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## Exploring the syndrome of spatial unilateral neglect through an illusion of length

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**Abstract** Both a neuropsychological syndrome (unilateral spatial neglect) and a visual illusion of length (the Brentano version of the Müller-Lyer illusion) bring about a misjudgement of the subjective centre of a horizontal line, with a unilateral shift. In experiment 1 we investigated, in patients with left unilateral neglect, illusory effects of horizontal length, with the aim of exploring the functional and neural basis of horizontal space perception, and the role of visual processing in shaping the patients' bisection performance. Fourteen right-brain-damaged patients with left spatial unilateral neglect, seven with and seven without left visual half-field deficits (assessed by confrontation, perimetry, and visual event-related potentials), entered this study. Two conditions of manual line bisection were assessed: setting the mid-point of a horizontal line, and of the shaft of the Brentano-Müller-Lyer illusion, with either a left- or a right-sided expansion. Both groups of patients set the subjective midpoint to the right of the objective centre of the line, consistent with the presence of left neglect. Patients with neglect and left hemianopia showed no illusory effects and a greater bisection error. The effects

of the illusion, by contrast, were fully present in neglect patients without hemianopia, in both illusory conditions, adding to, or subtracting from, the rightward bisection bias. Anatomoclinical correlations revealed an association of damage to the occipital regions with the lack of illusory effects. Conversely, more anterior damage, sparing these regions, did not disrupt the illusion, revealing a dissociation between visual and spatial processing of extension. These findings suggest that processing of the Müller-Lyer illusion of length is likely to occur in the occipital cortex, at a retinotopic level of representation. In neglect patients with left homonymous hemianopia the visual deficit adds to the spatial bias, yielding a greater error in line bisection, but not in other visual exploratory tasks, such as cancellation, where the contribution of retinotopic frames is likely to be comparatively minor. Experiment 2 showed preserved illusory effects in patients with homonymous visual field defects without spatial unilateral neglect, suggesting that preserved spatial processing may compensate for unilateral visual field defects.

**Keywords** Spatial unilateral neglect · Visual illusions · Homonymous hemianopia · Line bisection · Occipital lobe

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### Introduction

Visual illusions have long been used as a tool to explore the functional properties of the perceptual system. The dissociation, which is the essential feature of illusions, between what is perceived and what is objectively measurable, makes visual illusions a psychological counterpart of some neuropsychological effects of brain damage. One such case is the widely investigated Müller-Lyer's figure (1889, see Porac 1994) and its versions (Coren and Gircus 1978). This illusion consists of the phenomenon whereby two identical lines are seen as different in physical length because of the presence of fins with a particular orientation at the line ends: The line

with outgoing fins is seen as expanded, the line with ingoing fins as compressed. Versions of the illusion in which the left side is compressed with respect to the right one mimic a main aspect of spatial unilateral neglect, a neuropsychological syndrome whereby patients fail to explore the side of space contralateral to the lesion and, within a given coordinate system (e.g., ego-centric, object-based), to report stimuli presented in that portion of space (Vallar 1998; Bisiach and Vallar 2000). Such an illusory configuration induces in normal subjects a rightward displacement of the subjective midpoint of a horizontal line in the task of bisection (Mattingley et al. 1995; Fleming and Behrmann 1998; Post et al. 1998; Vallar et al. 2000). The similarity of this illusory shift of the subjective midline to the directional error of right-brain-damaged patients with left neglect suggests analogies in the underlying mechanisms, which may be conceived in terms of relative compression of the side of the stimulus contralateral to the lesion. A number of studies in brain-damaged patients with unilateral neglect have made use of versions of the Müller-Lyer illusion (Brentano and Judd figures), which induce a unilateral expansion/compression or a lateral shift. A consistent result has been that patients with left unilateral neglect show preserved illusory effects in both sides of space (Mattingley et al. 1995; Ro and Rafal 1996; Vallar et al. 2000). These findings indicate on the one hand that perception of visual length is preserved in these patients, suggesting that the spatial compression, which is, according to some accounts (Halligan and Marshall 1991), a main feature of neglect, arises at a level of representation different from that of the illusory effect (discussion in Vallar et al. 2000). On the other hand, they provide some indirect evidence concerning the neural correlates of illusory effects such as the Müller-Lyer figure, since patients with left unilateral neglect have extensive lesions, which most frequently include the right inferior parietal lobule, at the temporoparietal junction, but spare the occipital lobe (Vallar and Perani 1986; Vallar 1993; Leibovitch et al. 1998). Consistent with these findings, patients with left unilateral neglect show preserved illusory effects also in the case of subjective contours, the so-called Kanisza's triangle (Mattingley et al. 1997; Vuilleumier and Landis 1998).

In this study we investigated the neural correlates of length perception, making use of the Müller-Lyer illusion. In previous experiments we found preserved illusory effects of length perception in right-brain-damaged patients with left neglect and lesions involving the frontal or temporoparietal regions, but largely sparing the occipital lobe (Vallar et al. 2000). Here, we assessed the occurrence of illusory effects of length in right-brain-damaged patients with unilateral neglect with electrophysiological evidence of spared or defective early visual processing. As in our previous experiments (Vallar et al. 2000), we made use of the Brentano or combined form of the Müller-Lyer illusion, which makes one-half of the line longer than the other (Restle and Decker 1977; Coren and Gircus 1978; Porac 1994). This version

(see Fig. 3) includes both ingoing and outgoing fins together, embedding two opposite Müller-Lyer illusions in the same configuration.

## Experiment 1

### Materials and methods

#### Subjects

Fourteen patients, admitted to the IRCCS S. Lucia for neurological rehabilitation, participated in the study. All patients had suffered from an ischaemic cerebrovascular attack, were right handed, and showed no history or evidence of psychiatric disorders, or dementia. All subjects gave informed consent to the study, which had been approved by the Ethics Committee of the Fondazione S. Lucia IRCCS. The patients' demographic, neurological, and neuropsychological features are summarised in Table 1. All patients showed evidence of left spatial neglect (N+), as assessed by a standard diagnostic battery (Zoccolotti et al. 1989, and below). Patients were subdivided into two groups on the basis of the presence or absence of deficits of early visual processing. These were assessed by a standard neurological examination (Bisiach and Faglioni 1974), kinetic Goldmann perimetry and visual evoked potentials (VEPs). Patients with unilateral neglect may, however, show behavioural evidence of hemianopia on confrontation testing, associated with preserved VEPs (Vallar et al. 1991; Angelelli et al. 1996). This suggests that neglect may mimic hemianopia (Kooistra and Heilman 1989; Mesulam 2000). Accordingly, patients who exhibited *both* left homonymous hemianopia at the behavioural assessment *and* abnormal VEPs were classified as showing a visual field defect (N+VFD+). By contrast, patients with preserved VEPs were classified as not showing a visual field defect (N+VFD-), even if hemianopia was found on confrontation testing, perimetry or both. All patients were unaware of their visual field deficits, according to a standard interview (Bisiach et al. 1986).

