in a large number of saccades erroneously directed toward the distracter. Additionally, distracters presented at fixation severely disrupted saccade initiation irrespective of saccade direction, leading to disproportionately increased latencies of left and right saccades. This latency increase was specific to oculomotor responses of neglect patients and was not observed when a manual response was required. These results show that, in addition to their failure to inhibit reflexive glances toward ipsilesional items neglect patients exhibit a strong oculomotor bias favouring fixated stimuli. We conclude that impaired initiation of saccades in any direction contributes to the deficits of spatial exploration that characterize spatial neglect.

Keywords: visuospatial neglect; saccadic eye movements; visual attention; oculomotor function; parietal lobe

Abbreviations: ANOVA = Analysis of variance; RH = right hemisphere; RT = reaction time

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Introduction

Current accounts of spatial neglect consider two fundamental attentional impairments: a non-spatial deficit of sustained attention (Robertson, 2001; Husain and Rorden, 2003) and a spatially lateralized bias favouring attentional orienting toward ipsilesional stimuli (Duncan *et al.*, 1997; Driver and Mattingley, 1998; Pouget and Driver, 2000; Halligan *et al.*, 2003). Evidence for this lateralized bias is the failure of neglect patients to be aware of a contralesional stimulus when an ipsilesional stimulus competes for attentional resources (Driver and Vuilleumier, 2001; Geeraerts *et al.*, 2005) and their facilitated processing of right compared to left items (Smania *et al.*, 1998). Since the planning of eye movements is closely linked to spatial attention (Shepherd *et al.*, 1986), saccadic eye movements of neglect patients should be particularly affected by their spatial orienting bias. Indeed, neglect patients show a strong tendency to direct their first saccade ipsilesionally when exploring a visual scene (Behrmann *et al.*, 1997; Pflugshaupt *et al.*, 2004) and spend more time looking at details located in the right half of the scene (Ishiai *et al.*, 1987; Hornak, 1992; Behrmann *et al.*, 1997; Karnath *et al.*, 1998), often re-fixating the same ipsilesional items (Husain *et al.*, 2001; Mannan *et al.*, 2005). In spatial search tasks, ocular fixations and exploratory hand movements of neglect patients show a very similar rightward bias, suggesting that—irrespective of output modality—orienting responses of neglect patients are biased by the same mechanism favouring ipsilesional items (Karnath and Perenin, 1998; Schindler *et al.*, 2006). However, several studies have also revealed impairments in oculomotor tasks that suggest more fundamental oculomotor deficits, in particular severe hypometricity and increased latencies of contralesional

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saccades (Heide and Kömpf, 1998; confirming similar findings in monkeys with parietal damage, Lynch and McLaren, 1989; Pierrot-Deseilligny *et al.*, 1991). Visual search tasks are often too complex to allow inferences about the basic oculomotor mechanisms underlying target selection under conditions of competition. A more straightforward way to study such competitive interactions is to present an irrelevant distracter at different positions relative to the target and to measure its impact on the temporal and spatial parameters of saccades. Studies using this approach have identified two distinct effects of irrelevant distracters on saccade latency in healthy participants. First, in comparison to an overlap condition the offset of a central fixation stimulus shortly prior to appearance of the target significantly reduces saccade latency (Saslow, 1967), a phenomenon known as the *gap effect*. Second, a distracter presented simultaneously with the target, but in the opposite hemifield, systematically increases saccade latency, which has been termed the *remote distracter effect* (Walker *et al.*, 1995, 1997). Both effects are specific to eye movements and have been attributed to inhibitory interactions within the oculomotor system, in particular the superior colliculus (Munoz and Wurtz, 1992, 1993b; Walker *et al.*, 1997; Gandhi and Keller, 1999). Interestingly, a classic hypothesis has related the lateral orienting bias that characterizes spatial neglect to a loss of balance between the neocortex and the superior colliculus (Sprague, 1966). The plausibility of this hypothesis for a human model of spatial neglect would be supported when low-level oculomotor interactions such as the gap effect and the remote distracter effect were significantly affected by spatial neglect.

However, at present it is unclear how the lateralized orienting bias of neglect patients affects such inhibitory oculomotor interactions. A few studies suggested that a distracter presented at fixation does not affect right saccades of neglect patients, but increases latencies of left saccades. However, it is difficult to evaluate the significance of this finding since these studies involved patients with impaired visual fields (Girotti *et al.*, 1983; Walker *et al.*, 1991), examined patients in whom neglect signs were no longer observed (Pflugshaupt *et al.*, 2004), or failed to include a control condition without a central stimulus (Karnath *et al.*, 1991; Behrmann *et al.*, 2001). It is therefore not clear whether the patients' saccades were particularly affected by a distracter at fixation or rather exhibited a generalized slowing. A systematic examination of the gap effect and the remote distracter effect was only performed in a study by Walker and Findlay (1996). Two of the four neglect patients examined in this study had no hemianopia, and the results of these patients are therefore particularly relevant for the present report. Interestingly, these two patients were differently influenced by a central distracter: whereas one patient showed particularly slowed initiation of contralesional saccades, the other patient exhibited increased saccade latencies for left and right saccades. The results of this patient thus suggested the intriguing possibility that a central distracter might disrupt preparation of saccades directed to the impaired *and* the intact hemifield of patients with unilateral neglect. However, since this finding was based on the observation of a single patient, it neither influenced theoretical accounts of the neglect syndrome, nor did it present itself to the authors of the study, who concluded that in spatial neglect the reduction of saccade latency in the gap condition '*is comparable to that found with normal subjects*' (p. 500).

Here we report findings from neglect patients that contradict this conclusion. We presented to a group of carefully selected neglect and non-neglect patients visual targets and distracters at varying retinal positions left or right of a central fixation point. On some trials the target was presented alone while on other trials a distracter appeared simultaneously in the same hemifield, in the opposite hemifield, or at fixation. As expected given their strong bias favouring ipsilesional stimuli neglect patients made many erroneous saccades when a distracter appeared in the ipsilesional hemifield and the target was localized contralesionally, suggesting that the distracter captured gaze reflexively. However, in addition to this directional bias neglect patients showed a strong directionally unspecific bias when a distracter was presented at fixation. In this condition, initiation of saccades toward left and right targets was disproportionately slowed. This failure to initiate saccades in any direction when a distracter is presented at fixation is evidence of a strong non-lateralized bias favouring foveal stimuli in spatial neglect.

