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RESEARCH ARTICLE

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Modulating the attentional bias in unilateral neglect: the effects of the strategic set

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Abstract Left unilateral neglect is a neurological condition characterized by an impairment in orienting and responding to events occurring on the left side. To gain insight into the brain mechanisms of space processing and to provide theoretical foundations for patient rehabilitation, it is important to explore the attentional bias shown by neglect patients in the light of existing models of normal attentional orienting. Three experiments tested the hypothesis that attentional bias in neglect involves primarily exogenous, or stimulus-based, orienting of attention, with relatively preserved endogenous, or voluntary, orienting. Six patients with right hemisphere damage and left unilateral neglect and 18 age-matched participants without brain damage performed a cued reaction time (RT) task to targets which could appear in one of two lateral boxes. Cues consisted of a brief brightening of the contour of one of the boxes. The target followed the cue at 150, 550, or 1000 ms stimulus-onset asynchrony (SOA). In experiment 1, the cues were not informative about the future location of the target, and thus elicited a purely exogenous orienting of attention. Controls showed slowed RTs to the cued locations at SOAs > 150 ms, consistent with the notion of inhibition of return (IOR). Neglect patients had no evidence of IOR for right targets; they showed a disproportionate cost for left targets preceded by right (invalid) cues; this cost was maximal at the shortest SOA, consistent with the idea of a biased exogenous orienting in neglect. In experiment 2, 80% of the cues were valid (i.e., they correctly predicted the location of the impending target), thus inducing an initially exogenous, and later endogenous, attentional shift toward the cued box. Neglect patients showed again a cost for left invalidly cued targets, which this time persisted at SOAs > 150 ms, as if patients' attention had been cued to the right side not only exogenously, but also endogenously, thus rendering more difficult an endogenous reorienting toward the left. In experiment 3, only 20% of the cues were valid, so that the best response strategy was to endogenously orient attention toward the box opposite to the cued one. Controls were able to take advantage of invalid cues to rapidly respond to targets. In this condition, neglect patients were able to nullify their spatial bias; they achieved their fastest RTs to left targets, which were in the range of their RTs to right targets. However, for neglect patients fast responses to left targets occurred only at 1000 ms SOA, while controls were able to redirect their attention to the uncued box already at 550 ms SOA. Altogether, these results suggest that endogenous orienting is relatively spared, if slowed, in unilateral neglect.

Keywords Spatial attention · Exogenous orienting · Endogenous orienting · Unilateral neglect · Brain damage

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Introduction

Left unilateral neglect is a severely disabling condition resulting from right hemisphere damage. Its presence negatively affects patients' motor recovery (Denes et al. 1982) and social rehabilitation. Such patients live in a halved world, being unable to orient or respond to events occurring on the left side. Although deficits at different levels of impairment may be at work in different patients, the frequency and severity of attentional problems in neglect patients have been repeatedly underlined (see Bartolomeo and Chokron 2001 for review). A precise characterization of these deficits can shed light on the brain mechanisms of space processing, and is necessary in order to devise rational strategies of rehabilitation. Recent advances in the knowledge of the mechanisms of spatial attention in normals may help in characterizing these deficits.

The work of Posner and coworkers (see Posner 1980 for review) has contributed significantly to our understanding of the operations of spatial attention. These authors developed a manual reaction time (RT) paradigm to study the spatial orienting of attention. In this paradigm, subjects are presented with three boxes horizontally arranged on the computer screen. They fixate the central box and respond by pressing a key to a target (an asterisk) appearing in one of the two adjacent boxes. The target is preceded by a cue designating one of the lateral boxes. The cue can be either "central" (a centrally presented arrow pointing toward one of the two lateral boxes in which the target is to appear) or "peripheral" (a brief brightening of one lateral box). *Valid* cues correctly predict the box in which the target will appear, whereas *invalid* cues indicate the wrong box. Valid cues usually improve accuracy and RTs for target detection, whereas invalid cues have a detrimental effect on performance; the advantage for valid cue-target trials and the cost for invalid trials is referred to as cue validity effect. This effect suggests that the cue prompts an attentional orienting toward the cued location, which speeds up the processing of targets appearing in that region and slows down responses to targets appearing in other locations. The degree of predictiveness of cues influences the type of attentional processes. Typically, a majority (e.g., 80%) of cues are valid; in this case, most cues correctly predict the future site of the target, and are said to be spatially *informative*. The experimental paradigm may require the cue to be *non-informative*; in this case, the target will appear with equal probability in the cued or in the uncued location. Peripheral non-informative cues attract attention automatically, or exogenously (Jonides 1981; Müller and Rabbitt 1989).[1] This exogenous attentional shift (revealed by a cue validity effect) is typically observed only for short stimulus onset asynchronies (SOAs) between cue and target. For SOAs longer than ~300 ms, however, uncued targets are responded to faster than cued targets (Posner and Cohen 1984; Maylor and Hockey 1985; Rafal and Henik 1994), as if attention was inhibited from returning to previously explored objects (but see Berlucchi et al. 2000). This phenomenon has been labeled *inhibition of return* (IOR; Posner et al. 1985) or *ipsilateral inhibition* (Berlucchi et al. 1989). When peripheral informative cues are used, on the other hand, the cue validity

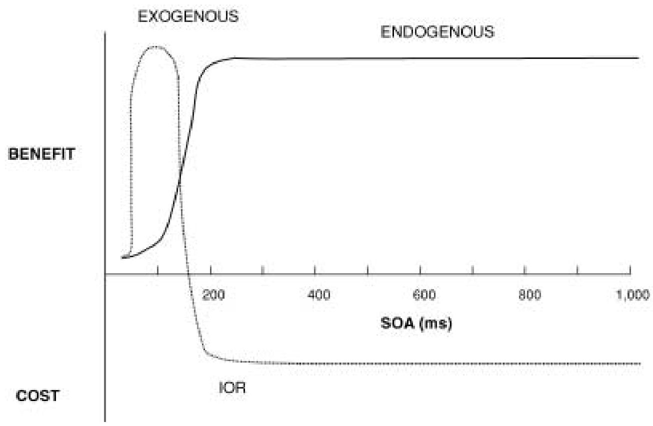

Fig. 1 Time course of the costs and benefits associated with exogenous and endogenous orienting of attention toward a cued location (*SOA* stimulus onset asynchrony) (modified from Müller and Findlay 1988)

effect persists even at longer SOAs, thus suggesting that the initial exogenous shift is later replaced by a slower, more endogenous shift toward the same location (Müller and Findlay 1988; see Fig. 1). This endogenous shift would be motivated by strategic considerations, because subjects are aware that targets will appear with high probability at the cued location.

