

Reflexive Orienting in Spatial Neglect Is Biased towards Behaviourally Salient Stimuli

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Patients with spatial neglect are impaired when detecting contralesional targets presented shortly after an ipsilesional cue. This 'disengagement' deficit is believed to reflect reflexive orienting towards ipsilesional stimuli that is independent of behavioural goals. Here, we show that the extent of this spatial bias depends on the behavioural salience of ipsilesional stimuli. Healthy participants, brain-injured patients without neglect and neglect patients reacted to ipsilesional and contralesional visual targets. Prior to target presentation, a visual cue similar or dissimilar to the target was presented at target position or opposite the target. Although participants did not react to the similar cue, it had high behavioural salience since it shared features with the target stimulus. Neglect patients showed dramatically increased reaction times to contralesional targets, but only when these followed behaviourally relevant ipsilesional cues. No decrease of performance was observed with irrelevant cues. This performance pattern was not due to perceptual similarity, since the same effect was found when cue and target were semantically related but differed perceptually. Importantly, semantically related cues ceased to attract attention when they were defined as behaviourally irrelevant. These results show that neglect patients only orient attention reflexively towards ipsilesional stimuli with high behavioural salience.

Keywords: behavioural salience, parietal lobe, reflexive orienting, selective attention, spatial neglect

Introduction

Capacity limitations of the visual system increase the demands on an efficient attentional orienting mechanism that selects among multiple sensory events those with greatest behavioural relevance. Studies with brain-injured patients suggest that the parietal lobe is particularly important for spatial orienting. Damage to this region leads to spatial neglect, a syndrome characterized by the lack of awareness for contralesional stimuli (Halligan and Marshall, 1993; Heilman *et al.*, 1993; Driver and Mattingley, 1998). Neglect patients exhibit a strong tendency to orient attention towards the side of space ipsilateral to their lesion, and this bias is exacerbated in the presence of ipsilesional stimulation (Gainotti *et al.*, 1991; Kinsbourne, 1993). Studies evaluating reaction time (RT) patterns of neglect patients in spatial cueing tasks have shown that these patients may fail to disengage attention from ipsilesional distracters. In a spatial cueing paradigm lateralized visual stimuli are preceded by a spatial cue that summons attention either to the location of the upcoming target (valid cue) or to the opposite location (invalid cue; Posner *et al.*, 1984). In this valid cue condition, patients with parietal damage show RTs comparable to ipsilesional and contralesional targets. In contrast, they are disproportionately impaired when reacting to contralesional targets

following ipsilesional cues (Egley *et al.*, 1994; Posner *et al.*, 1984, 1987; Friedrich *et al.*, 1998; Petersen *et al.*, 1989). The magnitude of contralesional slowing in the invalid condition correlates with the degree of spatial neglect (Morrow and Ratcliff, 1988; Bartolomeo *et al.*, 2001; Losier and Klein, 2001). Based on the supposition that attention must first be disengaged from the ipsilesional cue before a contralesional target can be detected, it has been suggested that the parietal cortex is crucial for the disengagement of attention and that a deficit in this operation might explain the occurrence of spatial neglect (Posner and Petersen, 1990; Rafal, 1998).

In the theoretical framework of Posner and collaborators (Posner and Petersen, 1990; Posner *et al.*, 1984) ipsilesional cues capture attention reflexively, and the disengagement deficit results from the spatial disparity between cue and target. In support of this prediction neglect patients show a disengagement deficit when cues are presented in a different modality than the target — even when these cues are unpredictable of the target location (Golay *et al.*, 2005), suggesting a stimulus-driven attentional capture that is independent of behavioural biases or goals of the patient. However, recent studies with healthy participants have reported that uninformative visual cues capture attention only when they are defined by features that also define the target (Gibson, 1996; Gibson and Jiang, 1998). For example, a coloured cue will only capture attention when an attentional set is created to attend to coloured targets (Folk *et al.*, 1992). That an attentional set may similarly influence the performance of patients with spatial neglect is suggested by the finding that neglect patients better detect features that define the target (e.g. colour) than other features (e.g. form), even if both describe the same object (Duncan *et al.*, 1999; Ptak *et al.*, 2002). However, whereas extensive research on the influence of spatial and temporal variables on the disengagement deficit after parietal lesions has been conducted (Losier and Klein, 2001), the extent to which behavioural salience of spatial cues may influence reflexive orienting of patients with spatial neglect towards ipsilesional stimuli has not been evaluated.

The aim of the present work was therefore to study whether the ipsilesional orienting bias of neglect patients could be modulated by induced behavioural biases in patients. In contrast to previous studies, we manipulated the identity of spatial cues to make them similar or dissimilar to the target. Similar cues possessed features that also defined the target and were thus of high behavioural salience, although patients had to withhold reactions to them. If, as predicted by the traditional spatial orienting account (Posner and Petersen, 1990), reflexive orienting of neglect patients is mainly stimulus-driven, contralesional RTs in the invalid cueing condition should not differ between similar (i.e. behaviourally relevant) and dissimilar (irrelevant) cues. In contrast, a larger disengagement deficit

with similar cues would indicate that spatial orienting is modulated by an observer bias towards relevant visual events.

Materials and Methods

All participants of this study gave informed consent according to the Declaration of Helsinki. Approval was obtained from the ethical committee of the University Hospital Geneva. Table 1 provides the demographical and clinical characteristics of all 26 patients participating in this study.

Experiment 1

Materials and Methods

Participants

Six patients (mean age = 64.3 years; range = 46–77 years) tested in experiment 1 had left neglect following right temporal-parietal damage after stroke (five patients) or haemorrhagic injury (one patient). These patients were tested on average 58.2 days post-injury. All manifested at least some behavioural signs of visual neglect (e.g. unawareness of persons or objects placed contralesionally, difficulty with dressing or grooming) as well as objective neglect signs in the 'Bells' cancellation test (mean = 11.8 of 15 contralesional omissions; Gauthier *et al.*, 1989) and on line bisection (mean = 13.6% ipsilesional deviation; Schenkenberg *et al.*, 1980). Patients 2 and 6 had an incomplete homonymous hemianopia with sufficient sparing (~10°) of the central visual field to allow perception of the entire experimental display.