#### Baseline neuropsychological assessment

A diagnostic battery, which included two visuomotor exploratory tasks (line and letter cancellation), a reading task, and a task requiring a perceptual judgement assessed the presence of unilateral visual neglect. In the cancellation tasks patients used the right hand. In all tasks the centre of the display was located on the mid-sagittal plane of the trunk of the patients, who were free to move their head and eyes (see a detailed description in Zoccolotti et al. 1989). All patients had a normal or corrected-to-normal vision.

1. Letter cancellation (Diller and Weinberg 1977): The scores were the number of omissions in the left- (range 0–53) and right- (range 0–51) hand sides of the sheet. The maximum number of omission errors for normal subjects is 4, and 2 is the maximum difference between errors on the two sides of the sheet (Vallar et al. 1994).

**Table 1** Demographic and neurological features of seven right-brain-damaged patients with spatial unilateral neglect and a left visual field defect (N+VFD+) and seven right-brain-damaged patients with neglect but no visual field defect (N+VFD-) (+/- presence/absence of left-sided deficit, *Upper/Lower* visual quadrant).

Patient	Sex	Age (years)	Time from stroke onset (months)	Left motor weakness	Confrontation		Goldmann perimetry	Letter cancellation		Line cancellation		Wundt-Jastrow		Sentence reading
					Upper	Lower		Left	Right	Left	Right	Left	Right	
<b>N+VFD+</b>														
1		77	1	+	+	+	+	0/53	28/51	0/11	8/10	20/20	1/20	6/6
2	M	60	16	+	+	+	+	1/53	51/51	11/11	10/10	1/20	0/20	1/6
3 <sup>a</sup>	M	79	2	+	+	+	+	0/53	21/51	0/11	9/10	5/20	0/20	0/6
4	M	53	3	+	+	+	+	0/53	35/51	6/11	9/10	4/20	0/20	4/6
5	F	46	5	+	+	+	+ <sup>b</sup>	4/53	34/51	10/11	10/10	13/20	0/20	4/6
6	M	57	10	+	+	+	+	2/53	45/51	11/11	10/10	6/20	2/20	0/6
7	F	56	5	+	+	+	+	Illiterate		3/11	10/10	19/20	0/20	Illiterate
Average		61.1	6					1.2	35.7	5.8	9.4	9.7	0.4	2.5
SD		12.3	5.3					1.6	10.9	4.9	0.8	7.6	0.8	2.5
<b>N+ VFD-</b>														
8 <sup>a</sup>	M	68	3	+	+	+	+	19/53	43/51	0/11	8/10	19/20	0/20	0/6
9 <sup>a</sup>	M	70	3	+	-	+	-	0/53	9/51	3/11	9/10	13/20	0/20	0/6
10	F	66	2	+	+	+	-	0/53	10/51	9/11	10/10	12/20	0/20	2/6
11	M	47	1	+	-	-	-	0/53	28/51	11/11	10/10	5/20	0/20	5/6
12	F	75	2	+	+	+	-	1/53	25/51	2/11	10/10	12/20	0/20	5/6
13	M	43	3	+	-	-	-	10/53	47/51	11/11	10/10	1/20	0/20	6/6
14	F	66	13	+	-	-	-	7/53	47/51	10/11	10/10	0/20	0/20	4/6
Average		62.1	3.9					5.3	30	6.6	9.6	8.8	0	3.1
SD		12.2	4.1					7.2	16.4	4.7	0.8	7	0	2.5

<sup>a</sup> Patients also tested in Vallar et al.'s (2000) study

<sup>b</sup> Macular sparing

- Line cancellation (Albert 1973): The scores were the numbers of omissions in the left- (range 0–11) and right- (range 0–10) hand sides of the sheet. Normal subjects perform this task without errors.
- Wundt-Jastrow Area Illusion Test (Massironi et al. 1988): The score was the number of responses not showing the illusory effect (“unexpected”), arising from the left (range 0–20) and right (range 0–20) sides of the stimulus. Patients with right brain damage and left neglect make errors only on stimuli with a left-sided illusory effect.
- Sentence reading: The score was the number of incorrectly read sentences (range 0–6). Normal subjects and patients with right brain damage without neglect make no errors on this test. Patients with left neglect make omission errors, substitution errors, or both, in the left half of the sentence.

All patients showed evidence of left neglect in the four tasks. Severity of neglect was comparable in the two groups.

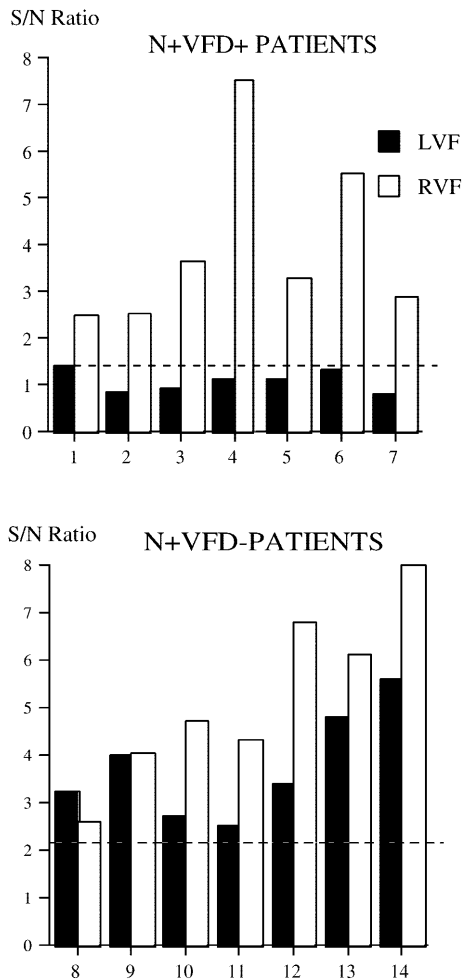
#### Evaluation of visual field defects

The assessment included:

- Standardised neurological examination, using the confrontation method (Bisiach and Faglioni 1974; see Table 1).