The present study aimed at exploring the characteristics of attentional orienting in left unilateral neglect. Though there is little doubt that neglect patients show a strong attentional bias, it is not clear which mechanisms of attentional orienting are precisely implicated in unilateral neglect. Posner et al. (1984) had six right brain-damaged (RBD) and seven left brain-damaged (LBD) patients with predominantly parietal lesions perform the cued detection task described above. Cues were either central or peripheral, but always informative of the future target location; 80% of cues were valid and 20% invalid. Patients were disproportionally slow when a target occurring on the side opposite to the brain lesion was preceded by an invalid ipsilesional cue. This RT pattern was present in both RBD and LBD patients, but considerably larger in RBD patients, and evident with both central and peripheral cues. Posner et al. (1984) termed this effect "extinction-like RT pattern" because it was reminiscent of extinction of contralesional stimuli in double visual stimulation, and argued that it resulted from an impaired disengagement of attention from the ipsilesional side, when attention had to move to a contralesional target. This notion may be used to explain the behavior of patients with unilateral neglect; these patients would neglect the contralesional side of space because their attention cannot easily disengage from ipsilesional objects. However, the parietal patients in Posner et al.'s (1984) study showed little or no neglect on paper-and-pencil tests (no neglect in five patients, minimal neglect in two, mild in five and moderate in one). Thus, in this study there was no direct evidence for a relationship between the observed extinction-like RT pattern and neglect.

[1] Other authors contend that the observed facilitation does not indicate attentional orienting, but is rather of sensory origin, because it results from energy summation between cue and target (see Maruff et al. 1999 for review and recent data about this debate).

Morrow and Ratcliff (1988) tested 12 RBD and 10 LBD patients using an RT paradigm with peripheral informative cues (75% of the cues were valid and 25% invalid). All patients had lesions including the parietal lobe, contralesional neglect, or both. Only RBD patients showed a significant extinction-like RT pattern. The observed cost for contralesional targets preceded by invalid cues correlated with a measure of left neglect, thus suggesting a causal relationship between the two phenomena.

However, for such a right-disengagement deficit to produce clinical left neglect, attention must logically have been engaged to the right *before* the occurrence of the disengagement problem. D'Erme et al. (1992) produced evidence for such an early rightward engagement by manipulating the Posner RT paradigm. D'Erme et al. contrasted the traditional task in which targets appeared in boxes with a condition in which targets appeared on a blank screen, not surrounded by boxes. The presence of the boxes considerably increased the left/right RT difference for neglect patients, as if the right-sided box acted as an invalid cue for left targets. Thus, the mere appearance on the computer screen of the placeholder boxes elicited a shift of patients' attention toward the rightmost box. Because the boxes were not informative about the future location of the targets, the type of orienting elicited by the boxes could best be characterized as reflexive, or exogenous, as opposed to the voluntary, or endogenous orienting elicited by central cues or by peripheral informative cues (Müller and Rabbitt 1989). Thus, D'Erme et al. (1992) proposed that the attentional imbalance in neglect was primarily one of exogenous attention, in keeping with previous similar suggestions based on the apparent "automaticity" of rightward attentional attraction in left neglect (Gainotti et al. 1991).

Làdavas et al. (1994) also addressed the issue of exogenous vs endogenous orienting of attention in neglect. They noticed that the use of informative cues in the Posner et al. (1984) study made it difficult to discriminate between these two modes of orienting, and contrasted the effects on target detection of central informative cues (an arrow presented near fixation) with that of peripheral non-informative cues (an arrow presented above one of the placeholder boxes). Làdavas et al. (1994) found that central cues pointing toward the left were able to decrease the number of omissions of left targets in neglect patients (RTs for left targets were not analyzed because of the high rate of omissions[2]), whereas peripheral cues presented on the left side had no significant effect on patients' accuracy. The authors concluded that neglect patients were not able to orient their attention leftward exogenously, but they could do so voluntarily (see also Smania et al. 1998). However, besides their different effects on exogenous and endogenous orienting, central and peripheral cues might act on distinct stages of information processing (an early perceptual stage for peripheral cues, and a late perceptual or a decision stage for central cues: Riggio and Kirsner 1997), thus rendering difficult any direct comparison between their respective effects on performance. Moreover, in the case of patients suffering from a spatial bias, the different spatial localization of central and peripheral cues may complicate the interpretation of the results.

In the present study, we explored attentional orienting in left unilateral neglect by using exclusively peripheral cues, whose informative value was systematically manipulated. In experiment 1, cues were not informative, and targets could appear either in the cued or in the uncued box with equal probability. This situation should evoke a purely exogenous shift of attention toward the cued box (Müller and Rabbitt 1989), particularly at short SOAs (Müller and Findlay 1988; see also Fig. 1). In experiment 2, cues predicted the future location of the target with 80% accuracy, thus evoking an exogenous orienting of attention at short SOAs and an endogenous orienting at long SOAs (Müller and Findlay 1988). In experiment 3, most cues (80%) were invalid. In this situation, cues should normally prompt an initial exogenous orienting toward the cued box, later followed by an inhibition of this exogenous shift, to be replaced by an endogenous shift toward the uncued box (Posner et al. 1982). Thus, for long enough SOAs this condition explores endogenous orienting in relative isolation. In a separate experiment, subjects performed a similar target detection task, but with cues occurring only at the central box (neutral condition).[3] Results of neutral condition were used to discriminate between costs and benefits of the various cueing conditions in experiments 1–3.

Materials and methods

Subjects

Six patients with right unilateral hemispheric lesions and signs of left unilateral neglect and 18 age-matched controls without neurological impairment participated in the study after giving informed consent. The study was carried out by following the guidelines of the Ethics Committee of the Cochin Hospital in Paris. All participants were right handed. Controls' mean age was 62.83 years (SD=10.19, range 44–77). Patients were selected on the basis of their having signs of unilateral neglect. No patient had hemianopia, but all showed visual extinction for left targets on double simultaneous visual stimulation. Unilateral neglect was assessed by means of tests of line, letter and shape cancellation, line bisection, and copy of a landscape (see Bartolomeo and Chokron 1999a for a detailed description of the tests). Table 1 shows the demographic and clinical characteristics of patients, as well as their performance on the neglect battery. Figure 2 shows the lesion location for five patients. All patients had predominantly retrorolandic lesions, with the exception of patient 5, who suffered from a subcortical frontal lesion as a consequence of a stroke in the territory of the anterior cerebral artery.

[2] Probably resulting from the very short time (75 ms) of target presentation.

[3] We chose a centrally presented cue rather than a simultaneous bilateral cueing of the peripheral boxes because the latter would probably have amounted to right cueing for left neglect patients (see D'Erme et al. 1992), who, by definition, do not process bilateral events in a symmetrical way.