Seven control patients with right-hemisphere (RH) damage (mean age = 58.2 years; range = 47–76 years) were tested on average 118 days following their ischemic stroke (five patients) or haemorrhagic injury (two patients). None of these patients presented behavioural or formal signs of neglect in the cancellation test (mean = 0.4 of 15 contralesional targets omitted) and on line bisection (mean = 0.6% ipsilesional deviation), and all had intact visual fields.

The neglect and RH-control groups did not differ significantly with respect to age [$t(11) = 1$, n.s.] or time since injury [$t(11) = 1.2$, n.s.]. In contrast, neglect patients had a significantly higher number of

contralesional omissions in the cancellation test (Mann-Whitney $z = 3.1$, $P < 0.01$) and a significantly larger ipsilesional bias on line bisection [$t(11) = 3.3$, $P < 0.01$].

The results of the two patient groups were compared with two healthy control groups of 10 younger (mean age = 30 years; range = 25–37 years) and 10 older (mean age = 63 years; range = 45–80 years) right-handed participants.

Stimuli and Procedure

The task in experiment 1 was to indicate by button-press whether a target display contained a red circle while disregarding a single cue stimulus presented shortly before. Stimuli were circles (diameter = 3.4°) and squares (side-length = 3°) of equivalent surface, filled with red or green colour and presented on black background. The target display consisted of two coloured forms, each presented with its inner border 1.5° left or right of fixation. Table 2 specifies the different stimulus conditions. On target-present trials the target display contained a red circle paired with a green square while on target-absent trials it contained a green circle paired with a red square. The cue was either identical to the target (a red circle; similar cue) or different (a green square; dissimilar cue), and it could appear at the same position as the target (valid cue) or at the opposite position (invalid cue). Variation of the physical resemblance (similar/dissimilar) and the spatial relation between cue and target (valid/invalid cue) resulted in four equiprobable experimental conditions: valid/similar, valid/dissimilar; invalid/similar and invalid/dissimilar.

The screen was placed at a distance of ~60 cm from the participant, aligned with his mid-sagittal line. On every trial participants first fixated a small white cross in the middle of the black screen (Fig. 1). The experimenter then started the stimulus presentation by pressing the mouse button. After a variable interval of 500–1250 ms the cue was presented for 300 ms, followed by 200 ms blank screen. The target display then appeared and remained on the screen until reaction of the participant. Participants were asked to depress with their index finger the left button of a button-box (labelled with 'yes') when the target display contained a red circle and the right button (labelled with 'no') with the middle finger when the red circle was absent. It was emphasized that they should not react to the cue stimulus presented first (though the cue could be identical to the target). Eye movements

Table 1

Patient description

Patient	Age	Days post-injury	Aetiology	Cancellation, omissions (%)		Line bisection deviation (in %)	Experiment
				Contra	Ipsi		
Neglect							
N1	77.4	56	CVI	100	33.3	6.2	1
N2	51.6	42	CVI	93.3	33.3	10.9	1
N3	74.7	38	CVI	40	0	16.9	1
N4	65.3	96	CVI	100	26.7	9.2	1
N5	46.2	58	Haemorrhage	40	13.3	5.7	1
N6	70.8	59	CVI	100	46.7	32.8	1 and 2
N7	83	58	CVI	100	33.3	12.2	2
N8	38.4	100	Tumour	100	0	3.6	2
N9	69.5	42	Haemorrhage	100	33.3	32.3	2
N10	82.3	37	Haemorrhage	100	60	10.3	2
N11	70.5	33	CVI	100	20	28.1	2
N12	40.6	88	Haemorrhage	100	47	25.3	2
RH-control							
C1	50.6	45	Haemorrhage	6.7	0	1.5	1
C2	46.9	108	CVI	0	0	1.7	1
C3	59.1	139	CVI	0	0	0	1
C4	63.6	387	CVI	0	0	2.4	1
C5	50.2	89	Haemorrhage	6.7	0	-0.2	1
C6	61.2	17	CVI	0	6.7	-1	1
C7	76	43	CVI	6.7	0	0.1	1
C8	78.7	136	CVI	13.3	20	-0.4	2
C9	81.5	43	CVI	0	0	2.4	2
C10	72.5	46	Haemorrhage	6.7	6.7	1.1	2
C11	70.2	71	CVI	0	0	5	2
C12	71.4	72	CVI	0	0	3.9	2
C13	58.5	39	CVI	13.3	0	0	2
C14	55.6	44	CVI	6.7	0	-0.3	2

Table 2

The composition of all possible target displays in experiments 1 and 2 (LVF/RVF: left/right visual field)

	Target display	Target location	Response
Experiment 1	Red circle + green square	LVF	Yes
	Green square + red circle	RVF	Yes
	Green circle + red square	-	No
	Red square + green circle	-	No
Experiment 2	Red circle + green square	LVF	Yes
	Word RED + green square	LVF	Yes
	Green square + red circle	RVF	Yes
	Green square + word RED	RVF	Yes
	Green circle + green square	-	No
	Green square + green circle	-	No
	Word GREEN + green square	-	No
	Green square + word GREEN	-	No

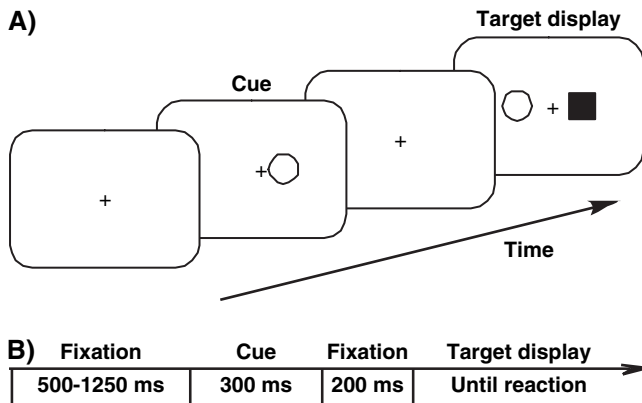


Figure 1. (A) Sequence of events presented in one trial of experiment 1. In this trial a target presented in the left visual field was invalidly cued with a similar cue. (B) Time course of experiments 1 and 2.

were controlled visually during a practice run, and checked periodically during the experimental runs. All participants responded with their right (dominant) hand.