Methods

Participants

Seven patients with left spatial neglect, seven right-hemisphere (RH) damaged patients without spatial neglect, and seven healthy control subjects participated in this study. All participants gave written consent, and the study was approved by the ethics committee at the University Hospital Geneva. Table 1 presents the demographic and clinical characteristics of the participants. Participants were matched with respect to age [ANOVA: $F(2,18) = 0.5$, $P = 0.61$], and time since injury (neglect and control patients, Mann–Whitney test: $P = 0.75$). Since visual field loss was an exclusion criterion, patients were carefully screened for the presence of visual field loss with detailed computer perimetry (white dot presented on black background at 110 different positions ranging between $-15°$ and $+15°$ on the horizontal and $-12°$ and $+12°$ on the vertical axis). All 14 patients had intact visual fields, though neglect patients occasionally missed targets in the left (mean: 6.5 out of 55) and right (mean: 3.3) visual field. Neglect patients all manifested clinical signs of left spatial neglect (e.g. unawareness of people or objects placed contralesionally, difficulty with dressing, grooming or displacement) and neglect-specific failures in formal neglect tests (Table 1): bell cancellation (Gauthier *et al.*, 1989), cancellation of inverted Ts among upright Ts, letter cancellation (Wilson *et al.*, 1987), line bisection (Schenkenberg *et al.*, 1980), sentence copying (Wilson *et al.*, 1987) and drawing of a landscape (Gainotti *et al.*, 1972). In contrast, none of the control patients showed any such failures

Table 1 Demographic and clinical characteristics of the three participant groups

Participant	Age (years)	Sex	Etiology	Time post (days)	Lesion volume (cm^3)	Bells cancellation (left omissions, out of 15)	Inverted T cancellation (left omissions, out of 27)	Letter cancellation (left omissions, out of 22)	Line bisection (% bias)	Sentence copying (word misses)	Drawing neglect (score)
RH1	56.6	m	Stroke	381	97.4	1	0	0	−1.03	0	2
RH2	77.1	m	Stroke	31	27.3	0	0	0	−0.05	0	2
RH3	67.4	f	Hemorrhage	56	48.6	0	1	0	2.31	0	2
RH4	57.9	m	Hemorrhage	70	7.7	1	2	0	−0.91	0	2
RH5	88.2	m	Stroke	53	1.5	1	1	0	−0.8	0	2
RH6	67.6	m	Hemorrhage	15	3.5	1	0	1	−0.43	0	2
RH7	72	m	Stroke	151	9.8	0	2	0	0.59	0	2
N1	60.5	m	Stroke	103	281.8	9	22	8	24.03	2	0
N2	59	f	Hemorrhage	72	162.8	7	18	12	8.49	1	1
N3	76.1	f	Hemorrhage	43	53.7	7	7	3	1.55	7	0
N4	75.4	f	Stroke	37	175.5	4	27	14	9.99	0	1
N5	74.6	f	Hemorrhage	33	78.5	13	9	4	3.22	10	2
N6	69.9	m	Hemorrhage	80	71.7	15	15	1	1.31	0	2
N7	60.3	m	Stroke	28	19.3	5	5	7	4.96	0	1
Controls	64.3 ± 11.1			–	–	–	–	–	–	–	–
RH-controls	69.5 ± 11			108.1 ± 127.9	28 ± 34.9	0.6 ± 0.5	0.9 ± 0.9	0.1 ± 0.4	0.0 ± 1.2	0.0 ± 0.0	2 ± 0.0
Neglect	68 ± 7.8			56.6 ± 28.5	120.5 ± 90	8.6 ± 4.1	14.7 ± 8.2	7 ± 4.8	7.7 ± 7.9	2.9 ± 4	1 ± 0.8

Drawing performance was scored as: 0 = flagrant omissions on the left side; 1 = distorted left side; 2 = intact.

in daily life or in the neglect tests. Neglect patients had significantly larger numbers of left omissions in the three cancellation tasks, a greater right bias in line bisection, a greater number of omissions in sentence copying, and a greater number of left omissions/transformations in drawing (Mann–Whitney tests: all $P < 0.05$).

Figures 1 and 2 show individual lesions and overlap maps of RH-control and neglect patients, and Table 1 shows estimated lesion volumes. Lesions were delineated on axial slices from the Montreal Neurological Institute (MNI) template brain using MRICro software (Rorden and Brett, 2000). Consistent with previous studies (Mort *et al.*, 2003; Malhotra *et al.*, 2005; Ptak and Valenza, 2005), lesions of neglect patients were larger than those of RH-damaged patients. Whereas location of lesions of RH-controls was highly variable, an area was identified that was damaged in six neglect patients. This area comprised the Centrum semiovale and the white matter beneath the posterior insula, extending into the posterior part of the internal capsule. Though the maximal lesion overlap is somewhat different than the results of previous anatomical studies, in these studies many neglect patients had relatively large lesions with a substantial cortical and subcortical overlap (Mort *et al.*, 2003; Karnath *et al.*, 2004).

Saccade task

The task was to make saccades from a central fixation point to a small (side length 0.6°) coloured square presented at 6 or 12° eccentricity in the left or right hemifield. Stimuli were presented on a neutral grey background on a 21″ colour monitor refreshed at 85 Hz. Participants viewed the display from a distance of 40 cm, their head supported by a chin-rest. Before each block of trials a calibration procedure was performed in which participants were required to sequentially fixate a white circle presented centrally and at 3, 6, 9, 12 and 15° in the left and right hemifield.

Each experimental trial started with the presentation of a black fixation cross (width 0.2°) in the centre of the screen. The experimenter checked fixation by inspecting the online output of the eye tracker and started a trial by pressing the mouse button when fixation was accurate. The fixation cross remained on screen for 1000 ms, but was extinguished 200 ms before the target (and eventually the distracter) appeared for 2000 ms. Targets were presented either alone or simultaneously with a distracter square of the same size, but different colour. On half of the trials the target was light green and the distracter light blue, and on the other half colours were reversed. The distracter appeared at 3, 9 or 15° in the left or right hemifield, or at the fixation position (0°). Within a block each target position was varied orthogonally with each distracter position, and the order of presentation of these conditions was completely randomized. Participants were instructed to move their eyes as quickly as possible to the colour-defined target and to disregard the distracter.

The horizontal position of the right eye was measured with a limbus eye tracker (Cambridge Research Systems, Rochester, UK), which uses the infrared light reflection technique. The analogue signal was digitized at 400 Hz and stored for later offline analysis. Only the first saccade was considered for analysis. Saccade onset and offset were defined using a velocity criterion of 50°/s. Anticipatory saccades (latency <80 ms) and saccades not triggered by the stimuli (latency >800 ms) were excluded from analysis. Saccade amplitude and latency were analysed with parametric methods while nonparametric methods were applied to analyse directional errors. To reduce the number of comparisons, we concentrated our analysis on effects of distracters presented in the same hemifield as the target for amplitude data and effects of distracters in the opposite hemifield or at fixation for error and latency data.