Table 1 Demographic and clinical characteristics of left neglect patients. Their performance (left/right correct responses) on the neglect battery is also reported

Patient	Sex, age, years of schooling	Onset of illness (days)	Etiology	Overlapping figures (max. 10/10)	Line cancellation (max. 30/30)	Letter cancellation (max. 30/30)	Bell cancellation (max. 15/15)	Line bisection (% rightward deviation)
1	M, 64, 12	22	Ischemic	8/9	21/27	14/19	4/12	17
2	M, 53, 5	186	Hemorrhagic	10/10	15/29	0/16	1/11	33
3	F, 45, 11	144	Hemorrhagic	10/10	14/28	13/28	8/14	10
4	M, 58, 8	82	Ischemic	10/10	2/28	10/23	0/9	9
5	M, 58, 8	90	Ischemic	9/10	29/29	0/18	1/11	37
6	M, 78, 13	38	Hemorrhagic	8/10	29/27	2/25	1/13	29

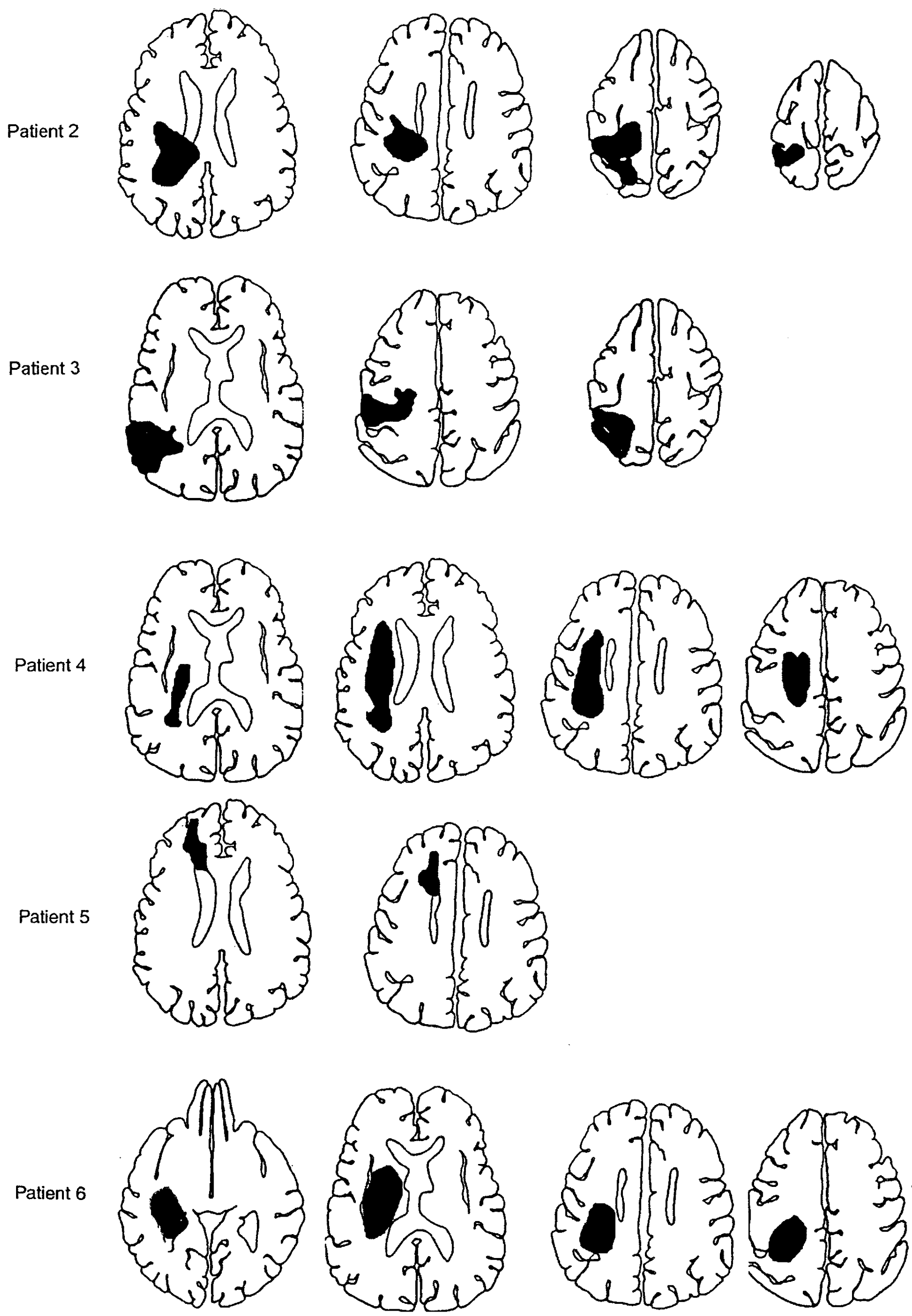

Fig. 2 Schematic representation of the lesion for five neglect patients on the Damasio and Damasio's (1989) templates

Apparatus and stimuli

Stimulus presentation and response collection were controlled by the Psychlab software (Gum 1996). Three black empty square boxes, with a 10-mm-long, 0.34-mm-thick side, were displayed on a white background. The boxes were horizontally arranged, the central box being located at the center of the screen. The central box contained a small black rectangular fixation point (1.02×1.34 mm). Distance between boxes was 30 mm. Cues consisted of a 300-ms thickening (from 0.34 to 0.68 mm) of the contour of one box. The target was an asterisk 4.40 mm in diameter, appearing inside one of the lateral boxes, at a retinal eccentricity of about 3.83°.

Procedure

Participants sat in front of a computer monitor at a distance of approximately 50 cm. Each trial began with the appearance of the three placeholder boxes for 500 ms. Then the cue followed during 300 ms. The target appeared at a variable SOA (150, 550 or 1000 ms) from the cue, and remained visible until a response was made, in order to minimize the possibility of omissions. Participants were instructed to maintain fixation on the fixation point and to respond to the target as quickly and accurately as possible, by pressing the center of the space bar with their right index finger. Eye movements were observed by one of the experimenters. After an intertrial interval of 1000 ms, a new trial began. Before each experiment, participants were informed about the level of predictiveness of the cue (50%, 80%, or 20%). They were instructed to respond exclusively to the targets, without paying attention to the cues. Before the conditions with informative cues (experiments 2 and 3), however, it was stressed that cues could in most cases help to respond more rapidly. On the other hand, before the conditions with non-informative cues (experiment 1 and neutral condition), it was explained that cues were useless to predict the target position. Each experiment consisted of two blocks of 150 trials preceded by 30 practice trials. A brief period of rest was allowed between blocks. Participants performed first experiment 2; after a 10-min rest, they performed experiment 3. The following day, they performed experiment 1 and the neutral condition, again separated by a 10-min rest.

Analysis of results

Response times exceeding the range of 150–5000 ms were discarded from analysis. This resulted in the exclusion of 2% of responses for controls and of 5.5% for patients. For each experiment and each group of participants, median RTs were entered in a repeated-measures analysis of variance (ANOVA), with side (left, right), cue (valid, invalid, neutral) and SOA (150, 550, 1000 ms) as factors. Theoretically relevant results were followed up by paired comparisons.