There were 72 trials in each block, consisting of 12 trials with left or right targets in each of the four experimental conditions, as well as 24 target-absent trials. Thus, every cue condition was presented on 25% of target-present trials, and the occurrence of a target could not be inferred from the presence of a particular cue. Every participant completed at least five blocks, yielding a total of at least 30 trials in every condition and on every side.

Results and Discussion

Response Time

Figure 2 presents the RT data of the four participant groups. Because of the large group differences in reaction times, group results were analysed with separate repeated-measures analyses of variance (ANOVAs) with cue validity (valid, invalid), cue identity (similar, dissimilar) and target position (left/right visual field) as factors. In order to compensate for violations of the independence assumption in the ANOVA, we determined the probability-level of the resulting *F*-values using corrected degrees of freedom according to Box's criterion. We report only the effects of highest order.

The results of both healthy control groups were characterized by a two-way interaction between cue validity and cue identity [younger controls: $F(1,9) = 9.1, P < 0.01$; older controls: $F(1,9) = 25.2, P < 0.001$]. Both groups detected targets faster in the valid/similar cue (RT = 411 and 609 ms, respectively) and the invalid/dissimilar cue condition (401 and 564 ms) than the valid/dissimilar cue condition (446 and 668 ms). Similar results were obtained from RH-damaged control patients. There

was a two-way interaction between cue validity and cue identity [$F(1,6) = 8.7, P < 0.01$] due to faster RTs to targets following valid/similar cues (666 ms) than targets following valid/dissimilar cues (764 ms) or invalid/similar cues (725 ms). Importantly, there was no sign of contralesional slowing (see Fig. 2), in agreement with our criterion to include only patients without signs of neglect in this group. Thus, a consistent finding in both control groups and RH-damaged patients was that similar cues presented at target location facilitated processing compared with dissimilar cues.

In contrast to healthy participants and patients without neglect, the performance of neglect patients clearly depended on the side of target presentation (see Fig. 2). Whereas the pattern of RTs to ipsilesional targets in the different cueing conditions was comparable to RH-damaged patients, reactions to contralesional targets in the invalid/similar condition were dramatically slowed. This was confirmed by an ANOVA revealing a three-way interaction between cue validity, cue identity, and target position [$F(1,5) = 6.1, P < 0.05$], indicating slower detection of contralesional targets following invalid/similar cues (1296 ms) compared with all other conditions (822–967 ms). Remember that the spatial orienting account of Posner and Petersen (1990) predicted that all ipsilesional cues should attract attention to the same degree. This prediction is clearly contradicted by the data: compared with invalid/dissimilar cues, similar cues increased RT to contralesional targets by 39% (range 23–60%) in neglect patients (RH-control mean = -0.4%, range = -17 to +14%).

In order to compare directly the results of older controls and both patient groups, we calculated a space-coherence index (SCI) as follows: $SCI = (RT_{invalid\ cue} - RT_{valid\ cue}) / (RT_{invalid\ cue} + RT_{valid\ cue})$. The SCI reflects the extent to which the speed of target detection depends on cue validity. A positive SCI indicates a processing cost, whereas a negative SCI reflects a processing advantage for targets following an invalid cue compared with a valid cue. An ANOVA with the factors group, cue identity, and target position revealed a significant three-way interaction [$F(2,22) = 3.38, P < 0.05$], which was explained by neglect patients having higher contralesional SCIs following similar cues than older controls and RH-controls, while these two groups did not differ from each other (Fig. 3A). A significant asymmetry between SCIs to ipsilesional and contralesional targets in the similar-cue condition was only found in the neglect group.

Response Accuracy

Omission rates were very low in all control groups (young controls = 0.7–3%; older controls = 0–2.7%; RH-controls = 0–4% across conditions). Neglect patients missed between 0.5–7.3% targets across conditions, except in the invalid/similar condition where they missed 14.1% of contralesional targets. Between-group comparisons showed that they missed more contralesional targets in the invalid/similar condition than older controls and RH-controls (Mann-Whitney test, $P < 0.05$) while error rates of the latter two groups did not differ.

We finally evaluated the number of false-positive responses in trials without a target. All participants occasionally reacted to the cue rather than the target, and all made more false-positive responses to similar cues than dissimilar cues (Fig. 3B). This was reflected in an ANOVA with group, cue validity and cue identity as factors by a significant effect of cue identity ($F(1,22) = 18, P < 0.001$). There was, however, no overall difference between groups or an interaction involving the factor group. This finding indicates that neglect patients attempted to control the interference from similar cues and succeeded to do this as well as the other groups.

In summary, performance of healthy participants and patients without neglect was mainly characterized by enhanced target processing following valid/similar cues. This effect is in accord with a recent study using a similar paradigm with parietal patients without spatial neglect (Marangolo *et al.*, 1998). One possible explanation of this enhancement is perceptual facilitation: according to this account, a similar cue presented at the target location gates processing due to perceptual 'priming' while a dissimilar cue will mask the upcoming target, thus increasing RTs. A second possibility is that similar cues activated a response prior to the appearance of the target and thus prepared for faster responding. We will consider both possibilities in more detail in the general discussion.