Baseline assessment: In the cancellation tasks the scores are the number of crossed targets, in the Wundt-Justrow Area Illusion Test the number of unexpected responses, in the reading task the number of correctly read sentences

- Kinetic Goldmann perimetry, using two spot sizes (area: 4 and 0.25 mm<sup>2</sup>) at the highest intensity (see Table 1).
- Steady-state VEPs: VEPs were recorded in response to horizontal gratings of 90% contrast, 0.6 cycles/deg spatial frequency, phase-reversed at 11 different temporal frequencies (5–10 Hz with steps of 0.5). The stimuli were generated by framestore (Cambridge Research VSG) and displayed on a monitor (Barco CDCT 6551) with a mean luminance of 16.5 cd/m<sup>2</sup> and frame rate of 100 Hz. The gratings were 17° wide and 20° high and were presented in the left or in the right visual field at an eccentricity of 1° from the central fixation point. An examiner monitored eye movements and interrupted data collection if fixation deviated. VEPs were recorded differentially with electrodes placed 3 cm above the inion (Oz) and at the vertex (Cz), with ground halfway between. Signals were amplified (50,000-fold), band-pass filtered between 1 and 100 Hz and averaged (200 repetitions) by computer, after artefact rejection (single sweeps over a threshold voltage, due to eye movements or eye blinks). The computer averaged the EEG in synchrony with the stimulus contrast reversal rate and performed an online Fourier analysis to calculate the amplitude of the second harmonic component (the principal modulation frequency). At the same time the program also averaged the signals asynchronously at 1.1 times the temporal frequency of the stimulus to



**Fig. 1** Individual mean signal-to-noise ratio values of VEPs from contralateral left visual half-field (*LVF*) and ipsilesional right visual half-field (*RVF*) stimulation, in N+VFD+ and N+VFD- patients

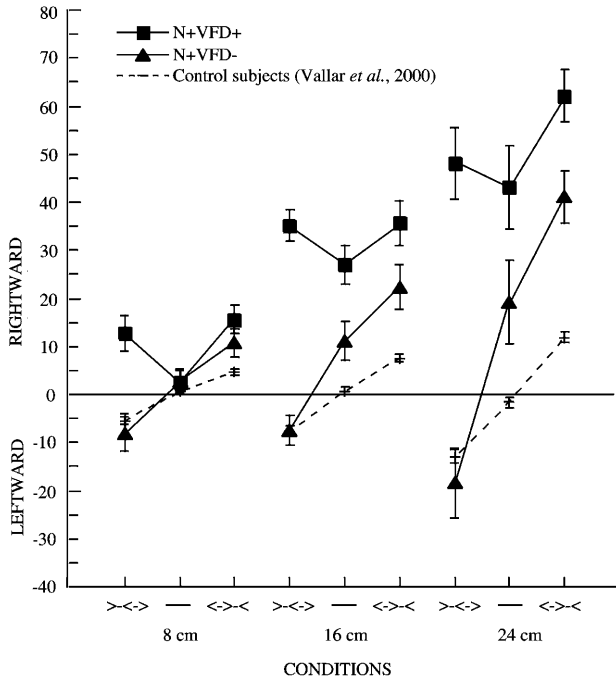
give an estimate of the background noise. VEPs were considered unreliable if the signal-to-noise ratio, averaged over all temporal frequencies, was less than 1.5, implying less than 50% signal above the noise level (Spinelli et al. 1994; Angelelli et al. 1996). Figure 1 shows the individual signal-to-noise ratios, averaged over all temporal frequencies for each half-field. Patients 1–7 did not present reliable VEPs to contralateral stimulation. The maximum signal-to-noise ratio for left visual field stimuli was 1.4, implying that less than 40% of the signal was above the noise level. On the contrary, in the same group, ipsilesional stimulation produced a clear evoked activity, synchronous to the stimulus and well above the baseline noise. In patients 8–14 reliable visual evoked potentials were recorded for both half-fields with signal amplitudes at least 1.5 times bigger than noise values. Accordingly, patients 1–7 were classified as N+VFD+, patients 8–14 as N+VFD-. As Table 1 shows, while all patients 1–7 exhibited a left hemianopia on the behavioural assessment, some of the re-

maining patients (8–10, 12) showed a dissociation between the behavioural evidence of hemianopia and reliable VEPs, confirming previous observations (Vallar et al. 1991; Angelelli et al. 1996). In such patients the behavioural visual field impairment may be interpreted as a manifestation of neglect (“unilateral visual inattention” or “pseudo-hemianopia”), rather than as a primary sensory disorder (Heilman et al. 1993; Vallar 1998).

### Experimental task

**Stimuli and procedure.** The Brentano version of the Müller-Lyer illusion was used (Coren and Gircus 1978). The stimuli were printed on A4 sheets using two different colours for the fins (black) and the line (red). The stimuli included two experimental illusory conditions, Left-expanded (left-sided outgoing fin/right-sided ingoing fin) and Right-expanded (left-sided ingoing fin/right-sided outgoing fin) illusions, and a Baseline control condition (a red line). Throughout the paper, the two types of illusory stimuli are distinguished with reference to the endpoint of the line (left or right) with the outgoing fins (expanded side). Examples are shown in Fig. 3. Three different line lengths were used for each condition (8 cm, 16 cm, and 24 cm). The fins were 2 cm long for 8-cm lines, 4 cm long for 16-cm lines, and 6 cm long for 24-cm lines. Lines and fins were 1 mm wide for 8-cm lines, 2 mm for 16-cm lines, and 3 mm for 24-cm lines. The fins formed with the line a 45° (ingoing) or a 135° (outgoing) angle. Two blocks were generated. Block A included the illusory stimulus with the right-expanded illusion and the baseline stimuli, block B the left-expanded illusion and the baseline stimuli. Each block comprised 18 stimuli, with three trials for each of two conditions (illusory and baseline control stimuli), for each of the three line lengths. Within each block the stimuli were presented in a random fixed order. Each block was presented twice, according to an ABBA sequence. In each trial the centre of the stimulus was aligned with the mid-sagittal plane of the trunk of the subject. The subject’s task was to mark the mid-point of the red horizontal line, using a soft pen, with no instructions about the fins being provided. Subjects sat in front of a table, where the stimulus display was laid. All subjects used their right hand and were allowed to move their eyes, head, and trunk throughout the task. These stimuli and procedures had been used in experiment 1 of the study by Vallar et al. (2000). Deviations from the objective midpoint of the red line were measured to the nearest millimetre. A positive score denoted a rightward transection displacement, a negative score a leftward displacement. These measures were submitted to an analysis of variance using a split-plot factorial design, with a between-subjects factor (Group: N+VFD+ and N+VFD-), and two within-subjects factors (Condition: right-expanded illusion, left-expanded illusion, and simple line; Length: 8 cm, 16 cm, and 24 cm).