Experiment 1: non-informative cues

In this experiment, the target could appear in the cued or in the uncued box with equal probability, thus prompting an exclusively exogenous orienting of attention toward their location (Müller and Rabbitt 1989). In normal subjects, this exogenous shift should result in a cue validity effect for short SOAs; for longer SOAs, valid trials should be affected by the IOR phenomenon, and show a cost as compared to invalid trials. If neglect patients' attentional bias involves exogenous orienting, then these patients should show disporportionally slow responses for left targets preceded by an invalid right-sided cue, despite being aware that cues have no informative value. If endogenous orienting is relatively spared in neglect, the cost for left invalidly cued targets should be especially evident at short SOAs; with longer cue-target inter-

Table 2 Neglect patients' median RTs (ms) for experiment 1 (50% cue predictiveness)

Patient	Left						Right					
	Valid			Invalid			Valid			Invalid		
SOA (ms)	150	550	1000	150	550	1000	150	550	1000	150	550	1000
1	646	565	680	957	803	564	649	576	588	602	569	575
2	963	960	1116	1270	1110	1133	812	965	819	918	783	1015
3	902	871	814	780	679	1198	599	648	640	617	693	636
4	539	583	691	811	713	602	574	531	645	603	595	689
5	876	791	900	1172	873	836	753	654	712	857	852	783
6	545	664	727	790	695	655	441	480	443	465	479	481

Table 3 Neglect patients' median RTs (ms) for experiment 2 (80% cue predictiveness)

Patient	Left						Right					
	Valid			Invalid			Valid			Invalid		
SOA (ms)	150	550	1000	150	550	1000	150	550	1000	150	550	1000
1	575	644	746	885	1226	1042	595	539	593	843	787	676
2	844	805	761	955	948	979	689	671	771	1249	1492	851
3	1300	2123	1216	1574	1691	1699	594	621	607	705	577	683
4	688	767	912	1328	1174	756	588	664	707	673	959	679
5	813	1086	882	1031	1063	984	751	675	713	1114	774	1283
6	649	771	513	1366	1263	1262	473	456	495	385	466	453

vals, patients should become able to use endogenous orienting to mitigate their attentional attraction toward a useless cue. The present experiment should also allow IOR to be explored in neglect patients. Using a target-target RT paradigm, we (Bartolomeo et al. 1999) have previously demonstrated that left neglect patients may show a facilitation for repeated rightward attentional shifts instead of the normal IOR. The present experiment should allow this notion to be tested in a different patient group and with a different (cue-target) paradigm.

Results and discussion

In order to facilitate comparisons, RTs for the three experiments and for the neutral condition are presented together in Fig. 3 for controls, and in Tables 2, 3, 4, 5 and Fig. 4 for neglect patients.

RTs for neglect patients were much slower than those of normal subjects, for all experiments and conditions. This pattern is consistent with the possibility of a general decrease in attentional resources in unilateral neglect (Robertson 1993; Bartolomeo and Chokron 1999b). In contrast to controls, who successfully maintained fixation, patients produced occasional saccades toward the targets, apparently without a definite preference for either side. Problems maintaining fixation, as well as other stable postures, are indeed to be expected in right brain-damaged patients, who often demonstrate motor impersistence (Kertesz et al. 1985; De Renzi et al. 1986). However, the occasional eye movements produced by our neglect patients are unlikely to have confounded the observed results, as discussed below.

Controls

The only main effect that emerged from the analysis of variance carried out on the results of experiment 1 was an effect of SOA, $F_{(2,34)}$=12.23, P<0.0001; RTs were faster with longer SOAs, consistent with the notion of an increasing anticipatory set with time elapsing after cue onset (see, e.g., Niemi and Näätänen 1981). The effect of SOA interacted with the type of cue, $F_{(4,68)}$=9.46, P<0.0001; at 150 ms SOA, validly cued trials evoked faster responses than invalid trials, $F_{(1)}$=24.05, P<0.0001, as expected by an effect of exogenous orienting toward the cued box. Consideration of the neutral condition suggests that the observed cue validity effect depended more on a cost for invalid trials than on an advantage for valid trials. It is possible that the central cue of the neutral condition alerted participants to respond rapidly, thus perhaps acting similarly to the non-predictive peripheral cues. At 550 ms SOA, there was no effect of validity of the cue (F<1); this could result from an interplay of decreasing facilitatory processes and increasing inhibitory processes (see Maylor 1985 and Fig. 1). At 1000 ms SOA, invalid trials were responded to faster than valid trials, $F_{(1)}$=13.87, P<0.005, as expected by the occurrence of an IOR phenomenon, now

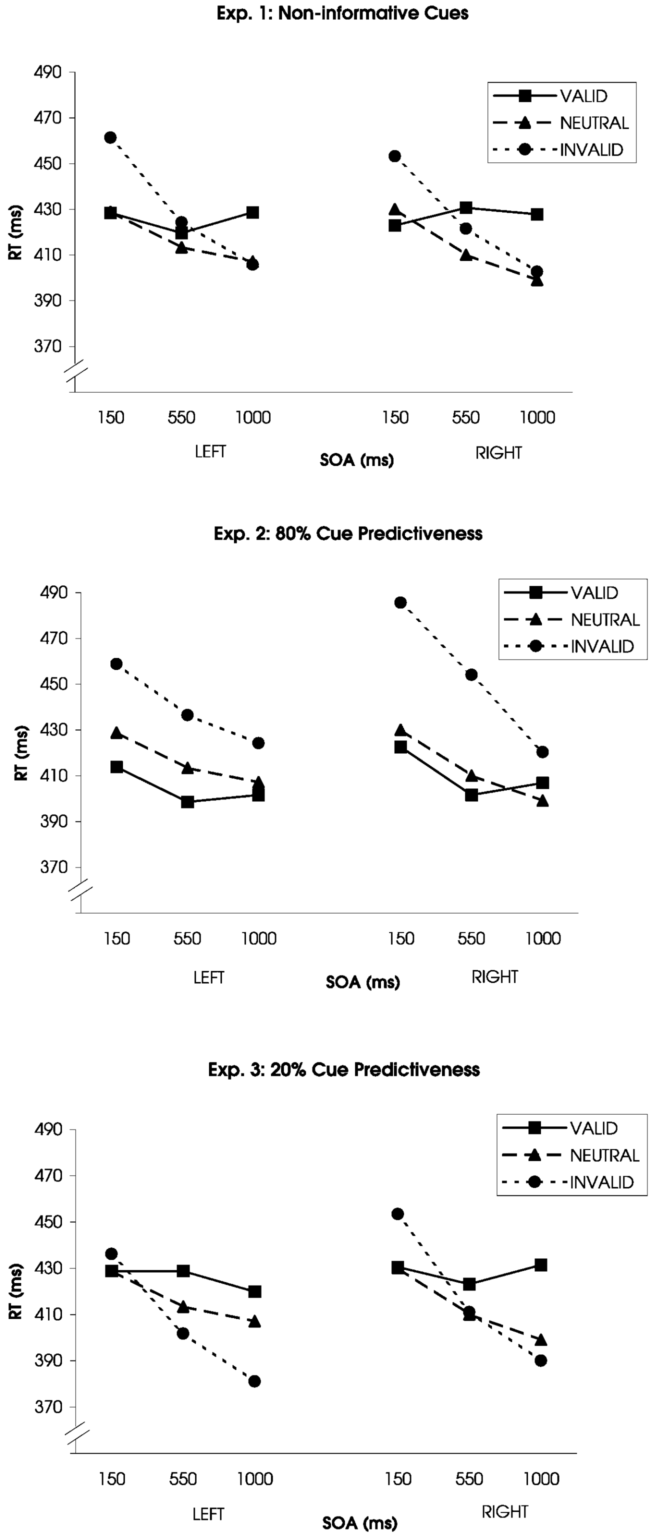

Fig. 3 Response times for normal participants in experiments 1–3

predominating on earlier facilitation. Comparison with RTs for the neutral condition reveals that the valid-invalid difference observed at 1000 ms SOA is indeed a true cost for valid trials (as predicted by the occurrence of IOR, Maylor and Hockey 1985), and not an advantage for in-

Table 4 Neglect patients' median RTs (ms) for experiment 3 (20% cue predictiveness)