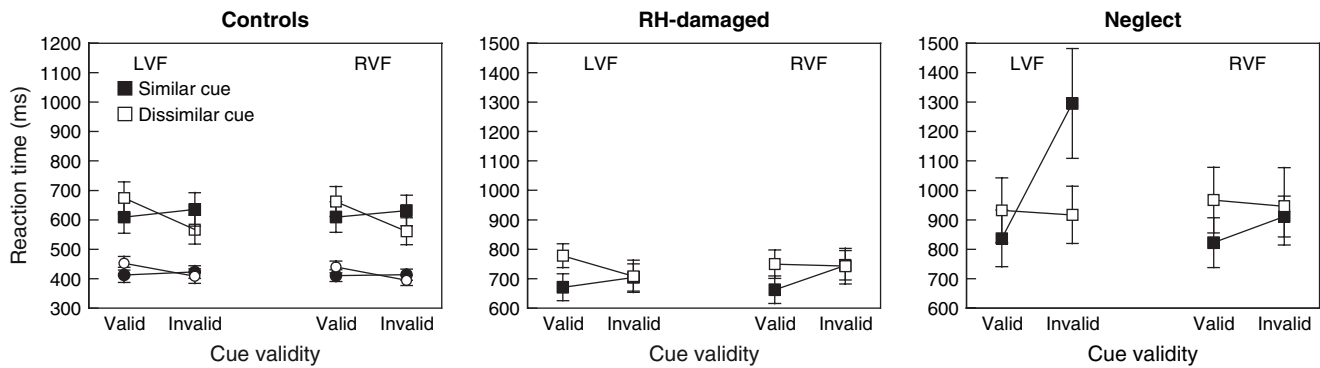


Figure 2. Mean reaction times in experiment 1 depending on cue validity, cue identity and target position for younger (circles) and older (squares) healthy controls, right-hemisphere-damaged patients without neglect, and neglect patients. Note that the data of healthy participants and patients are presented in different scales. Error bars represent the standard error of the mean (LVF/RVF: left/right visual field).

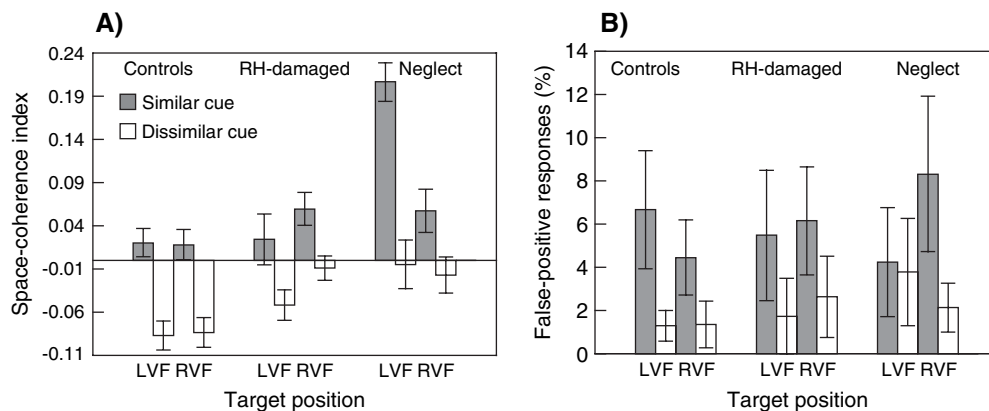


Figure 3. (A) Mean space-coherence indices in experience of older controls, right-hemisphere-damaged patients, and neglect patients for targets presented left or right of fixation that were cued with similar or dissimilar cues. (B) Mean per cent false-positive responses of these three groups to similar and dissimilar cues. Error bars represent the standard error of the mean (LVF/RVF: left/right visual field).

Neglect patients showed a clearly different response pattern. While similar cues presented at target location enhanced performance compared with dissimilar cues, invalid/similar cues produced a dramatic increase of RTs to contralesional targets. Critically, contralesional slowing of RT was not observed with invalid/dissimilar cues, suggesting that only cues that shared features with the target attracted attention ipsilesionally. We argued in the introduction that such a pattern would indicate that reflexive orienting of neglect patients depends on the behavioural salience of the cue. However, previous studies have reported that ipsilesional stimuli sharing visual features with contralesional stimuli may decrease awareness of the latter (Baylis *et al.*, 1993; Vuilleumier and Rafal, 2000; Ptak and Schnider, 2005). An alternative is therefore that similar cues had increased salience because of their visual relatedness, not their high behavioural relevance. In order to exclude this hypothesis, we examined in experiment 2 whether the same reaction time pattern as in experiment 1 would be found when the ipsilesional cue shared semantic attributes with the target, but was perceptually different.

Experiment 2

Materials and Methods

Experiment 2 used the same experimental design as experiment 1 with the exception that participants reacted to a target feature that was defined perceptually (the colour red) or conceptually (the word RED). Our first question was whether the critical finding of experiment 1, i.e. the slowing of RT to contralesional targets following invalid/similar cues, would be replicated in the condition where cue and target were

perceptually identical (i.e. both were colours or both were words). The more critical question was whether this slowing would be maintained when a contralesional target presented in one modality (e.g. colour) followed an invalid cue presented in the other modality (word). The hypothesis of purely perceptual interactions would be excluded if contralesional RTs following invalid/similar cues were slowed whether cues were perceptually similar or semantically similar to the target.

Participants

Thirteen new patients were recruited for the second experiment (see Table 1). Six patients, together with patient 6 from the first study presented left spatial neglect following right hemisphere stroke (three patients), haemorrhage (three patients) or parietal-temporal glioma (patient 8). The mean age was 65 years (range = 38–83 years), and patients were tested on average 60 days post-injury. All seven patients showed severe neglect as assessed with a cancellation task (mean = 15 of 15 contralesional omissions) and line bisection (mean = 20.7% ipsilesional deviation). Their performance was compared with seven RH-damaged patients without neglect (mean age = 69.8 years; range = 56–82 years), tested on average 64 days post-injury, who presented normal cancellation (mean = 0.9 contralesional omissions) and line bisection (mean = 1.6% ipsilesional deviation).

There was no significant difference between neglect and RH-control patients with respect to age [$t(12) = 0.6$, n.s.] or time since injury [$t(12) = 0.7$, n.s.]. However, neglect patients had a significantly higher number of contralesional omissions in the cancellation test (Mann-Whitney $z = 3.4$, $P < 0.001$) and a significantly larger ipsilesional bias on line bisection [$t(12) = 4.2$, $P < 0.001$].