Manual task

The saccade task was followed by a manual reaction task, which used the same experimental setup except that manual reaction times (RTs) were measured. In order to prevent participants from

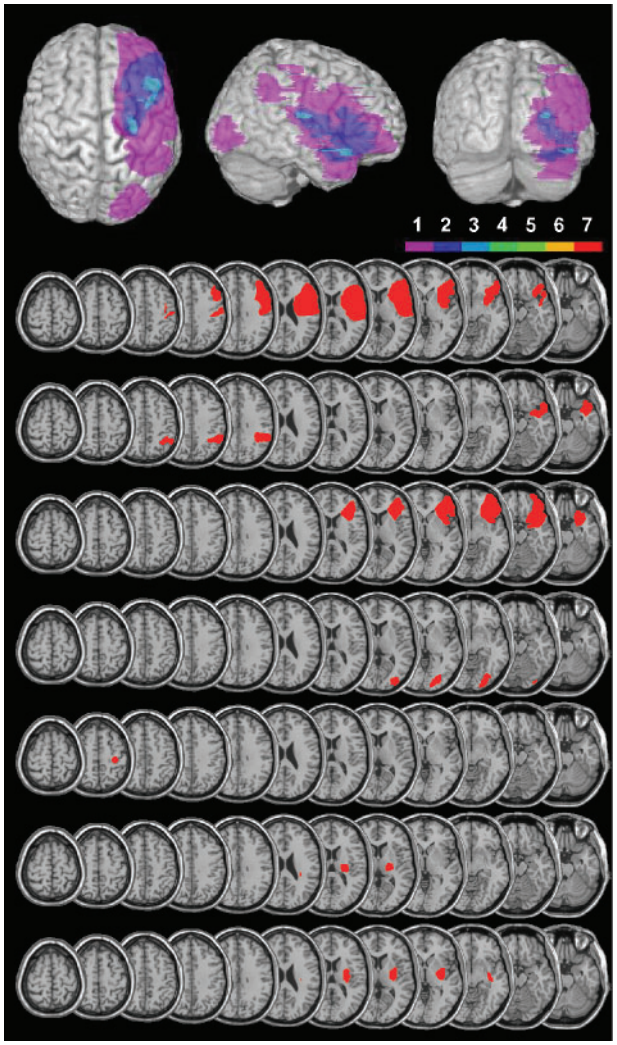

Fig. 1 Overlap map and individual lesions of RH-damaged control participants. The colour scale indicates the absolute number of shared lesions for every damaged area. The order of cases is the same as in the upper half of Table 1.

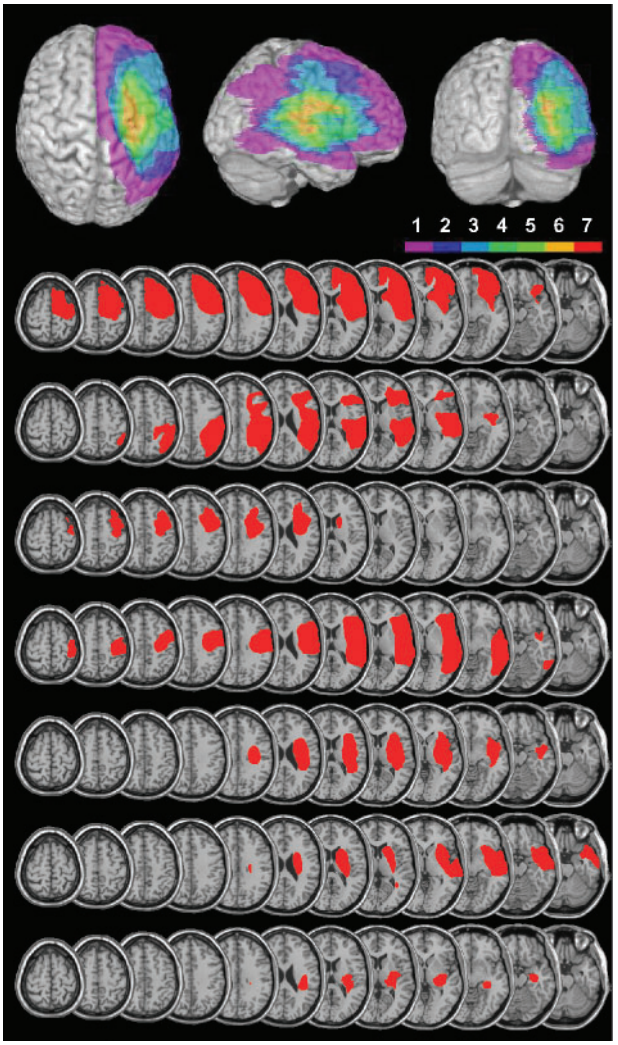

Fig. 2 Overlap map and individual lesions of neglect patients. The order of cases is the same as in the lower half of Table 1.

making anticipatory reactions, in one-third of the trials both stimuli were distracters. Participants were instructed to depress as quickly as possible the space bar upon appearance of the target, and to withhold reaction when no target appeared.

Results

Directional errors

Our first analysis focused on erroneous saccades. Directional errors—that is saccades directed to the hemifield opposite the target—occurred in all participants and were generally followed by a corrective saccade. Figure 3 shows that such errors occurred almost exclusively when a distracter was presented in the hemifield opposite the target, suggesting that they reflect the capture of gaze by the distracter. To analyse capture of gaze statistically we compared the proportion of saccades directed toward distracters in the opposite hemifield with the no-distracter condition. In control participants and RH-controls the proportion of directional errors reached significance when distracters were at 3, 9 and 15° in the hemifield opposite to a 12° left or right target, and when distracters were at 9° opposite to a 6° target (all $P < 0.05$, Wilcoxon test). The right attentional bias of neglect patients was expected to lead to an exaggerated number of directional errors toward distracters located in the right hemifield. This pathological bias also predicted a reduced number of directional errors toward distracters in the left hemifield. The data confirmed the first prediction: neglect patients made many more saccades toward right than left distracters. This priority of right-sided over left-sided items was stable for each distracter position and whether the target was closer (6°) or farther (12°) from fixation ($P < 0.05$). However, surprisingly, the proportion of directional errors toward the *left* hemifield was not reduced compared to the control groups (controls: 24.7%; RH-controls: 21.4%; neglect: 19.9%; Kruskal–Wallis test, $P = 0.63$). Thus the reflexive capture