Patient	Left						Right					
	Valid			Invalid			Valid			Invalid		
SOA (ms)	150	550	1000	150	550	1000	150	550	1000	150	550	1000
1	874	584	986	968	1023	586	742	795	726	763	613	637
2	817	840	952	1126	1144	1157	803	873	952	1062	1092	1038
3	448	516	2223	495	730	598	663	583	567	519	643	669
4	596	756	857	551	615	564	687	560	641	623	660	783
5	1412	1264	1156	1266	1123	985	819	867	1066	1064	1359	1184
6	722	605	554	992	793	544	551	477	393	563	504	485

Table 5 Neglect patients' median RTs (ms) for neutral condition

Patient	Left			Right		
SOA (ms)	150	550	1000	150	550	1000
1	742	745	692	705	707	638
2	992	1089	1213	1045	1038	1051
3	1258	1471	1134	580	609	585
4	633	649	668	562	549	588
5	934	995	973	852	922	857
6	1028	1220	1252	600	614	624

valid trials; RTs for valid trials are indistinguishable from those for the neutral condition at 150 ms SOA, $F<1$, but at longer SOAs they become slower, $F_{(1)}=8.28$, $P<0.01$. These findings confirm that exogenous orienting and its associated phenomena are normal in healthy elderly persons (Danckert et al. 1998).

In the present study, the condition with spatially non-informative cues was run the day after a condition with 80% cue predictiveness. This may raise the concern that participants found it difficult to treat the cues of experiment 1 as truly non-informative. Indeed, Hughes (1984) showed that when a test session employing non-informative cues follows another session employing informative cues an advantage for valid trials in the session using non-informative cues may occur which is greater than when the task with non-informative cues is performed first. This suggests that participants having previous experience with informative cues exerted some endogenous orienting also toward the non-informative cues. Note, however, that Hughes employed long SOAs, from 1000 to 2000 ms, whereas we found an advantage of valid over invalid trials at 150 ms SOA, an interval more apt to probing exogenous orienting. At 1000 ms SOA, our controls showed a typical IOR effect, consistent with the assumption that non-informative cues truly elicited an exogenous attentional orienting (compare the different pattern of results induced by informative cues in experiment 2). Surprisingly, Hughes found no signs of IOR with non-informative cues at SOAs≥1000 ms, even when the condition with non-informative cues was performed first (see his Table 1). This difference between the Hughes' study and ours probably results from the fact that Hughes explicitly instructed his participants to pay attention to the cues (Hughes 1984, p. 179), whereas we carefully avoided giving such instructions. Hughes' subjects might have thus endogenously oriented their attention toward the non-informative cues in order to comply with the test instructions. Preliminary data (reported in Appendix A) obtained in our laboratory with a test procedure similar to the one used in the present study, involving a different group of normal participants, who either performed the 50% cue validity condition previous to or subsequent to the 80% cue validity condition, clearly do not conform to Hughes' results. One can thus be reasonably confident that our experiment 1 primarily explored exogenous orienting of attention.

Neglect patients

Patients with left neglect responded faster to right than to left targets, $F_{(1,5)}=11.95$, $P<0.05$. They also showed an effect of the type of cue, $F_{(2,10)}=6.94$, $P<0.05$, because responses for valid trials were overall faster than RTs for neutral trials, $F_{(1)}=13.84$, $P<0.005$. In contrast to controls', neglect patients' RTs did not decrease with increasing SOAs, $F<1$. A cue validity effect was present for left targets at 150 ms SOA, $F_{(1)}=14.84$, $P<0.005$. The size of this effect was much larger for patients than it was for controls: 218 ms compared to 33 ms. For neglect patients, the observed validity effect for left targets is consistent with the phenomenon of extinction-like RT pattern (Posner et al. 1984). According to this interpretation, right cues summon patients' attention[4]; if the target

[4] Before cue onset, patients' attention was presumably already biased toward the right by the onset of the placeholder boxes (see D'Erme et al. 1992); this, however, was true for all experiments and conditions.