Stimuli and Procedure

Experiment 2 was identical to the previous experiment except for three differences. First, participants were now instructed to press the 'yes' button when a target was presented, but to withhold reaction when the target display did not contain a target. This change in methodology was introduced in order to test whether the principal findings of experiment 1 could be reproduced with a go/no-go in contrast to a go/go paradigm that has more demands on set-shifting capacities. Secondly, the target display was presented simultaneously with four white horizontal lines situated above and below the left and right item. The lines were irrelevant to the task, but were presented in order to indicate precisely when the target display appeared on the screen. Given that neglect patients have difficulty to differentiate the onset times of ipsilesional and contralesional events (di Pellegrino *et al.*, 1997; Rorden *et al.*, 1997), a possible confounding factor for the findings of experiment 1 is that they confused cue displays with target displays. Thus, the white lines were an additional cue marking the onset of the target display and a signal to start search for the target. The most important difference of experiment 2 was that in addition to the stimuli used in experiment 1, the words 'ROUGE' ('red' in French) and 'VERTE' ('green') were used in the cue and target displays. The words were 1.3 cm high and 6.6 cm large, and were presented in white print with their inner border at the same position as the coloured forms.

The task was to react as quickly as possible and only when the target display contained either the red colour or the word 'red'. The different conditions are specified in Table 2. On trials with cue and target presented in the same modality, cues were perceptually similar to the target (the red circle when the target was the red circle OR the word 'red' when the target was the word 'red') or dissimilar (a green square when the target was the red circle OR the word 'green' when the target was the word 'red'). On trials with cue and target presented in a different modality, the similar cue carried the same meaning as the target but was perceptually dissimilar (the word 'red' when the target was the red circle OR a red circle when the target was the word 'red'), while the dissimilar cue carried a different meaning and was also perceptually dissimilar to the target (the word 'green' when the target was the red circle OR a green square when the target was the word 'red').

The target display contained two forms or a form and a word. On target-present trials there was a red circle or the word 'red' paired with a green square. On target-absent trials there was a green circle or the word 'green' paired with a green square. The target display remained on screen until reaction of the participant or for a maximum of 3 s. However, with this presentation time neglect patients 10 and 11 missed nearly all contralesional targets when these followed an invalid/similar cue. For these two patients presentation time of the target display was therefore increased to eight seconds. Patients completed at least five blocks of 96 trials, each containing 32 target-absent trials as well as 64 target-present trials that were orthogonally varied according to the factors cue validity, cue identity, cue modality (same as target, different than target) and target side.

Results and Discussion

The omission rates of RH-controls (0.9%) and neglect patients (3.2%) were low, and there were no statistical differences between cueing conditions. Neglect patients made not significantly more false positive responses than RH-controls (5.7 versus 1.9%).

As Figure 4 shows, the RT patterns of the two patient groups were comparable for ipsilesional targets, but clearly differed for contralesional targets. Irrespective of whether the modality of cue and target were the same or different, both groups showed a performance pattern that closely resembled the pattern of their respective groups in experiment 1. A repeated-measures ANOVA with factors cue validity, cue identity, target position and the new factor cue modality was performed on the data of RH-control patients. The highest-order effects of this analysis were significant two-way interactions between cue validity and identity [$F(1,6) = 13.92, P < 0.001$; explained by a tendency of valid/similar cues to enhance RTs compared with valid/dissimilar cues], and between cue identity and modality [$F(1,6) = 8.56, P < 0.01$], indicating that similar cues enhanced RTs more compared with dissimilar cues when they were presented in the same modality. In experiment 1, no effect involving target side reached significance, confirming that there was no contralesional slowing of RH-damaged control patients.

Neglect patients showed a clearly different pattern (Fig. 4). Just as in experiment 1, their data were described by a significant three-way

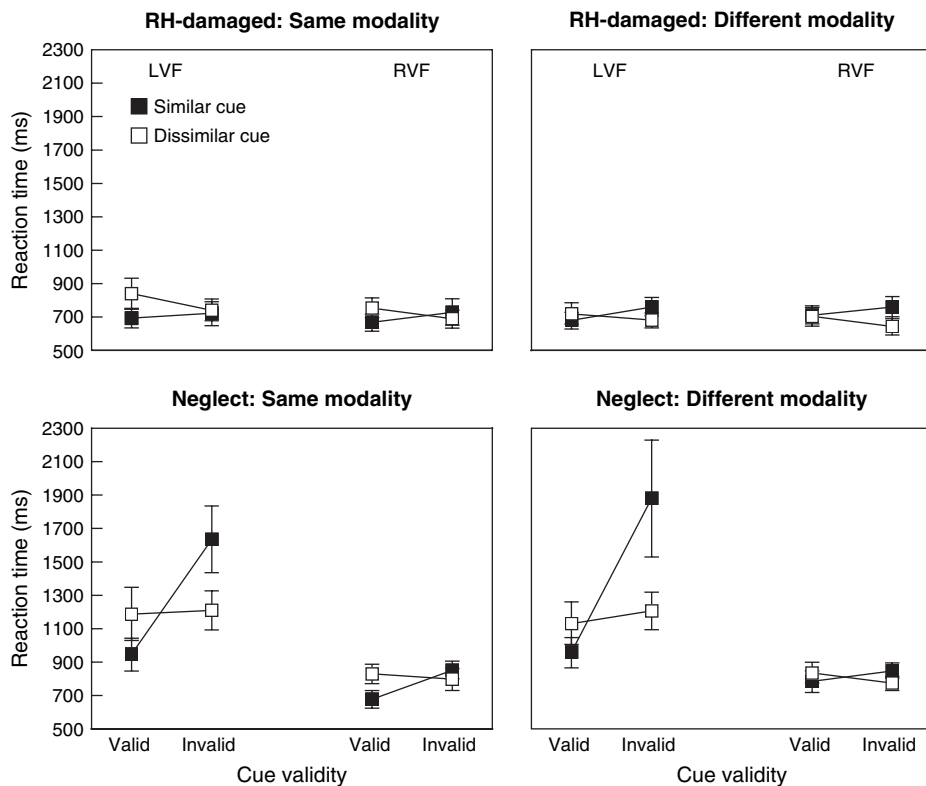


Figure 4. Mean reaction times in experiment 2 depending on cue validity, cue identity and target position for right-hemisphere-damaged control patients and neglect patients. Targets were presented in the same or in a different modality than the cue. Error bars represent the standard error of the mean (LVF/RVF: left/right visual field).