MEAN TRANSECTION DISPLACEMENT (mm)



**Fig. 2** Mean transection displacement (mm) and standard error, by group (N+VFD+ and N+VFD-), line length (8 cm, 16 cm, and 24 cm), and condition (baseline control, left-, right-expanded Brentano-Müller-Lyer illusion). Control data from Vallar et al.'s (2000) study are shown

Analysis of lesion site

CT or MRI scans were performed and axial images of the brain (rotated between 0° and 10° above the canthomeatal line) were obtained. Lesions were localised on each axial section and plotted on corresponding digitalised templates from the third set of Damasio and Damasio's (1989) templates. The individual templates were digitally superimposed in order to individuate the region of maximal overlapping in the N+VFD+ and

N+VFD- patients. The subcortical localisation of the lesion was analysed using the atlas of Matsui and Hirano (1978).

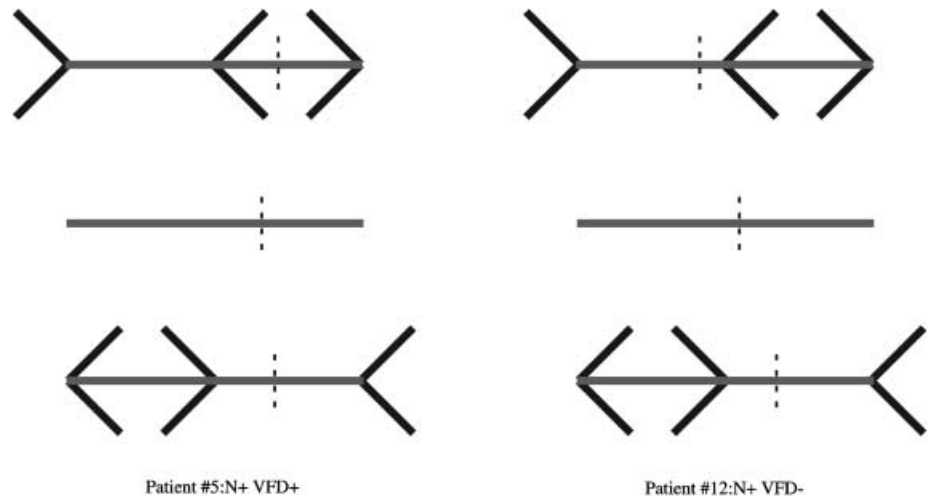
Results

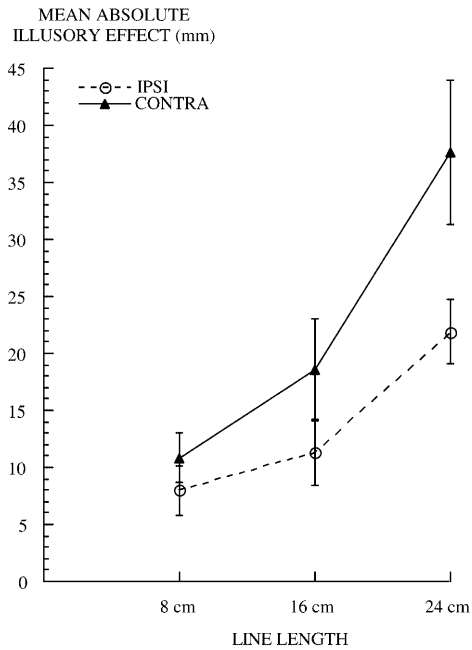
Experimental task

Figure 2 shows the mean bisection errors of patients with left neglect, with and without an associated visual field defect. For comparison with normal performance, data from the control group of the study by Vallar et al. (2000) are shown. In the baseline control condition all neglect patients made a rightward bisection error, which was greater in the N+VFD+ group, with the exception of 8-cm lines. Such an error increased with line length. The subjective mid-point was affected by the direction of the illusion in a different fashion in the two groups. Compared to the baseline, the right-expanded condition brought about a rightward shift of the subjective mid-point in both groups, while the left-expanded condition produced a leftward displacement in N+VFD- patients, but a rightward displacement in N+VFD+ patients. The different effects of illusory stimuli on the bisection performance of patients with and without a visual field defect are illustrated in Fig. 3.

An analysis of variance showed significant main effects of Group ( $F_{(1,12)}=20.48, P<0.001$ ), Condition ( $F_{(2,24)}=34.38, P<0.0001$ ), and Length ( $F_{(2,24)}=37.62, P<0.0001$ ). The Condition by Group ( $F_{(2,24)}=19.31, P<0.0001$ ), Length by Group ( $F_{(2,24)}=9.32, P=0.001$ ), and Condition by Length ( $F_{(4,48)}=33.03, P<0.0001$ ) interactions were significant. The significant Condition by Length by Group interaction ( $F_{(4,48)}=5.82, P<0.001$ ) was further explored with Duncan's post hoc comparisons. The bisection performances of the N+VFD+ and N+VFD- patients differed in all conditions with 16-cm and 24-cm lines ( $P<0.005$ ); with 8-cm lines the two groups differed only in the left-expanded condition ( $P<0.001$ ). In both groups the right-expanded condition

**Fig. 3** Stimuli (left-expanded, control baseline, and right-expanded condition) and representative performances with 16-cm stimuli by two patients. In N+VFD+ patient 5 both left- and right-expanded stimuli brought about an increase in the rightward transection error (dashed vertical line). In N+VFD- patient 12 left-expanded stimuli reduced the rightward error, which was further increased by right-expanded stimuli