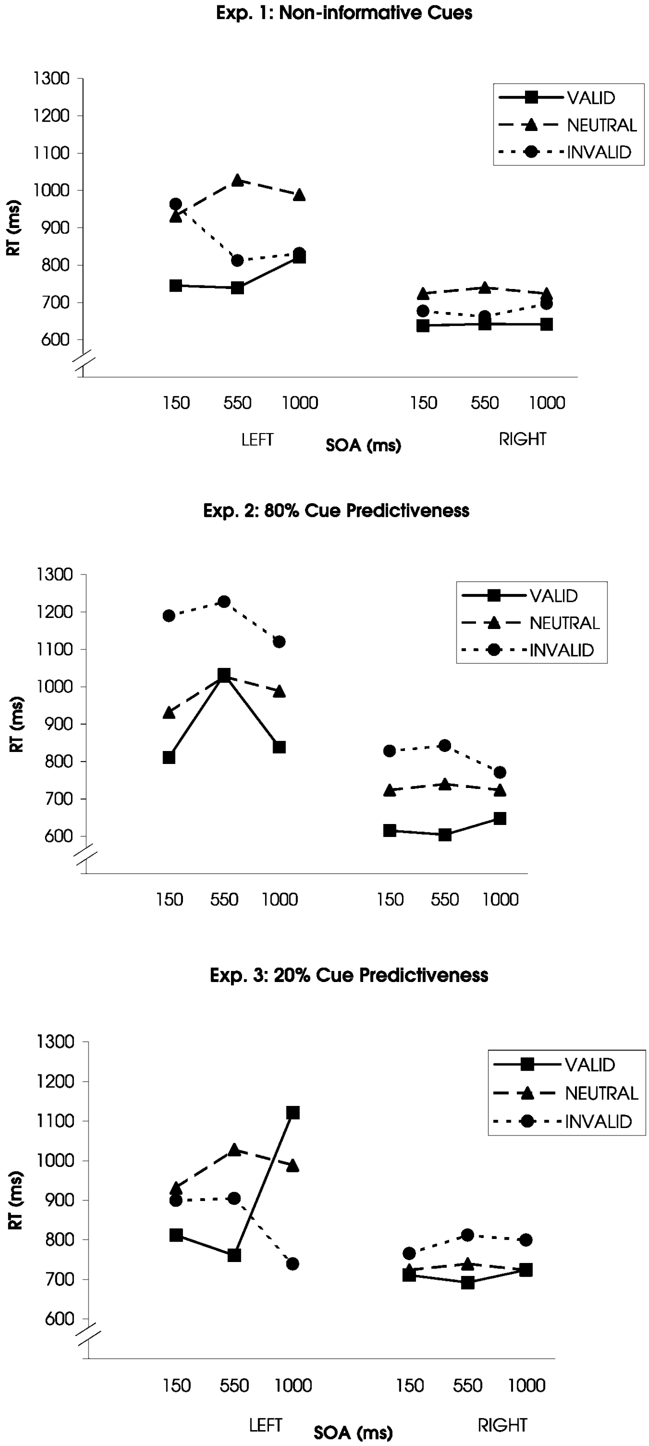

Fig. 4 Response times for neglect patients in experiments 1–3

then appears on the left side, responses are considerably slowed down by the fact that patients are unable to rapidly disengage attention from the right-sided box in order to move it toward the left. In the present experiment, cues were not informative, thus eliciting a purely exogenous orienting of attention; our findings thereby confirm that the attentional bias in unilateral neglect concerns exogenous orienting. Also consistent with the hypothesis that exogenous orienting is particularly biased in unilateral neglect is our finding that the validity effect for left targets was evident at 150 ms SOA, an interval which allows exogenous, but not endogenous, attentional shifts[5] (Müller and Findlay 1988). Similarly, Posner et al. (1984) and Morrow and Ratcliff (1988), using a paradigm in which most cues were valid, and Friedrich et al. (1998), who also employed a paradigm with non-informative cues, found the strongest evidence of extinction-like RT pattern at the shortest SOA employed (50 ms). In the present experiment, at 150 ms SOA neutral and invalid trials evoked similar RTs; these findings, analogous to those obtained by Posner et al. (1984) and by Morrow and Ratcliff (1988), argue against the possibility that eye movements might have determined the observed extinction-like RT pattern; should this have been the case, the centrally presented neutral cues would not have produced such a cost for left-sided targets. In the present experiment, at SOAs longer than 150 ms the deficit of disengagement was even greater with neutral trials than with invalid trials; this further confirms that eye movements played no role in this effect. The shortening of RTs to invalidly cued left targets with increasing SOAs might be due to the fact that patients, who were aware of the non-informative nature of the cues, could on some occasions endogenously inhibit their reflexive orientation toward right-sided cues, and try to spread their attention over the entire stimulus display. This would explain why the cost for left targets was more long-lasting in the neutral condition than in the condition with lateralized cues; in the neutral condition, with central cues, no such location-based inhibition was possible. Indeed, as Rafal and Henik (1994) have proposed, people might be able to "inhibit their reflexive orienting only when they can predict its location and develop a strategic set to inhibit signals there" (p. 18). Alternatively, the central cues used in the neutral condition might have been more perceptually conspicuous, being presented at the fovea, than the laterally presented cues; if so, patients might have experienced a more persistent difficulty in disengaging their attention from the central cues than from the invalid right cues. The notion that neglect patients might progressively reorient their attention toward the left after an invalid right-sided cue is consistent with the idea, outlined in the "Introduction," that endogenous orienting can be relatively spared in unilateral neglect (Gainotti et al. 1991; Làdavas et al. 1994). This putative process, however, was not sufficient to ensure an unbiased performance for our patients, because RTs to invalidly cued left targets at SOAs≥550 ms were still slower than the corresponding RTs for right targets with neutral cues, $F_{(1)}$=5.04, P<0.05.

Responses to right targets were in general faster for valid than for invalid or neutral trials, but this effect did

[5] In principle, an endogenous shift was still possible at 150 ms SOA, because the target remained on until response, which was generally slow for neglect patients; however, we deem this unlikely, given the non-informative nature of the cues.

not reach significance (all Fs≤2.96). The non-significant advantage of valid over invalid and neutral trials persisted at long SOAs; thus, no evidence emerged for the IOR phenomenon,[6] consistent with the finding that neglect patients may not show this phenomenon for targets appearing on the non-neglected side (Bartolomeo et al. 1999). The impairment of a mechanism normally used to sample novel spatial locations, such as IOR (Klein 1999), may explain why neglect patients' exploration of space often cannot extend beyond a few right-sided objects. More generally, the absence of IOR, a phenomenon which seems exclusive to the dynamics of exogenous orienting (Maylor and Hockey 1985), constitutes a further argument supporting the notion of a relatively selective bias of exogenous orienting in unilateral neglect.

Experiment 2: 80% cue predictiveness

In this experiment, cues were informative about the future location of the target. Targets appeared in the cued box 80% of the time, and in the uncued box 20% of the time. This setting is expected to provoke an attentional orienting toward the cued box. This attentional shift should be initially (within 150 ms SOA) exogenous, and later on (after 300 ms SOA) endogenous (Müller and Findlay 1988; also see Fig. 1). In this situation, when a left target is preceded by a right (invalid) cue, neglect patients should not be able to use endogenous orienting even at long SOAs; this is because most cues reliably predict target location; thus the best strategy is to maintain attention on the cued box. We would not expect the cost for invalidly cued left targets to decrease with increasing SOAs, because patients' attention should remain fixed on the right-sided box.

Results and discussion

Controls

A main effect of the cue type was present, $F_{(2,34)}$=3.85, P<0.05. This effect was principally due to a cost for invalid trials, which elicited slower responses than both valid trials, $F_{(1)}$=6.81, P<0.05, and neutral trials, $F_{(1)}$=4.51, P<0.05. An advantage for valid trials over neutral trials was marginally significant only for the shorter SOAs (for 150- and 550-ms SOAs pooled together, $F_{(1)}$=3.59, P=0.06). The absence of a consistent advantage for validly cued targets with respect to the neutral condition probably resulted from the fact that targets remained on until response, thus reducing stimulus uncertainty and rendering detection particularly easy even in the neutral condition. Consequently, no additional advantage resulted from the presentation of a valid lateralized cue at long SOAs. When the cue was invalid, on the other hand, participants had to inhibit their exogenous orienting toward it; this could be the source of the observed cost. As in experiment 1, RTs decreased with increasing SOAs, $F_{(2,34)}$=10.04, P<0.001. No cost for valid trials (i.e., IOR) was observed at long SOAs, similarly to data obtained with central cues (Posner and Cohen 1984), and consistent with the idea (Maylor and Hockey 1985) that IOR is a phenomenon exclusively related to exogenous orienting (see also Fig. 2). These results of course leave open the possibility that IOR did occur after the peripheral cue onset, but it was overcome by the concomitant benefit resulting from endogenous orienting to the cued location (Berlucchi et al. 2000). That this could indeed be the case is suggested by the tendency of RTs for valid trials to increase between 550 and 1000 ms SOA, whereas RTs for neutral and invalid trials continued to decrease (see Fig. 3, central panel). This tendency resulted in a marginally significant interaction between cue and SOA, $F_{(4,68)}$=2.48, P=0.0518.

Neglect patients

Patients showed a tendency to respond faster to right than to left targets, $F_{(1,5)}$=4.60, P=0.086. The type of cue had an effect, $F_{(2,10)}$=7.84, P<0.005, because invalid trials evoked slower responses than both valid trials, $F_{(1)}$=15.51, P<0.005, and neutral trials, $F_{(1)}$=5.40, P<0.05, similarly to controls' pattern of performance. An effect of SOA was also present, $F_{(2,10)}$=4.98, P<0.05, but it originated from the fact that RTs at 550 ms SOA were slower than those at the two other SOAs, $F\text{s}_{(1)}$≥7.25, P<0.05, probably a spurious finding. A cue validity effect was present for all conditions, all $F\text{s}_{(1)}$≥6.73, P<0.05, except for right targets at 1000 ms SOA, $F_{(1)}$=2.69. The cue validity effect for left targets amounted to 378 ms at the shortest SOA, almost twice the size of the similar effect observed in experiment 1 (218 ms), and remained large at longer SOAs, in contrast with the results of experiment 1. It mainly consisted of a cost for invalid trials, as demonstrated by the RT pattern in the neutral condition. This large and persistent cue validity effect for left targets could depend on patients' attention being directed toward right-sided cues not only exogenously, but also endogenously (given the high predictiveness of the cues); the stronger attentional engagement on the right-sided box could have produced additional difficulties for patients to respond to invalidly cued left targets. This additional endogenous bias could have influenced RTs already at 150 ms SOA, because the