interaction between cue validity, cue identity and target position [$F(1,6) = 8.28, P < 0.01$]. Contralesional targets were detected slower following invalid/similar cues (1758 ms) than in all other conditions (953–1208 ms). Importantly, the invalid/similar cue generated the slowest RTs whether cue and target were presented in the same modality or not. Accordingly, the four-way interaction including the factor modality was not significant [$F(1,6) < 1$], indicating that the performance pattern was similar for same-modality cues and different-modality cues.

In order to compare directly the performances of the two groups, we performed a mixed ANOVA with factors group, target position, cue identity and modality on the SCIs of the patients (Fig. 5). Remember that a positive SCI indicates a processing cost and a negative SCI a processing advantage for targets following an invalid cue compared with a valid cue. The analysis revealed a three-way interaction between factors group, target position and cue identity [$F(1,13) = 8.01, P < 0.01$], indicating that neglect patients had higher contralesional SCIs following similar cues (mean = 0.28) than RH-controls (mean = 0.04). Further, only neglect patients showed a significant asymmetry between SCIs to ipsilesional and contralesional targets in the similar-cue condition. Importantly, the four-way interaction involving the factor modality was not significant [$F(1,13) < 1$], suggesting that same-modality and different-modality cues affected performance comparably.

These data confirm the finding of experiment 1 that ipsilesional stimuli similar to the target attract attention of neglect patients far more than dissimilar cues. Experiment 2 extends this finding by showing that ipsilesional attraction of attention is at least as strong with semantically similar cues as with perceptually similar cues. However, since the colour cue and the word cue were behaviourally relevant, there are two possibilities to explain this finding. The first is that all semantically related cues attract attention, whether they are behaviourally salient or

not. The second is that only relevant cues attract attention, whether they are semantically related or not. In order to distinguish between these possibilities, we repeated experiment 2 with neglect patients 6, 11 and 12, but instructed them to react only to the colour target while disregarding the word target. If semantic similarity was crucial, reflexive orienting towards ipsilesional, semantically related word cues should still be observed, although these cues were now irrelevant. In contrast, if behavioural salience of the cue was crucial, the word cue should cease to attract attention ipsilesionally since it was now behaviourally irrelevant.

The new instruction did not influence RTs to the colour target when it followed the colour cue. In the critical invalid/similar condition, mean RTs to contralesional targets were 1356 ms when colour and word were relevant and 1294 ms when only colour was relevant. Accordingly, a four-way ANOVA with cue validity, cue identity, target position, and relevance of the word cue as factors revealed a three-way interaction between cue validity, cue identity and target position [$F(1,2) = 5.86, P < 0.001$] due to slowed RTs to contralesional targets following invalid/similar cues. Importantly, this effect did not interact with the factor relevance [$F(1,2) < 1$], indicating that the relevance of the word cue did not alter the impact of the colour cue. In contrast, when only colour was relevant, RTs were clearly faster when the target followed the (now irrelevant) word cue (Fig. 6). In the invalid/similar condition, contralesional targets were detected on average after 1968 ms when the word was relevant, but after 884 ms when it was irrelevant. This was reflected in a four-way interaction between cue validity, cue identity, target position and relevance of the word cue [$F(1,2) = 4.96, P < 0.001$].

Summarized, these data confirm that ipsilesional cues similar to the target attract attention of neglect patients, resulting in a reflexive orienting bias. The new finding of experiment 2 is that cue–target

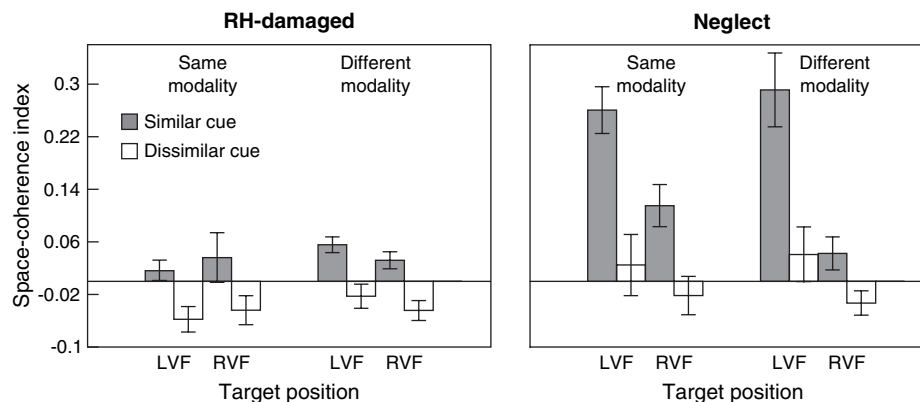


Figure 5. Mean space-coherence indices in experiment 2 for targets presented left or right of fixation that were cued by similar or dissimilar cues. Targets were presented in the same or in a different modality than the cue. Error bars represent the standard error of the mean (LVF/RVF: left/right visual field).