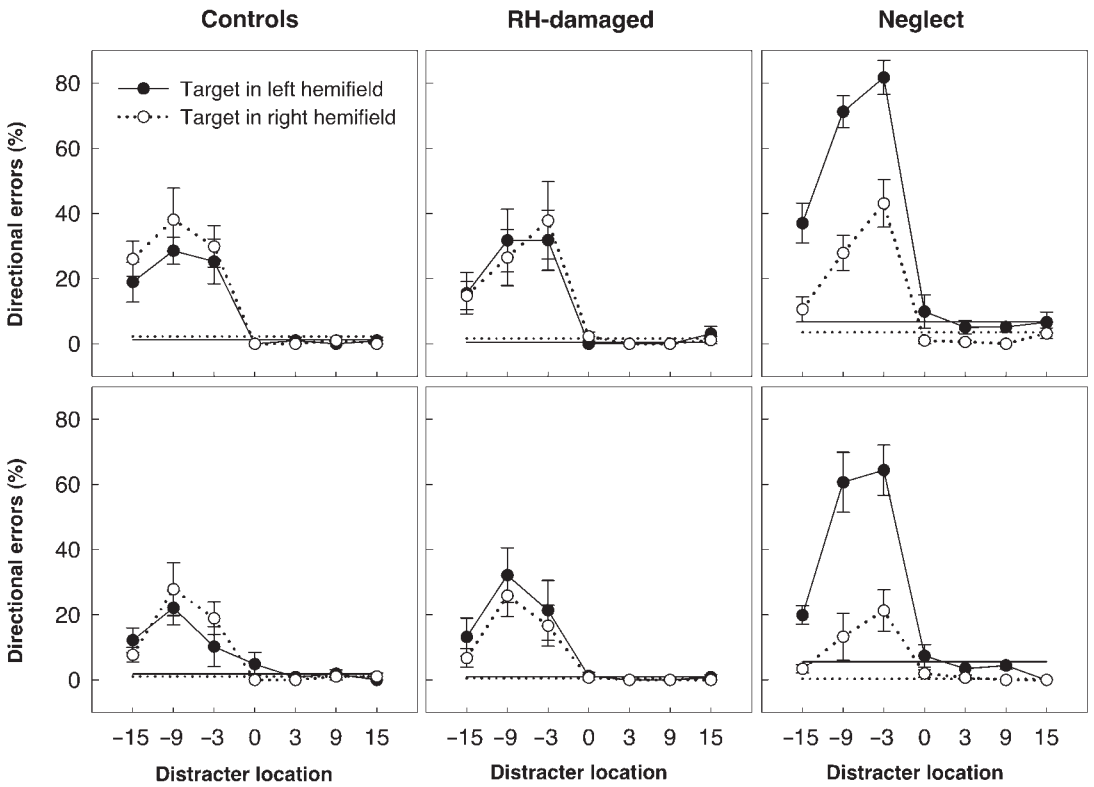

Fig. 3 Mean percent directional errors (±SEM) as a function of distracter location (upper row: target at 12°; lower row: target at 6°). Positive numbers denote distracter positions in the same hemifield as the target; hence for left targets distracters in the left hemifield are shown on the right side and distracters in the right hemifield on the left side of each graph. The straight horizontal lines show mean percent directional errors in the no-distracter condition.

of gaze by left distracters was unaffected by the right spatial bias that characterizes visual neglect.

Saccade amplitude

We next evaluated whether distracters presented in the opposite hemifield modify the spatial parameters of saccades directed toward the target. Figure 4 shows saccade amplitude of the three groups for left and right targets as a function of distracter position. In healthy controls amplitude was unaffected by distracters presented in the hemifield opposite the target or at fixation, but was modulated by ipsilateral distracters. When the distracter was closer to the fovea than the target (3° for targets at 6°; 3° and 9° for targets at 12°) saccades typically landed between the distracter and the target, but closer to the distracter. When the distracter was farther away (9° and 15° for targets at 6°; 15° for targets at 12°), a slight overshoot of the target was observed. RH-controls had slightly smaller saccade amplitudes than controls, but showed no difference between left and right saccades, and the modulation of their amplitudes by distracters ipsilateral to the target was very similar. Neglect patients, in contrast, showed a severe reduction of amplitude of left saccades that was evident in target-alone trials and in all target-distracter pairings. However, despite this marked hypometria the modulating effect of a distracter appearing in the same hemifield as the target was still observed (Fig. 4). To evaluate the degree of undershoot/overshoot relative to the no-distracter condition, we performed paired *t*-tests. All groups showed significant undershoot of targets at 6 and 12° in both hemifields when the distracter was at 3° (all $P<0.01$). Undershoot was less important when the target was at 12° and the distracter at 9°. Overshoot was significant in the left and right hemifields of both control groups when targets were at 6° and the distracter at 9° ($P<0.05$). In this condition, neglect patients only showed significant overshoot of right targets. In sum, the effect of right distracters on saccade amplitude was comparable between the three groups and even the left saccades of neglect patients were significantly modulated when target and distracter were presented in the same hemifield. However, due to severe hypometria left saccades often had smaller amplitude than the less eccentric of both items.

Saccade latency

When analysing saccade latency we distinguished between directional errors and correct saccades. Directional errors were generally followed by a corrective saccade, suggesting that they reflected a reflexive, precipitated release of a