[6] The meaning of the absence of IOR in the present data might be questioned. RTs for invalidly cued right targets might be abnormally slowed down if patients neglected left-sided cues, which consequently failed to exert their warning effect. If so, IOR for valid trials might have been masked by the concurrent slowing of RTs for invalid trials. This account, however, does not apply to neutral trials, which also failed to induce faster RTs than valid trials, as if IOR were not operating. Neutral cues were adequately processed by neglect patients, as shown by the extinction-like RT pattern that they induced for left targets. The issue is not, however, completely settled by the present data because the neutral condition was administered in a separate session, thus rendering difficult a fine-grained comparison between conditions.

target remained on until the subjects' response, which was generally slow for neglect patients, thus allowing enough time to permit endogenous orienting. The persistence of the cue validity effect at longer SOAs is exactly what the dynamics of endogenous orienting would have predicted (see Müller and Findlay 1988 and Fig. 1). Thus, the stronger and more persistent cost for invalidly cued left targets observed in experiment 2 as compared to experiment 1 might essentially depend on the fact that in experiment 2 endogenous orienting, directed toward the right box by right-sided cues, was less available than in experiment 1 to compensate for the biased exogenous orienting.

In agreement with our results, Friedrich et al. (1998) found in patients with lesions involving the temporal-parietal junction an enhancement of the cue validity effect on contralesional targets in a 80% cue predictiveness experiment, as compared with an experiment with non-informative cues. At variance with our results, however, patients in the Friedrich et al. study (who had no clinical evidence of neglect or extinction) were able to take advantage of valid predictive cues to improve their performance on targets appearing on the contralesional side; our patients' inability to do so can be explained by the possibility that the 300-ms cues presented in the left, neglected hemispace sometimes failed to attract attention in our patients.

The presence of a validity effect for right targets at the shorter SOAs was due to a slowing of RTs to invalid trials, whereas RTs to valid trials were similar to those produced in experiment 1. Thus, a possible explanation of this difference between the two experiments is that patients could have been more motivated to attend to left-sided cues in experiment 2 than in experiment 1, given the different levels of cue predictiveness; this could have led to a better processing of some of these cues, producing in turn the observed cost for invalid trials. Despite the putative better processing of left cues, valid left-sided cues still failed to produce consistent advantages on RTs in experiment 2 as compared to experiment 1; this parallels the results for normal participants, who showed principally costs associated with invalid cues, but much less evident benefits for valid cues.

Experiment 3: 20% cue predictiveness

In experiment 3, the cues were predictive of the target location only 20% of the time; for the remaining 80%, the target appeared in the uncued box. This pattern should result in normals in a validity effect at short SOAs, followed by an inverted validity effect, i.e., an advantage of invalid over valid trials, at long SOAs (Posner et al. 1982). This advantage for invalid trials can be interpreted as resulting from an endogenous, strategic-based orienting of attention.

Results and discussion

Controls

As in the preceding experiments, RTs were faster with increasing SOAs, $F_{(2,34)}=10.29$, $P<0.001$. This effect interacted with the cue type, $F_{(4,68)}=6.08$, $P<0.001$; at 150 ms SOA, there was a tendency for RTs to be faster for the valid than for the invalid condition, $F_{(1)}=3.51$, $P=0.06$, as if attention were exogenously attracted by the cue despite the subjects' awareness that this was an unsound strategy, given that most cues were invalid. The use of shorter SOAs would have probably demonstrated a stronger validity effect (see Posner et al. 1982). For SOAs ≥ 550 ms, invalid trials evoked faster responses than valid trials (all $Fs_{(1)}\geq 5.87$, $P<0.05$). Thus, normal participants are able to inhibit an exogenous orienting of attention on the basis of strategic considerations (see also Yantis and Jonides 1990), if they have enough time to do it.

Neglect patients

The only main effect that emerged from the ANOVA was the expected left/right RT difference, $F_{(1,5)}=7.29$, $P<0.05$. Once again, increasing SOAs were not able to shorten patients' RTs, $F<1$. The interaction cue/SOA approached significance, $F_{(4,20)}=2.36$, $P=0.08$. In contrast to the first two experiments, invalid right-sided cues produced no significant slowing of RTs to left targets at SOAs ≤ 550 ms, as compared to validly cued targets on the same side, $Fs_{(1)}\leq 1.46$. An effect of the validity of the cue was only present for the left side at 1000 ms SOA, $F_{(1)}=10.34$, $P<0.005$, and consisted of faster RTs for invalid trials (739 ms) than for valid trials (1121 ms); the source of this effect was thus neglect patients' ability to use right-sided, invalid cues to orient their attention toward the left-sided box. Importantly, neglect patients attained in this condition their fastest RT for left targets of all the present experiments (equaled only by valid trials at 550 ms SOA in experiment 1). This RT was in the range of responses to right targets in the neutral condition; thus, neglect patients were able to successfully counter their spatial bias on this occasion. It is worth stressing that, in this condition, the strategic set was able to reverse the extinction-like RT pattern usually observed in neglect patients. However, this process apparently required a longer time than for normal participants, who showed an advantage of invalid over valid trials already at 550 ms SOA.

General discussion

In the present study, we examined the effect of the strategic set on performance of neglect patients in a series of cued reaction time experiments. This was in order to define neglect patients' attentional bias with respect to the proposed distinction between exogenous, or reflexive, and endogenous, or voluntary, modes of attentional orienting. Our results allowed us to better characterize patients' attentional impairments and their spared capacities. Our patients demonstrated several signs of biased exogenous orienting of attention, in the presence of a relatively spared, if slowed, endogenous orienting.

Previous clinical and experimental evidence, such as the finding that neglect patients typically orient their attention to the rightmost object as soon as the visual scene unfolds (Mark et al. 1988; De Renzi et al. 1989; Gainotti et al. 1991; D'Erme et al. 1992; see also Kinsbourne 1993), had already suggested that spatial bias in unilateral neglect primarily involves exogenous orienting. Both the immediacy of this "magnetic attraction" of attention and its compulsory character are indicative of a relationship with exogenous, automatic orienting. Our present evidence, that spatial bias (as indexed by a cue validity effect) is maximal at short SOAs and tends to decrease with longer SOAs (see also Posner et al. 1984; Morrow and Ratcliff 1988), confirms this notion. Furthermore, we demonstrated that this effect was evident even with non-informative peripheral cues (experiment 1), that is, in a situation in which cues elicit an exogenous shift of attention toward their location; predictive cues, on the other hand, caused the validity effect to persist at longer SOAs (experiment 2). This suggests that the disengagement deficit is maximal when attention is directed to the right side not only exogenously, but also endogenously, on the basis of strategic considerations. Results of experiment 3 demonstrate that neglect patients are capable of endogenously inhibiting their severe attentional bias toward right-sided objects. Under appropriate conditions (i.e., a long enough SOA), our patients were indeed able to attain a remarkably symmetrical performance for left and right targets. This result provides converging evidence with that of Làdavas et al. (1994), who found that central informative cues induced in neglect patients a better, albeit still asymmetrical, performance on left targets than peripheral non-informative cues. Làdavas et al. interpreted their findings as indicating spared endogenous orienting in neglect. Our results replicate and extend these results with a task paradigm that, employing exclusively peripheral cues, allowed a more rigorous comparison between conditions. Other converging evidence for preserved endogenous orienting in neglect comes from a study employing simple RTs to lateralized visual stimuli (Smania et al. 1998). In this study, neglect patients had faster RTs for both hemifields when the side of stimulus presentation was predictable as compared to the case when stimuli were presented randomly.