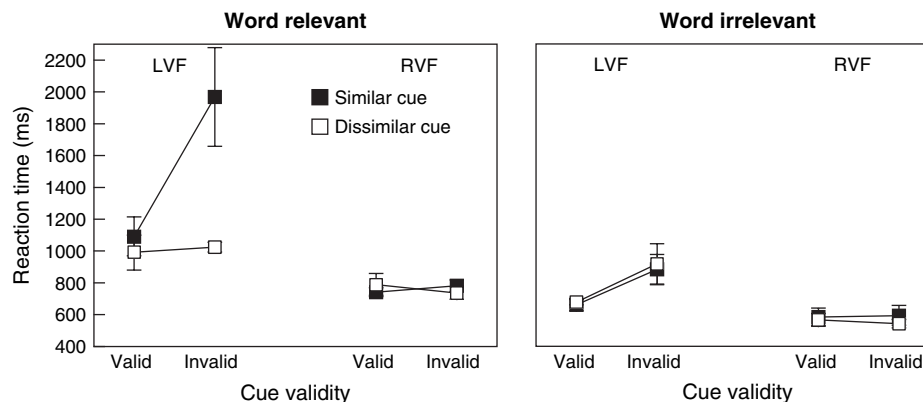


Figure 6. Mean reaction times in experiment 2 to colour targets following word cues depending on cue validity, cue identity and target position when the word cue was relevant and when it was irrelevant. Error bars represent the standard error of the mean (LVF/RVF: left/right visual field).

similarity does not have to be perceptually defined; semantic similarity is sufficient to generate attentional attraction. However, as the results of three neglect patients showed semantically similar cues only attracted attention when the semantically related stimulus was also an action-target, indicating that attentional attraction was determined by the behavioural salience of the cue stimulus.

General Discussion

Pathological attraction of attention by ipsilesional items is one of the most predominant signs of the neglect syndrome (Mark *et al.*, 1988; Marshall and Halligan, 1989; De Renzi *et al.*, 1989; Gainotti *et al.*, 1991; Kinsbourne, 1993). In contrast to previous work mostly evaluating perceptual interactions between items presented in the intact and the impaired visual field (e.g. Eglin *et al.*, 1989; Ward *et al.*, 1994; Gilchrist *et al.*, 1996), our study provides evidence that the behavioural salience of an ipsilesional stimulus may interact with awareness of contralesional visual stimuli.

The principle finding of this study is a reflexive orienting bias of neglect patients towards ipsilesional cues that share behaviourally relevant features with the target. Similar cues were behaviourally salient for the participants because they had visual (experiment 1) or semantic features (experiment 2) that would have triggered a reaction if the identical stimulus was part of the target display. In contrast, target detection was unaffected by irrelevant ipsilesional cues. Prior to discussing the possible reasons for the absence of an orienting bias towards irrelevant cues and attempting an explanation of the bias towards relevant cues, we will first discuss facilitation effects observed in our results.

Facilitation Effects

Facilitation of stimulus detection was observed when a similar cue was presented at the position of the upcoming target. In this condition RTs of healthy participants and RH-damaged control patients were faster compared with when a valid cue was perceptually dissimilar to the target. In a similar paradigm, Marangolo *et al.* (1998) found that RTs of patients with chronic parietal damage were accelerated by similar cues and inhibited by dissimilar cues compared with a neutral cue, indicating that the difference between similar and dissimilar cues was attributable to perceptual facilitation as well as inhibition effects. Interestingly, although their patients did not have spatial neglect, they had decreased perceptual facilitation in the visual field contralateral to the lesion. In accord with this, our neglect patients tested in experiment 1 had decreased contralesional facilitation (95.5 ms compared with 145.1 ms ipsilesionally). However, in the mixed-modality experiment neglect patients also showed contralesional facilitation. This finding is incompatible with perceptual facilitation, as cue and target were always perceptually different, independent of whether the cue was relevant or not. It is therefore more plausible that relevant cues presented at the same location as the upcoming target activated a 'yes' response before the target was presented, and that patients were therefore prepared to generate a 'yes' response when the target appeared. It is interesting to note that facilitation due to response activation was more than three-times as large in the contralesional than in the ipsilesional visual field in experiment 2 (171 ms compared with 50 ms). This finding contrasts with the finding of Marangolo *et al.* (1998) of decreased contralesional perceptual facilitation after parietal damage.

Absence of a Disengagement Deficit with Irrelevant Cues

A surprising result was that neglect patients detected contralesional targets as fast as ipsilesional targets when these followed an invalid/dissimilar cue. This finding clearly contradicts the prediction outlined in the introduction that all ipsilesional cues should attract attention reflexively and should therefore lead to a large cost in contralesional target detection. The failure to find a validity effect with dissimilar cues might be explained by temporal aspects of our paradigm. In healthy participants peripheral cues trigger a fast-rising automatic (exogenous) as well as a slower-rising controlled (endogenous) orienting mechanism (Müller and Rabbitt, 1989). Automatic orienting has a transitory effect of 100–300 ms after cue onset and is thereafter replaced by the controlled mechanism. Studies that systematically varied the cue-target interval and the cue predictability suggest that the disengagement deficit of patients with spatial neglect mainly reflects impaired exogenous orienting, while controlled orienting mechanisms are slowed but relatively well preserved (Bartolomeo *et al.*, 2001; Bartolomeo and Chokron, 2002). According to this account, the absence of a detrimental effect of invalid/dissimilar cues may therefore reflect the fact that the exogenous ipsilesional bias had faded at onset of the target display (500 ms after cue onset) and had been replaced by the controlled mechanism — hence that at target onset neglect patients had voluntarily disengaged attention from the ipsilesional cue and shifted it back to the centre.

However, there are two difficulties with this interpretation. First, previous studies have shown that uninformative peripheral cues attract attention of neglect patients even if an interval between cue onset and target onset of 500 ms or more is used, suggesting that the automatic orienting mechanism may persist longer than in healthy participants (Bartolomeo *et al.*, 2001; Losier and Klein, 2001). This finding raises the question whether neglect patients would be able to shift attention to the peripheral cue and back to the centre within 500 ms after cue onset. A second problem is that the concept of purely stimulus-driven attentional capture by irrelevant cues has been challenged in recent psychological literature. Attentional capture has been observed with stimuli that differ from surrounding distracters with respect to a unique feature or their onset characteristics (Treisman and Gelade, 1980; Jonides and Yantis, 1988; Treisman and Gormican, 1988), and reflexive attentional capture by ipsilesional items appeared to be a major determinant of the neglect syndrome (Eglin *et al.*, 1989; Ptak and Valenza, 2005). However, there is increasing evidence that attentional capture is contingent on expectations and other observer biases (Folk *et al.*, 1992; Gibson and Jiang, 1998). In accord with this, some studies with neglect patients have shown that goal-directed processes may also influence the degree of contralateral neglect (Duncan *et al.*, 1999; Ptak *et al.*, 2002). Thus, if the degree of attentional capture depends on an induced observer bias, irrelevant cues will not capture attention to the same degree as similar cues. According to this possibility, in the present experiments irrelevant cues captured attention to a much lesser degree than relevant cues did because neglect patients were not set to attend to them.