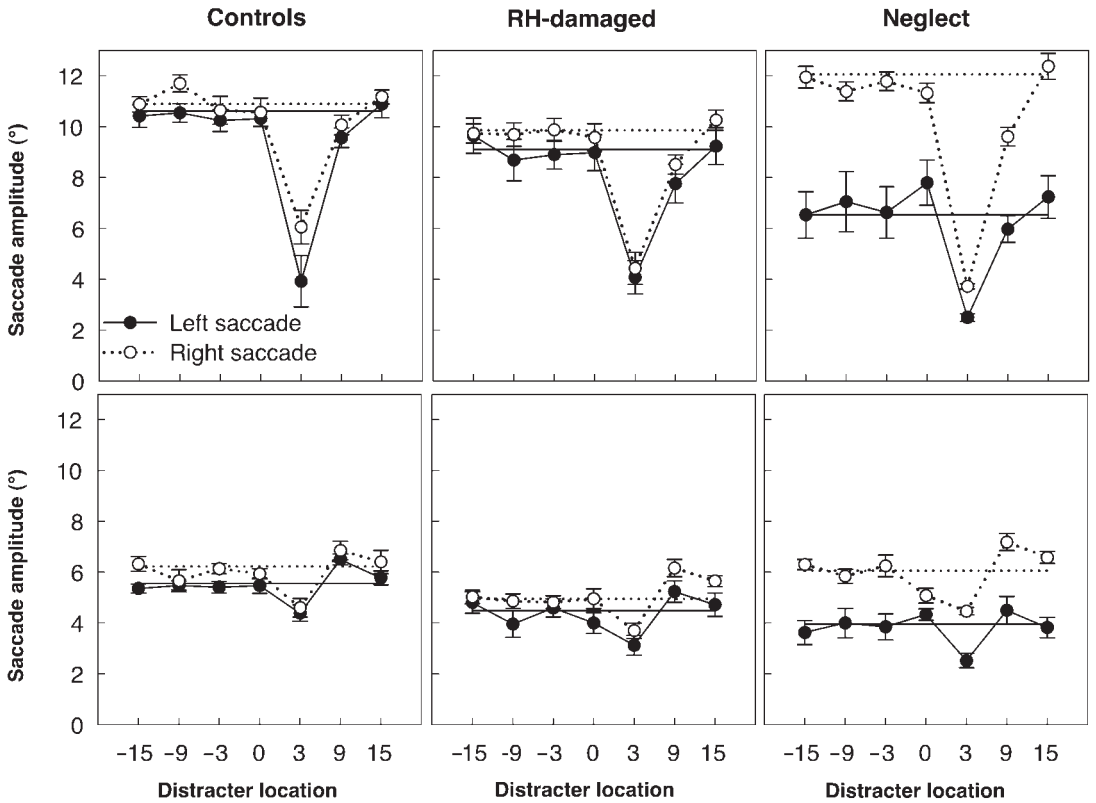

Fig. 4 Mean amplitude (±SEM) of correct saccades directed toward the target as a function of distracter location (upper row: target at 12°; lower row: target at 6°). As in Fig. 3, positive numbers denote distracter positions in the same hemifield as the target. The straight horizontal lines show mean saccade amplitude in the no-distracter condition.

saccade. If this hypothesis is correct, directionally erroneous saccades should be initiated faster than saccades executed correctly despite the presence of a distracter in the opposite hemifield. To test this prediction we compared saccade latencies in the no-distracter condition to saccades directed toward the target despite the presence of an opposite distracter and to directionally erroneous saccades. An ANOVA with group, hemifield and saccade type as factors confirmed that directional errors and saccades in the no-distracter condition were faster compared to correct saccades with a distracter [directional errors: 215 ms; targets without distracter: 208 ms; targets with distracter: 236 ms; $F(2,36) = 21.73$, $P < 0.001$, no other significant effects]. This acceleration of directionally erroneous saccades compared to correct saccades supports the hypothesis that the former reflect the capture of gaze by an irrelevant distracter, and that this process is comparable between the three groups.

Next, we investigated whether the presence of a distracter interfered with initiation of a correct saccade. Figure 5 shows mean latency of correct saccades plotted as a function of distracter position. Healthy participants had slightly increased latencies compared to the no-distracter condition when a distracter appeared at fixation or in the opposite hemifield. In contrast, a distracter in the ipsilateral hemifield did not affect or even slightly shortened saccade latency. ANOVAs examining the factors hemifield and distracter position revealed significant effects of distracter position for targets at 6° [$F(7,42) = 11.78$, $P < 0.0001$] and 12° [$F(7,42) = 13.87$, $P < 0.0001$], but no difference between hemifields. We therefore pooled data across hemifields and compared the latency increase elicited by distracters at fixation or contralateral to the target with the no-distracter condition. The latency increase resulting from the conjoint effect of all contralateral distracters was significant for both target positions, as was the latency increase when a distracter appeared at fixation ($P < 0.01$, planned contrasts). Similar to healthy participants, the latency data of RH-controls were only characterized by effects of distracter position [6°: $F(7,42) = 4.34$, $P < 0.01$; 12°: $F(7,42) = 5.65$, $P < 0.001$], but revealed no differences between hemifields. Planned comparisons revealed a reliable increase of saccade latency when distracters appeared at fixation or in the contralateral hemifield, but only for targets at 12° ($P < 0.05$).

Figure 5 illustrates that in contrast to the control groups, neglect patients showed a massive latency increase of saccades in both directions when a distracter appeared at fixation. ANOVA revealed highly significant effects of distracter position [6°: $F(7,42) = 18.86$, $P < 0.0001$; 12°: $F(7,42) = 19.54$, $P < 0.0001$], and a main effect of hemifield for the 6° target [$F(1,6) = 8.37$, $P < 0.05$], but no interaction between both factors. For all target positions, neglect

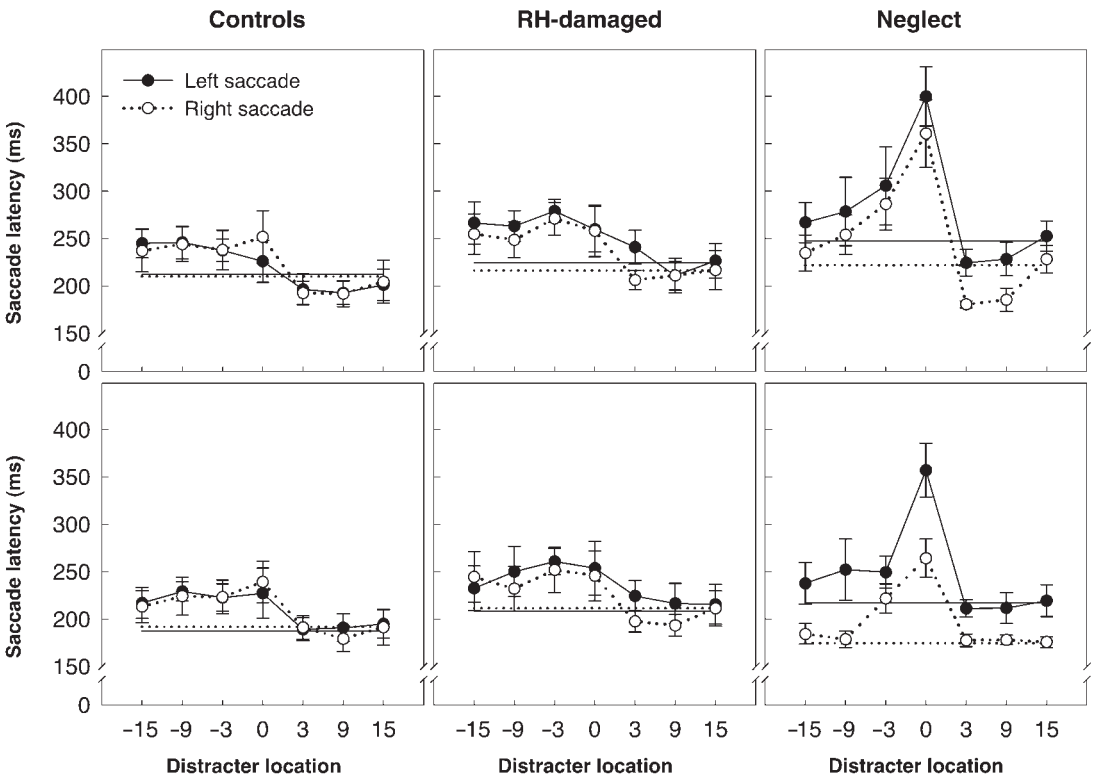

Fig. 5 Mean latency (±SEM) of correct saccades directed toward the target as a function of distracter location (upper row: target at 12°; lower row: target at 6°). The straight horizontal lines show mean saccade latency in the no-distracter condition.

patients showed reliable increases of saccade latency following contralateral distracters ($P < 0.05$). Planned comparisons also showed that regardless of saccade direction, saccade latency was significantly increased compared to the no-distracter condition when a distracter appeared at fixation ($P < 0.0001$).