The apparent absence of inhibition of return in neglect patients (see the present experiment 1 and Bartolomeo et al. 1999) may be interpreted as still another sign that exogenous orienting is abnormal in unilateral neglect, because IOR appears to be specifically related to exogenous shifts (Maylor and Hockey 1985). From this point of view, our results, which show abnormal IOR in the face of relatively normal endogenous orienting in unilateral neglect patients, stand in striking contrast to those obtained with a similar paradigm in patients with Alzheimer's disease (Danckert et al. 1998). These patients showed normal IOR, together with normal validity effects for conditions involving exogenous orienting; however, they were unable to endogenously redirect attention toward the uncued side in a condition similar to our experiment 3 (80% of invalid cues). The authors interpreted these findings as resulting from a dysfunction of frontal lobe attentional areas in Alzheimer's disease, consistent with other neuropsychological and neuroimaging findings that they review.

The fact that patients with frontal damage are impaired in orienting attention in response to central informative cues (Alivisatos and Milner 1989), as well as in executing antisaccades (i.e., saccades toward the direction opposite to an abrupt-onset target; Guitton et al. 1985), suggests that endogenous orienting might involve cognitive operations subserved by the frontal lobes. Furthermore, a functional MRI study (Rosen et al. 1999) contrasting exogenous and endogenous orienting demonstrated largely overlapping activations in the parietal and dorsal premotor regions for both modes of orienting, except for an activation in the right dorsolateral prefrontal cortex (BA 46), which was exclusive to the endogenous condition. It is thus conceivable that the frontal lobes (and perhaps particularly their dorsolateral aspects) are important for endogenous orienting, whereas the integrity of more posterior brain regions, whose damage frequently causes unilateral neglect, might be essential for an unbiased exogenous orienting. One important aspect of endogenous orienting that is likely to be subsumed by frontal cortical areas is the inhibitory suppression of distractor activity (LaBerge et al. 2000), a process that might be the basis of performance in situations similar to our experiment 3, where cues asked for an attentional shift away from their location. These considerations are compatible with a hierarchical model of attentional orienting (Posner and Petersen 1990), in which a frontal system controls more posterior areas. Also consistent with these ideas is the proposal (Bartolomeo 1997, 2000) that frontal cognitive abilities are important for recovery from neglect; this recovery is indeed more rapid in patients without injury to the right frontal cortex (Hier et al. 1983), and is related to the restoration of metabolism in the ipsi- and contralesional frontal cortices (Pantano et al. 1992; Perani et al. 1993; Pizzamiglio et al. 1998).

An important question raised by the present findings is the following: If neglect patients have relatively intact capacities to endogenously orient their attention, why do they not employ these capacities to compensate for their neglect in everyday life? There are at least two possible answers, which are not mutually exclusive, to this question. First, one might think that our patients could endogenously orient toward the left only under narrow test conditions, that is, when right-sided cues were either non-informative (experiment 1), or explicitly prompted participants to expect a left-sided target (experiment 3).

In both of these conditions, the task contingencies invited an active inhibition of the location where the cue had occurred. In natural situations, on the other hand, there is no specific incentive to inhibit orienting to right-sided objects; thus, patients in daily life are confronted with a situation more similar to our experiment 2, in which informative right-sided cues induced a rightward spatial bias which was both severe and persistent. A second reason why neglect patients may be unable to effectively use endogenous orienting in everyday life is that this mode of orienting appeared to be slower than normal in our neglect patients. Indeed, the results of experiment 3 demonstrated that left neglect patients are able to use right-sided invalid cues to orient toward the left, neglected side on the basis of a strategic set. This process, however, took time; patients required at least 1000 ms after cue onset to contrast a strategically inappropriate exogenous shift toward the right, whereas 550 ms was sufficient for normal controls. Persons without brain damage may require less than 300 ms to accomplish such a process (Posner et al. 1982; Danckert et al. 1998). Also experiment 1 produced some evidence of spared endogenous orienting capabilities in neglect patients; their RTs to invalidly cued left targets decreased with increasing SOAs, as if after the cue onset they were progressively able to ignore it because it was not informative about the future target location. This process was already evident at 550 ms SOA, but, on the other hand, it was not sufficient to ensure an unbiased performance, because RTs to left targets were beyond the range of responses to right targets. This is in contrast to the results of experiment 3, in which patients managed to nullify their spatial bias for left invalidly cued targets at 1000 ms SOA. These findings suggest that time may be a crucial factor in the compensation of spatial bias; patients might perhaps offset their neglect if they learned to be fast enough in endogenously reorienting their attention leftward. Using a paradigm consisting of a majority of invalid trials, and in this respect similar to the present experiment 3, Warner et al. (1990) found that, after extensive practice, normal individuals learned to exert the attentional shift from the cued to an uncued location in less than 150 ms. Thus, practice can influence exogenous attentional shifts, perhaps by speeding up the development of the inhibition associated with endogenously redirecting attention from an unwanted target. In support of this notion, Lambert and Hockey (1991) showed that practice decreased the cost for invalid trials[7] at SOAs≤100 ms in a paradigm employing non-informative cues. On the other hand, in the same study practice had no effect on the size of IOR. It might then be that two different types of inhibition are involved in redirecting attention away from a cued location: an automatic process, strictly linked to exogenous orienting, and corresponding to IOR; and a more controlled, or endogenous, process, which can be trained with practice. To respond to left targets after right-sided cues, our patients with left neglect were apparently unable to use IOR (as shown by the lack of cost for right validly cued targets at long SOAs in experiment 1; see also Bartolomeo et al. 1999), but could use the endogenous process inspired by the strategic set (as demonstrated by the shortening of RTs for left invalidly cued targets with increasing SOAs in experiment 1, and by the striking advantage of invalid over valid trials for left targets in experiment 3 at 1000 ms SOA). It is thus possible that neglect patients cannot use their capacity to actively inhibit their compulsive rightward orienting tendency in their everyday life because its activation is too slow to cope with a continuously changing environment.

[7] And not, as maintained by the authors, the advantage for valid trials (see Fig. 1 in Lambert and Hockey 1991).

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Appendix A

Mean difference scores (invalid mean–valid mean, expressed in milliseconds) for the 50% validity condition performed by 11 normal participants (mean age 66.54 years, range 40–80 years), who either received the 50% validity condition first (*n*=5) or received it after the 80% validity condition (*n*=6) at 100, 500 or 1000 ms SOA

	SOA (ms)		
	100	500	1000
50% validity first	59	32	–8
80% validity first	63	20	–19

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