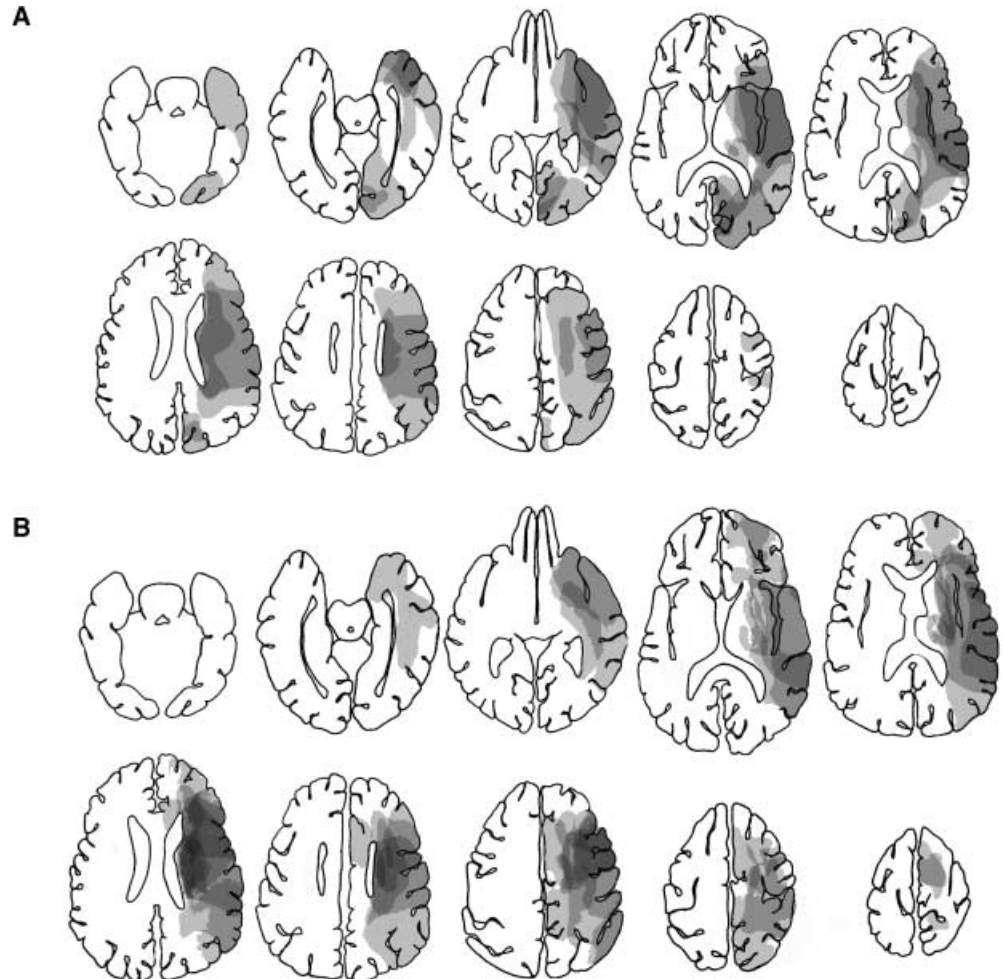


**Fig. 4** Mean absolute illusory effect (mm) and standard error in seven N+VFD- patients, by line length (8 cm, 16 cm, and 24 cm) (*Ipsi* illusion size with ipsilesional, right-expanded stimuli, *Contra* illusion size with contralesional, left-expanded stimuli)

was different from the baseline at all lengths ( $P < 0.05$ ). In N+VFD- patients the left-expanded condition was different from the appropriate baseline and the right-expanded condition at all lengths ( $P < 0.005$ ). In N+VFD+ patients the left-expanded condition differed from the appropriate baseline at 8-cm ( $P < 0.05$ ) and 16-cm ( $P < 0.005$ ) line lengths, but not from the right-expanded condition. At 24-cm lines, vice versa, the left-expanded condition differed from the right-expanded condition ( $P < 0.0001$ ) but not from the appropriate baseline.

Inspection of Fig. 2 suggests that N+VFD- patients may exhibit a larger illusory effect with stimuli expanded towards the left, contralesional, "neglected" side. In order to compare in these patients the amplitude of the illusory effects in the contralesional (left-sided) and in the ipsilesional (right-sided) directions, an analysis of variance was performed on the *absolute mean illusory effects* [illusion size: mean transaction error in each illusory condition (left-expanded, right-expanded) minus mean transaction error in the appropriate control baseline], in the three line lengths (8 cm, 16 cm, and 24 cm). Figure 4 shows that the size of the illusion was larger with contralesional, left-expanded stimuli, compared with ipsilesional, right-expanded stimuli, and increased with line length. The main effect of Illusion size was not

**Fig. 5** Maps of lesion overlapping in N+VFD+ (A) and N+VFD- (B) patients



**Table 2** Lesion localisation in 14 patients. *MFG* (BA 46): middle frontal gyrus, dorsolateral prefrontal region; *FO* (BA 44, 45, 47): frontal operculum; *FPR* (BA 6): frontal premotor region; *preC* (BA 4): precentral gyrus; *postC* (BA 3, 1, 2): postcentral gyrus; *S/PL* (BA 7, 39 and 40): superior/inferior parietal lobule; *TP* (BA 38): temporal pole; *AC* (BA 41, 42): primary auditory cortex; *supT* (BA 22): superior temporal gyrus and auditory association cortex; *midT*

(BA 21): middle temporal gyrus; *postT* (BA 37): posterior sector of middle, inferior and fourth temporal gyri; *postGC* (BA 23, 31): posterior half of cingulate gyrus; *VAC* (BA 18, 19): visual association cortex; *PVC* (BA 17): primary visual cortex; *Th* thalamus, *CN* caudate nucleus, *P* putamen, *GP* globus pallidus, *i/e c* internal/external capsule, *or* optic radiation, *pvwm* paraventricular white matter, *ant/post* anterior/posterior, minor damage *in brackets*

Patient	MFG	FO	FPR	PreC	postC	SPL	IPL	TP	AC	supT	midT	postT	postGC	VAC	PVC	Subcortical
<b>N+VFD+</b>																
1												x		x	x	Th, CN tail
2										x	x			x		P, ec, ic, ant-post pvwm, or
3											x			x	x	post pvwm, or
4		x	x	x	x		x	x	x	x	x					post pvwm, or
5						x					x	x		x	x	post pvwm
6	x	x	x	x	x		x	x	x	x						P, ec, ic, post pvwm, or
7													x	x	x	Th post, post pvwm
<b>N+VFD-</b>																
8		x	x	x	x				x	x	x					P, ec, ant (post) pvwm
9	x	x	x	x	x		x	x		x	x	x				ic, ant (post) pvwm
10		x	x		x			x	x	x	x	x				P, GP, CN head, ant (post) pvwm
11								x								P, CN head, ic, pvwm
12		x	x	x	x		x		x	x						P, GP, CN head, ec
13	x		x	x	x	x	x				x					GP, ic, ant (post) pvwm
14	x	x	x	x	x		x						x			(ant pvwm)

significant ( $F_{(1,6)}=4.28$ ,  $P=0.083$ ). The main effect of Length was significant ( $F_{(2,12)}=86.04$ ,  $P<0.0001$ ), as well as the Illusion size by Length interaction ( $F_{(2,12)}=4.38$ ,  $P<0.05$ ). Duncan's post hoc comparisons revealed that the illusory effect increased with longer segments ( $P<0.05$ ), with the exception of the 8-cm vs 16-cm comparisons in the ipsilesional condition. The size of the illusion was greater in the contralesional condition than in the ipsilesional condition ( $P<0.05$ ), with the 16-cm and 24-cm lines, but not with the 8-cm stimuli.

### Analysis of lesion site

Figure 5 shows the composite contour lesion maps of the two groups of patients. N+VFD+ patients showed a maximal overlap in the occipital and posterior temporal regions. In N+VFD- patients the regions of maximal overlap were more anterior, in the frontal premotor cortex, the frontal operculum, and the pre- and postcentral regions. The individual lesion sites are shown in Table 2.