While these within-group analyses show that saccade latency was modulated by the same variables in all three groups, it is evident from Fig. 5 that only neglect patients exhibited an exaggerated increase of saccade latency following a foveal distracter. The degree of latency increase became apparent when the distributions of left and right saccades following distracters at fixation were compared with the no-distracter condition. To better visualize the differences between distributions, we smoothed the latency distributions with a negative exponential function. Figure 6 shows that both control groups produced right-skewed distributions with a strong peak at ~180 ms. In contrast, the distributions of neglect patients only exhibited a distinctive peak in the no-distracter condition, but not when a distracter was presented at fixation. Importantly, Fig. 6 shows that there was no difference between left and right saccades in neglect patients' data.

The increase of saccade latency and the modified latency distribution following a foveal distracter might reflect inhibitory effects specific to the oculomotor system or a general difficulty to disengage attention from a fixated item. The latter hypothesis predicts that the distracter interferes with attention independently of output modality and should therefore similarly affect saccade latencies and manual reaction times (RTs). In order to examine this possibility, we conducted a control experiment in which we measured manual RTs rather than saccade latencies. The rates of target misses (controls: 0.1%; RH: 0.4%; neglect: 3.4%) and of false-positive responses initiated when only the distracter, but not the target was shown (controls: 3.5%; RH: 4.4%; neglect: 1.3%) were comparably low in all three groups. We found that in all three groups manual RTs were unaffected by distracter position (Table 2), though RH-controls showed slightly (left: 559 ms; right: 521 ms) and neglect patients severely (left: 812 ms; right: 681 ms) slowed RTs to targets in the left hemifield. In order to compare the effect of a distracter on saccade latency and manual RT directly, we calculated the increase of latency following a foveal distracter relative to the no-distracter condition. Figure 7 shows that a foveal distracter significantly affected saccade latencies, but not manual RTs, and that saccade latency increase was significantly larger in neglect patients than in the two control groups. Confirming this finding, an ANOVA with group, hemifield, target eccentricity, and task as factors revealed as highest-order effect a significant group by task interaction [$F(2,18) = 18.69$, $P < 0.0001$], reflecting the exaggerated bilateral saccade latency increase in patients with left neglect.

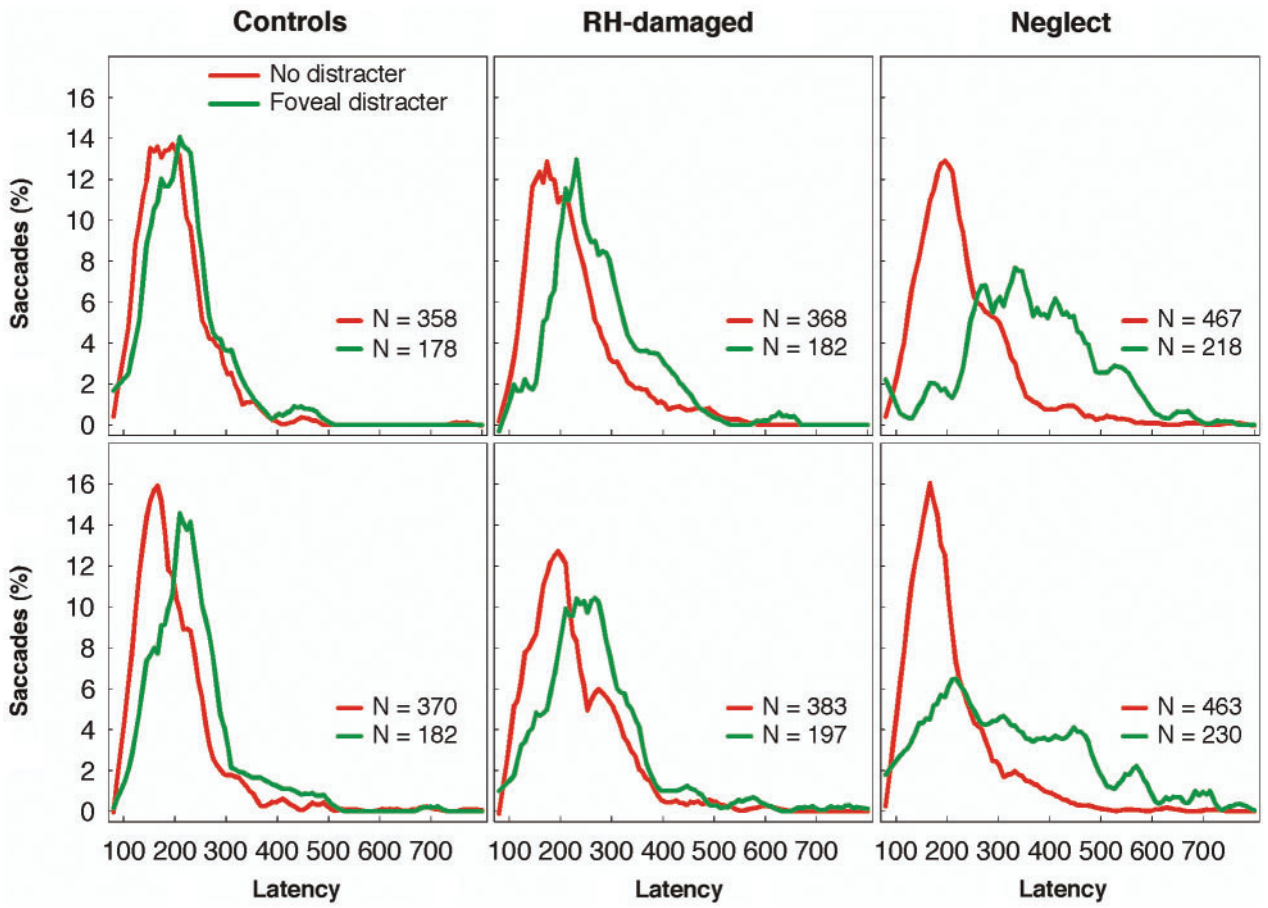

Fig. 6 Distribution of latencies of all left (upper row) and right saccades (lower row) made when no distracter was presented (red) or when a distracter appeared at fixation (green). Distributions were smoothed with a negative exponential function. Ns indicate the numbers of saccades on which the distributions are based.