Our data do not allow a definite distinction between the two hypotheses outlined above. Both possibilities raise the question whether a disengagement deficit with dissimilar cues would be found with shorter cue-target intervals — that is, when neglect

patients do not have enough time to shift attention from the cue back to the centre. For that case, the hypothesis of an exogenous ipsilesional bias predicts that a disengagement deficit should be observed with irrelevant cues while the hypothesis that attentional capture is contingent on the behavioural set of the subject predicts that even at shorter intervals irrelevant cues should not capture attention.

Disengagement Deficit with Behaviourally Relevant Cues

The essential finding of this study was the large disengagement deficit when contralesional targets followed an invalid/similar cue contrasted with the absence of a disengagement deficit with dissimilar cues. Why did similar cues presented to the intact visual field capture attention of patients with spatial neglect?

Current understandings of attentional failures in spatial neglect relate the ipsilesional shift of attention to biased competition processes (Desimone and Duncan, 1995; Duncan *et al.*, 1997). According to this account stimuli presented at ipsilesional locations might appear perceptually more salient and therefore dominate over the contralesional percept. However, this perceptual account would predict at least some capture of attention by dissimilar items, as reported in many extinction studies (e.g. Ward *et al.*, 1994; Gilchrist *et al.*, 1996; Ptak and Schneider, 2005). Further, a purely perceptual account is incompatible with the finding of attentional attraction by a word when a coloured form was the target and vice versa in experiment 2 since both word cues were perceptually different from the colour target.

An alternative possibility is that attentional competition occurred between stimuli that shared the same cognitive representation — be it perceptual or semantic (e.g. the abstract concept ‘red’). Several previous studies have shown that attentional capture by ipsilesional stimuli was higher when these stimuli shared features with the contralesional stimulus (Baylis *et al.*, 1993; Rafal *et al.*, 2002; Ptak and Schneider, 2005). This account has the advantage to explain why neglect patients were slowed following an ipsilesional/similar cue when it was presented in a different modality than the target. However, it also predicts cross-modal interactions independently of the behavioural salience of the cue and does not therefore explain why the word cue influenced processing of the colour target only when it was behaviourally relevant. This finding demonstrates that cross-modal inhibition of a colour target by a word cue depends on whether the word cue is also defined as target — that is, whether it is behaviourally salient. The effect is reminiscent of our previous report of a patient who showed less extinction for target features to which he was cued to attend and more extinction for unattended features (Ptak *et al.*, 2002). Both findings demonstrate that neglect patients are able to generate arbitrary action-goals and that these goals will influence the degree of attentional attraction by ipsilesional stimuli.

In our discussion of the lack of a disengagement deficit with dissimilar cues, we proposed that attention of neglect patients is reflexively captured by ipsilesional cues and then voluntarily shifted back to fixation prior to target appearance. The distinction of two attentional processes — one fast and automatic, the other slow and voluntary — predicts that

disengagement deficits for large cue-target intervals are based on the fact that attention is maintained voluntarily on the cue, which is in accord with the finding that the disengagement deficit persists for longer cue-target intervals when cues are predictive of target location compared with when they are unpredictable (Bartolomeo *et al.*, 2001). However, in our study cues were always unpredictable of the target location and there was no reason for maintaining attention voluntarily more on the relevant than the irrelevant cues. Moreover, disengagement deficits of neglect patients have been shown to persist for cue-target intervals of 500 ms (the interval used in our experiments) or more even when unpredictable cues were used (Farah *et al.*, 1989), suggesting that attention of neglect patients may be controlled exogenously for much longer than attention of healthy participants. This would explain the disengagement deficit with relevant cues, but conflicts with the absence of a disengagement deficit with irrelevant cues. However, it is possible to resolve this difficulty by assuming that the duration of exogenous cueing effects depends on the type of cue used: reflexive attentional capture is short-lasting with irrelevant cues but long-lasting with relevant cues. One possible shortcoming of this interpretation is that the claimed covert attentional effects could partly be confounded with eye movements towards ipsilesional cues. Even though we instructed participants to keep fixation steady throughout an experimental trial, patients may have fixated occasionally the ipsilesional cue. However, there is ample psychological and physiological evidence that the systems underlying visual attention and eye movements are closely linked (Kustov and Robinson, 1996; Corbetta *et al.*, 1998; Perry and Zeki, 2000), and that attentional orienting precedes eye movements (Hoffman and Subramaniam, 1995; Deubel and Schneider, 1996). Even if we assumed that neglect patients made eye movements on every trial (which is implausible as we periodically checked for the presence of eye movements) attentional capture by relevant ipsilesional cues would not be refuted.

A final implication of our study concerns the neural systems involved in evaluation of behavioural salience. The inferior parietal lobule and the temporal-parietal junction have been identified as the critical regions for reflexive spatial orienting (Friedrich *et al.*, 1998; Rafal, 1998). Neurophysiological studies have shown that activity of some cells in the parietal cortex is modulated by the behavioural salience of a stimulus (Gottlieb *et al.*, 1998; Colby and Goldberg, 1999; Constantinidis and Steinmetz, 2001). These cells are not activated by visual stimuli presented in their receptive fields unless the stimuli are defined as saccade targets. It is not known to what extent cells in the human inferior parietal lobe and the temporal-parietal junction are involved in the evaluation of stimulus relevance. Nevertheless, our results provide a demonstration that reflexive orienting may directly be modulated by the behavioural salience of a stimulus.

Notes

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