## Experiment 2

The previous experiment showed that the association of left unilateral neglect with homonymous visual field defects disrupts the illusory effects produced by the left-expanded Brentano version of the Müller-Lyer figure. In order to tease apart the contribution of these two component deficits, the bisection performance of patients with homonymous hemianopia without neglect was assessed. The possibility may be entertained that the lack of ef-

fects of the left-expanded stimuli reflects a combined pathological action by neglect and visual field deficits, whereby the defective exploration of the left side of space, which characterises neglect, prevents the building up of a visual representation of both sides of the stimulus in the spared contralateral left visual cortex. If this is the case, the prediction can be made that patients with homonymous hemianopia without neglect (N-VFD+) would be sensitive to the illusion in both lateral directions, being able to compensate for the homonymous visual field deficit with eye movements (Barton et al. 1998).

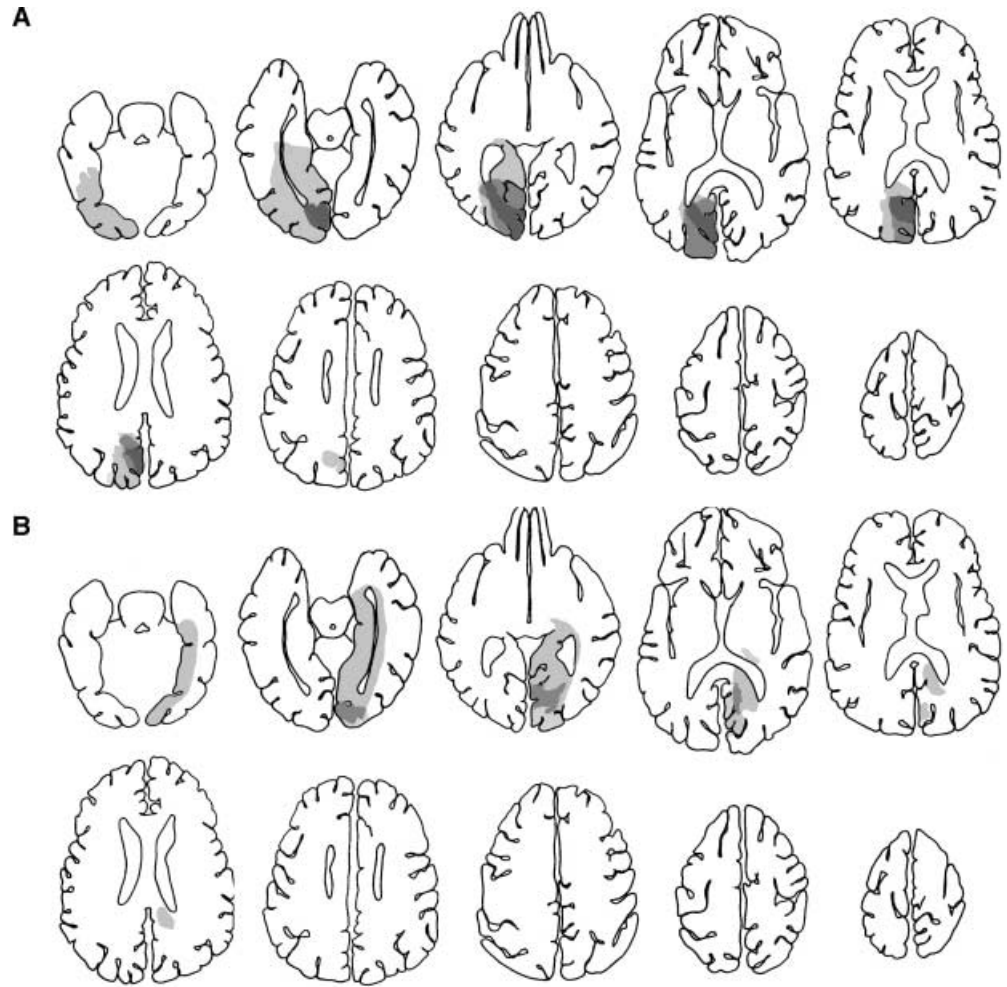
## Materials and methods

### Subjects and procedure

Six N-VFD+ patients entered this study. Four patients had a left hemispheric lesion and a right homonymous hemianopia, two patients a right hemispheric lesion and a left homonymous hemianopia. The visual field deficits were assessed by confrontation and Goldmann perimetry.

All subjects gave informed consent to the study. All six patients had suffered an ischaemic cerebrovascular attack in the vascular territory of the posterior cerebral artery. In five patients the maps of lesion overlapping showed an involvement of the primary and association visual cortices (Fig. 6, Table 3). The CT of one patient was not available for mapping. All patients showed no evidence of dysphasia or spatial unilateral visual neglect on a standard assessment. All patients were fully aware of their visual field deficit.

**Fig. 6** Maps of lesion overlapping in three left-brain-damaged patients (A) and in two right-brain-damaged patients (B), with contralesional hemianopia without spatial unilateral neglect



**Table 3** Lesion localisation in five patients. L/R: left/right hemispheric damage; *SPL* (BA 7): superior parietal lobule; *postT* (BA 37): posterior sector of middle, inferior and fourth temporal gyri; *paraH* (BA 28, 27): parahippocampal (fifth temporal) gyrus; *post-*

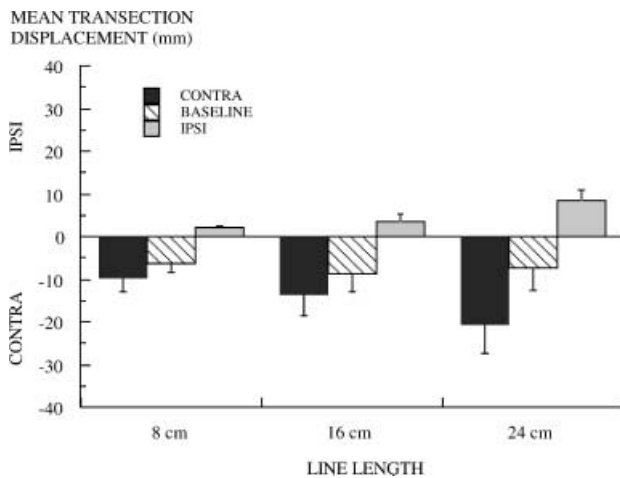
*GC* (BA 23, 31): posterior half of cingulate gyrus; *VAC* (BA 18, 19): visual association cortex; *PVC* (BA 17): primary visual cortex; *Th* thalamus, or optic radiation, *pvwm* paraventricular white matter, *ant/post* anterior/posterior, minor damage in brackets