Table 2 Mean manual reaction times as a function of distracter location

Group	Target position	Distracter position							
		No distracter	–15	–9	–3	0	3	9	15
Controls	–12°	492	494	506	482	490	497	494	500
	12°	503	467	487	502	486	502	487	487
	–6°	469	464	455	462	481	475	467	444
	6°	470	465	458	455	462	487	473	472
RH-controls	–12°	586	579	573	547	602	564	606	636
	12°	522	541	515	523	515	524	544	564
	–6°	521	526	520	516	530	533	544	562
	6°	508	488	524	498	498	518	517	544
Neglect	–12°	895	910	861	913	837	777	824	853
	12°	687	708	692	689	734	700	711	721
	–6°	765	795	787	712	741	734	819	765
	6°	657	653	653	663	642	651	698	646

Note that negative target positions indicate targets in the left hemifield and that negative distracter positions stand for distracters in the hemifield opposite the target.

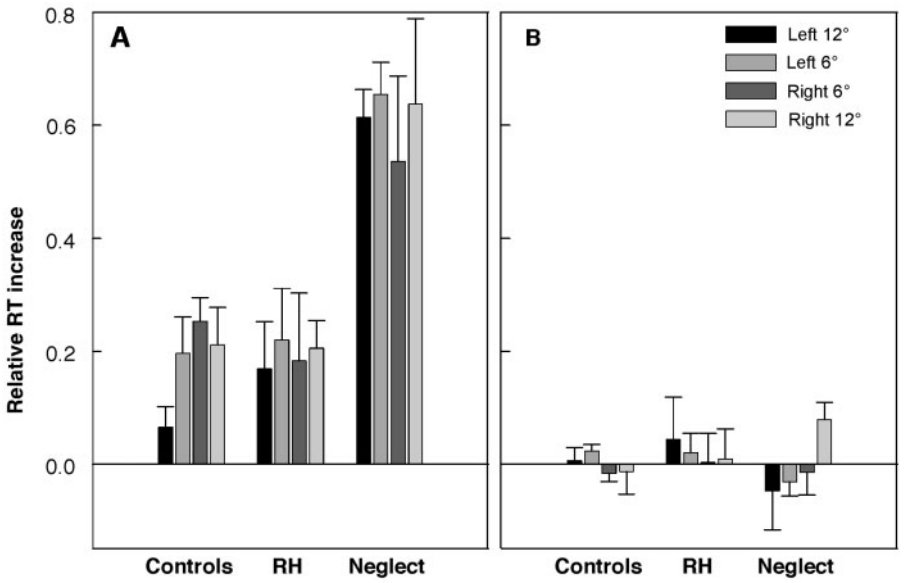

Fig. 7 Mean increase (±SEM) of saccade latency (**A**) and manual reaction time (**B**) when a distracter appeared at fixation relative to when no distracter was presented. Relative increase is shown for each group as a function of target position.

Discussion

The present results show that competition between target and distracter for sensory resources produces a distinctive pattern of saccadic responses in patients with spatial neglect. Since a neural bias only becomes apparent when processing capacity is limited, our findings allow us to make conclusions about the neural biases affecting the representation of stimuli in neglect patients' oculomotor system. Depending on the position of the distracter neglect patients showed a distinct pattern of directional errors, saccade metrics and saccade latencies. Regarding directional errors, neglect patients performed almost perfectly in target-alone trials. In contrast, they exhibited a strong directional bias in favour of ipsilesional distracters, which was expected given their attentional bias toward ipsilesional space. Nevertheless, an interesting aspect of the error data is that the frequency of errors was highest for distracters located close to fixation and decreased for more lateral distracters. Thus the proportion of reflexive glances toward right distracters was inversely related to their eccentricity, which contradicts a simple gradient model predicting a linear relation between attentional capture and stimulus eccentricity (Kinsbourne, 1993; Behrmann *et al.*, 1997). This finding shows that stimuli closer to fixation have higher saliency compared to peripheral stimuli, and this saliency difference appears to be unaffected by spatial neglect. A second interesting point regarding error data is that neglect patients made as many directional errors toward *contralesional* distracters as controls. This finding shows that the reflexive capture of gaze by left distracters is unaffected by the right bias characterizing spatial neglect, which is difficult to explain in terms of a generalized right attentional bias. Instead, it suggests the presence of a low-level—possibly preattentive—retinotopic bias in the oculomotor system that is unaffected by spatial neglect. A finding confirming such a preattentive bias is the slowing of saccade initiation by a distracter presented in the hemifield opposite saccade direction (remote distracter effect), which also was comparable for left and right distracters.

Regarding spatial parameters, our neglect patients showed severely hypometric contralesional saccades, confirming similar findings from earlier studies (Heide and Kömpf, 1998; Behrmann *et al.*, 2001). In all three groups saccade amplitude was unaffected by contralateral distracters, but clearly modulated by distracters presented in the same hemifield as the target. Neglect patients showed a normal modulation of ipsilesional saccade amplitude by ipsilesional distracters and a significant modulation of contralesional saccade amplitude by contralesional distracters despite severe hypometria. An interesting implication of the latter finding is that the averaging process underlying the modulation of saccade amplitude by a distracter presented in the same hemifield might take place prior to the computation of final saccade amplitude. Such a pattern would be expected from a system that computes saccade amplitude in two steps: in a first step, stimulation is integrated over a wide area of visual space and in a second step, final saccade amplitude is computed based on this integrated visual information (Findlay and Gilchrist, 2003).

The most important finding of the present study is the exaggerated, bilateral increase of saccade latency in neglect patients when a distracter appeared at fixation. This finding contrasts with the previous findings in patients with slight or recovered neglect, who only showed a latency increase for contralesional saccades (Pflugshaupt *et al.*, 2004; with the notable exception of patient RR, who showed a bilateral latency increase of some 50 ms for stimuli close to fixation,

Walker and Findlay, 1996). In contrast to these studies, in our experiment the fixation stimulus appeared simultaneously with the target, which might have increased its degree of interference with saccade initiation.