Patient	Sex	Age (years)	Time from stroke onset (months)	SPL	postT	paraH	postGC	VAC	PVC	Subcortical		
N-VFD+												
1-L	M	68	26	x	x	x	x	x	x	post pvwm		
2-L	F	53	33	x			x	x	x	post pvwm, or		
3-L	F	26	23	x			x	x	x	(Th), post pvwm		
4-L	F	71	4	CVA in the vascular territory of the posterior cerebral artery (CT/MRI not available)								
5-R	M	53	6				x	x	x			
6-R	F	66	25		x	x	x	x	x	post pvwm, or		

The stimuli and procedures were the same as in experiment 1. The measures were firstly submitted to a repeated measures analysis of variance with two within-subjects factors (Condition: illusion expanded in the contralesional or in the ipsilesional direction, line; Length: 8 cm, 16 cm, and 24 cm). The contralesional side was the left side in right-brain-damaged patients, the

right side in left-brain-damaged patients. The ipsilesional side was the right side in right-brain-damaged patients, the left side in left-brain-damaged patients. Secondly, in order to compare the amplitude of the illusory effects in the contralesional and in the ipsilesional directions, an analysis of variance was performed on the absolute mean illusory effects [Illusion size: mean transection error in





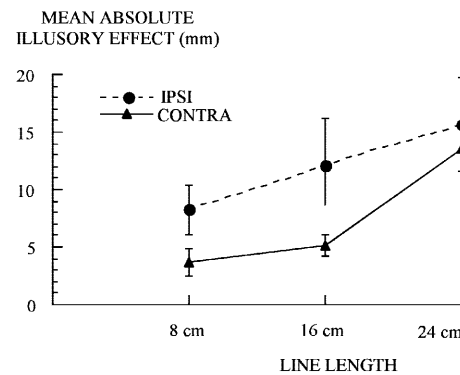
**Fig. 7** Mean transection displacement (mm) and standard error (*CONTRA*/*IPSI* contralesional/ipsilesional displacement of the subjective midline), by line length (8 cm, 16 cm, and 24 cm), and condition (*BASELINE* control, *CONTRA*/*IPSI* illusion expanded in the contralesional/ipsilesional direction), in six brain-damaged patients with homonymous hemianopia without neglect

each illusory condition (contralesional, ipsilesional expansion) minus mean transection error in the appropriate control baseline], in the three line lengths (Length: 8 cm, 16 cm, and 24 cm).

## Results

Figure 7 shows the mean bisection errors of the six N-VFD+ patients. At all three line lengths patients showed a contralesional displacement of the subjective midline in the baseline control condition. The two opposite illusory conditions brought about further contralesional or ipsilesional displacements of the subjective midline. The analysis of variance showed a significant main effect of Condition ( $F_{(2,10)}=16.56$ ,  $P<0.001$ ), but not of Length ( $F_{(2,10)}<1$ ). The Condition by Length interaction was significant ( $F_{(4,20)}=26.12$ ,  $P<0.0001$ ), and was further explored with Duncan's post hoc comparisons. All differences between the contralesional and the ipsilesional expanded conditions and their control baselines were significant ( $P<0.05$ ). In the baseline condition, the bisection error was comparable in the three line lengths. In both expanded conditions the differences between 8-cm and 24-cm lines, and between 16-cm and 24-cm lines, were significant ( $P<0.001$ ). The difference between 8 cm and 16 cm was significant only in the contralesional illusory condition ( $P<0.005$ ).

Figure 8 shows the mean absolute illusory effect, which increased with line length. The main effect of Length was significant ( $F_{(2,10)}=31.11$ ,  $P<0.0001$ ). The main effect of Illusion size ( $F_{(1,5)}=3.58$ ,  $P=0.12$ ) and the interaction ( $F_{(2,10)}=2.79$ ,  $P=0.10$ ) were not. The absolute illusory effects of each patient are shown in Table 4. A perusal of the individual data does not reveal differences



**Fig. 8** Mean absolute illusory effect (mm) and standard error in six brain-damaged patients with homonymous hemianopia without neglect, by line length (8 cm, 16 cm, and 24 cm) (*CONTRA*/*IPSI* illusion expanded in the contralesional/ipsilesional direction)

**Table 4** Mean absolute illusory effect in six N-VFD+ patients, by direction of the illusion: contralesional (*Contra*), and ipsilesional (*Ipsi*) (*L/R* left-/right-brain-damaged patient)

Patient	Line length (cm)					
	8		16		24	
	Contra	Ipsi	Contra	Ipsi	Contra	Ipsi
1-L	0.87	6.71	4.54	5.21	14.50	10.75
2-L	6.29	16.62	9.41	29.17	21.79	32.13
3-L	1.42	2.50	4.09	2.58	8.46	5.79
4-L	0.83	5.16	3.00	5.17	10.34	7.75
5-R	6.83	5.67	5.5	11.83	13.67	15.33
6-R	5.92	12.75	4.08	18.42	12.25	22.08

between left- and right-brain-damaged patients, showing, however, some tendency towards minor illusory effects in the contralesional direction of the illusion.

## Discussion

The main result of the present study is a behavioural and anatomical dissociation within patients with unilateral neglect. Patients with visual field defects, documented electrophysiologically, showed no sensitivity to an illusion of length. These patients treated the Brentano-Müller-Lyer stimuli independent of the leftward or rightward direction of the illusory effect, with a rightward ipsilesional shift of the subjective midline. As Figs. 2 and 3 show, the illusory stimuli appear to exert a rightward cueing effect, independent of their illusory properties. By contrast, patients with preserved visual processing showed bidirectional illusory effects, replicating a previous observation (Vallar et al. 2000). Finally, in neglect patients without visual field deficits, the size of the illusion was larger on the left contralesional side than on the right ipsilesional side (see Fig. 4). By contrast, hemianopic patients without neglect did not show such a difference (see Fig. 8).

The preserved vs impaired processing of the Brentano-Müller-Lyer illusion of length has an anatomical counterpart. As Fig. 5 and Table 2 show, patients who did not exhibit illusory effects had lesions involving the striate and extrastriate visual cortex, or the optic radiation. Consistent with these findings, the preservation of illusory effects assessed by line bisection is associated with lesions involving the frontal, temporal and parietal regions, but largely sparing the occipital areas (Ro and Rafal 1996, Judd and Müller-Lyer figure; Vuilleumier and Landis 1998, illusory contours; Vallar et al. 2000, Brentano-Müller-Lyer illusion). By contrast, the illusory effects are disrupted when the damage extends more posteriorly to the occipital lobe (Vallar et al. 2000, patient G.M.; Vuilleumier et al. 2001). Kartsounis and Warrington reported the case of a patient with a cortical degeneration, with a left hemianopia and a mild left neglect, who presented with a severe impairment of visual object recognition, traced back to a breakdown of figure-ground discrimination. The patient failed to perceive a number of illusions, including subjective contours and the Müller-Lyer figure.