The disproportional increase of saccade latency with a foveal distracter suggests that besides their strong directional bias toward ipsilateral items neglect patients exhibit a second, directionally unspecific bias favouring fixated stimuli. Confirming previous studies using tasks evaluating global alertness (Robertson, 1989), the attentional blink (Husain *et al.*, 1997), global attentional processing capacity (Duncan *et al.*, 1999) or speed of visual processing (Battelli *et al.*, 2003) this central bias shows that neglect patients have severe spatially unspecific processing deficits. An influential hypothesis explains the increase of saccade latency by a fixated distracter in terms of impaired disengagement of attention from fixation (Fischer and Breitmeyer, 1987). Since attentional disengagement is an important component of spatial neglect (e.g. Morrow and Ratcliff, 1988; Losier and Klein, 2001; e.g. Posner *et al.*, 1987), a critical question is whether attentional deficits can explain the present findings. A number of factors suggest that disengaging covert attention and withdrawing the gaze from a fixated stimulus are based on different underlying processes. First, neglect patients only exhibit deficient attentional disengagement when reacting to a contralesional stimulus following an ipsilesional distracter, while no deficit is observed in the reverse direction (Posner *et al.*, 1987; Morrow and Ratcliff, 1988; Losier and Klein, 2001; Ptak and Schnider, 2006). Thus, in contrast to the present findings the disengagement deficit is clearly unidirectional. Second, most studies showing impaired attentional disengagement have examined manual RTs of neglect patients, which in some patients were excessively long (Posner *et al.*, 1984; Morrow and Ratcliff, 1988; Làdavas *et al.*, 1994; Bartolomeo *et al.*, 2001; Ptak and Golay, 2006; Ptak and Schnider, 2006). Thus, even though manual RTs were about three times as long as saccadic latencies in our study, deficient disengagement of attention should have similarly affected oculomotor and manual reactions. Instead of that, we observed a bilateral increase of saccade latency following a foveal distracter, but no effect of the distracter on manual RTs. Moreover, our patients even showed *shorter* saccade latencies compared to the foveal distracter condition when the distracter appeared ipsilesionally and the target was in the contralesional hemifield, a situation that should have induced a disengagement deficit. Finally, it has been shown that whether attention is engaged at fixation or not does not change the extent of facilitation observed in the gap condition (Kingstone and Klein, 1993; Walker *et al.*, 1995). These considerations suggest that attentional disengagement primarily affects processing of stimuli presented in the visual periphery, but is unlikely to explain the bilateral effect of a foveal distracter on saccadic latencies and the absence of an effect on manual RTs.

An alternative to the attentional account is to consider the present findings as result of enhanced fixational activity within the oculomotor system of patients with spatial neglect (see also Walker and Findlay, 1996). Such a mechanism is offered by a model of spatial orienting assuming mutual inhibitory interactions between the parieto-occipital cortex and the superior colliculus (Sprague, 1966), a structure involved in saccade initiation and maintenance of active fixation. In animals, impaired orienting responses toward stimuli contralateral to a parieto-occipital lesion are restored if the contralateral colliculus is functionally inactivated (Sprague, 1966; Payne *et al.*, 1996). This finding suggests that parieto-occipital cortex normally exerts a facilitatory influence on the ipsilateral and an inhibitory influence on the contralateral colliculus. In spatial neglect following a cortical lesion, the ipsilesional colliculus has a lower (inhibition) and the contralesional colliculus a higher glucose metabolism (disinhibition, Rushmore *et al.*, 2006), which could contribute to the directional bias favouring ipsilesional items. An important feature of the superior colliculus is its subdivision in two functionally distinct regions. The rostral colliculus contains neurons that discharge when a stimulus in the central $\sim 2^{\circ}$ of the visual field is actively fixated (Munoz and Wurtz, 1992; 1993b; Gandhi and Keller, 1999), while neurons in the caudal colliculus show activity related to the preparation and execution of saccades (Dorris *et al.*, 1997). In patients with neglect following a right cortical lesion, a functionally disinhibited left colliculus would exhibit increased fixational activity in its rostral region and increased saccade-related activity in its caudal region. Thus, disinhibition of the left caudal colliculus can explain the high number of right directional errors of our patients. On the other hand, the bilateral increase of saccade latency following a foveal distracter can be understood in terms of functional interactions between the two colliculi. Fixation neurons pause before saccades in all directions (Munoz and Wurtz, 1992, 1993*b*) and stimulation of these neurons in one colliculus activates fixation neurons and deactivates saccade-related neurons in the other colliculus (Munoz and Istvan, 1998), suggesting that rostral colliculi work as a unit that maintains active fixation. Disinhibition of one rostral colliculus delays saccades in all directions (Munoz and Wurtz, 1993*a*), which would explain the bilateral increase of saccade latency in our neglect patients. Such disinhibition would produce an increase of saccade latency via a mechanism that amplifies the neural response to fixated items relative to peripheral items. Supporting this cortico-tectal hypothesis is the finding that six of our seven neglect patients had damage to the posterior internal capsule, which is the subcortical region through which cortico-collicular connections travel (Gaymard *et al.*, 2003). This finding might be a particularity of our patient sample; however, previous anatomical studies showed that neglect patients often have large cortical and subcortical lesions that may undercut cortical connections to the midbrain

(Mort *et al*., 2003; Karnath *et al*., 2004). Lack of facilitation of the ipsilesional colliculus could therefore be a consequence of a disconnection of these cortico-collicular connections.

This interpretation of the present results in terms of cortico-tectal interactions is appealing, yet in absence of neurophysiological data its applicability to spatial neglect in humans remains hypothetical. A critical point is that while the manual RT task required a simple reaction, in the saccade task a goal-directed action had to be planned and executed. However, in previous studies examining goal-directed hand movements, neglect patients needed much more time to initiate leftward compared to rightward arm moves (e.g. Behrmann and Meegan, 1998; Mattingley *et al*., 1998), even if the starting point was dissociated from the fixation point. It is therefore unlikely that a pathological slowing would be observed in goal-directed manual responses. An additional argument for a specific effect of a central distracter on saccadic reactions is the fact that neurons exhibiting fixation-related activity are not only located in the superior colliculus, but also in cortical regions involved in oculomotor programming such as the frontal eye fields (e.g. Hanes *et al*., 1998). An imbalance between cortical regions might therefore contribute to the increased activity of the fixation system in neglect patients.

In sum, our findings show that in addition to spatially lateralized attentional failures, spatial neglect is also characterized by a strong directionally unspecific bias in favour of foveated stimuli. This strong non-lateralized bias may be understood in terms of increased fixational activity of the oculomotor system in spatial neglect. Since only saccade latency but not saccade amplitude was influenced by the presence of a foveal stimulus, we conclude that distracters presented in the fovea of neglect patients impair saccade timing (WHEN-processes) without affecting the spatial properties of saccades (WHERE-processes, Becker and Jürgens, 1979; Findlay and Walker, 1999). Our results imply that such impaired saccade timing processes contribute to the deficient orienting responses of neglect patients.

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