A number of neurophysiological studies in the monkey and neuroimaging experiments in humans have focused on another type of visual illusion, namely, the perception of subjective contours. This, as noted earlier, is preserved in patients with spatial neglect (Mattingley et al. 1997; Vuilleumier and Landis 1998). Recording from neurons in the monkey's visual cortex indicates that the perception of these kinds of subjective contours arises as early as in V1 (Grosop et al. 1993) and V2 (von der Heydt et al. 1984; von der Heydt and Peterhans 1989; Peterhans and von der Heydt 1991). Functional studies in normal subjects suggest an association between perception of subjective contours and activation in the occipital striate and extrastriate cortex (Hirsch et al. 1995, BA 18; Ffytche and Zeki 1996, V2; Larsson et al. 1999, V1 and V2; Mendola et al. 1999, retinotopic areas V3A, V4v, V7, V8). These related data concur with the present findings to suggest that visual illusions, such as the Müller-Lyer figure, arise posterior to the inferior parietal lobule, in the occipital regions. The present results, however, do not allow a further teasing apart of the relative contribution of specific occipital regions.

The lack of sensitivity to the Brentano-Müller-Lyer illusion does not reflect a more severe visuospatial exploratory deficit in patients with both unilateral neglect and visual field defects. As shown in Table 1, the performance of the two groups of neglect patients, who were free to move their head and eyes in the bisection task, is comparable in a number of visuomotor cancellation, reading and perceptual tasks. The defective sensitivity to the illusory figure, on the other hand, is not dependent on the presence of a visual field deficit per se. The six patients with homonymous hemianopia without neglect, who were able to explore and attend the whole of peripersonal space, showed illusory effects (see Fig. 7). It is the combined effect of visual field deficits and neglect to bring about the patients' complete insensitivity to the

illusion: The deficit of spatial exploration and perceptual awareness, which characterises unilateral neglect, is likely to prevent the execution of strategies, which, in hemianopic patients without neglect, may compensate for the disrupted processing of visual input from the contralesional half-field.

The two groups of neglect patients were, however, differentially impaired in the line bisection task. Patients with visual field deficits showed an overall greater rightward directional error, compared to patients with preserved early visual processing. These findings are in line with an observation by Doricchi and Angelelli (1999), who found that neglect patients with hemianopia (documented electrophysiologically, as in the present study), and lesions involving the occipital lobe, made a rightward error in line bisection greater than that committed by neglect patients without hemianopia, and more anterior lesions (see also D'Erme et al. 1987, for an early observation of a greater bisection error in patients with left neglect and hemianopia). Right-brain-damaged patients have been described who show left neglect in line bisection, but not in cancellation tasks and vice versa (Halligan and Marshall 1992). In a study by Binder et al. (1992), right-brain-damaged patients with abnormal line bisection had more posterior damage, clustering in the inferior parietal lobule, in the posterior and middle temporal gyrus, and in the anterolateral occipital lobe. By contrast, patients with cancellation deficits and normal line bisection had lesions clustering in precentral and premotor frontal regions. In Binder et al.'s (1992) study, left hemianopia was more frequent in patients with defective line bisection (4 out of 11) than in patients with a normal performance (1 out of 10). Taken together, these findings indicate that lesions involving the occipital lobe bring about a more severe contralesional error in line bisection, but not in other tasks assessing neglect, such as cancellation. McGlinchey-Berroth et al. (1996), in a large series of right-brain-damaged patients, confirmed the double dissociation between impairments in line bisection and cancellation tasks, but did not find any specific anatomical correlate: the lesions, classified by a neurologist with no reference, however, to standard templates, were equally likely in the temporoparietal region, in the dorsolateral frontal cortex, and in the deep frontal structures.

There is an apparent paradox in the observation that visual field deficits worsen the bisection error in patients with left neglect. Patients with hemianopia in line bisection tasks make an error in the opposite direction, that is, contralateral to the side of the lesion, into the blind field (Axenfeld 1894; D'Erme et al. 1987; Kerkhoff 1993; Doricchi and Angelelli 1999; Kerkhoff 1999). The contralesional shift of the subjective midline in patients with hemianopia without neglect is not confined to the visual modality, extending to the subjective auditory straight ahead (Kerkhoff et al. 1999). In the present study, in line with these findings, brain-damaged patients with homonymous hemianopia without neglect showed a tendency to bisect the line with an error towards the

contralesional side (see Fig. 7), into the hemianopic half-field. By contrast, patients with neglect make an ipsilesional directional error both in line bisection (Bisiach et al. 1983; Riddoch and Humphreys 1983; Halligan and Marshall 1988; Marshall and Halligan 1989; Mozer et al. 1997) and in setting the subjective straight ahead (Heilman et al. 1983; Mark and Heilman 1990; Karnath 1994). Given these opposite effects of homonymous hemianopia and unilateral neglect on the direction of the bisection error, their association could bring about a reduction of it (see Kerkhoff 1993, for a discussion of this hypothesis). The present empirical evidence, however, is that homonymous hemianopia increases the ipsilesional rightward directional error made by right-brain-damaged patients with left neglect, as shown by both experiment 1 and previous studies (see D'Erme et al. 1987; Halligan et al. 1990, for a trend; Doricchi and Angelelli 1999). Using a different task (setting the subjective straight ahead), Ferber and Karnath (1999) found that the opposite directional errors of right-brain-damaged patients with left hemianopia without neglect (left contralesional deviation) and of patients with left neglect without hemianopia (right ipsilesional deviation) cancelled out in patients with associated impairments, namely: In right-brain-damaged patients with left neglect and left hemianopia, the subjective straight ahead was within the normal range. Other studies, however, found a marked ipsilesional rightward deviation of the subjective straight ahead in right-brain-damaged patients with both left neglect and hemianopia (Farnè et al. 1998; Rossetti et al. 1998). The precise relationship between the different components of unilateral spatial neglect and visual half-field deficits are at present controversial and call for further research.

The contralesional bias of hemianopic patients may reflect a compensatory strategy set up to overcome the visual field defect. Consistent with this view, in patients with hemianopia without neglect the pattern of eye movements during line bisection is characterised by fixations towards the blind field (Ishiai et al. 1989; Barton et al. 1998). In patients with neglect, by contrast, fixations towards the neglected side of space are typically reduced (Chedru et al. 1973; Girotti et al. 1983; Ishiai et al. 1989; Karnath and Fetter 1995; Barton et al. 1998). Finally, patients with hemianopia without neglect are usually aware of their disorder (Warrington 1962; Koehler et al. 1986), facilitating the setting up of compensatory exploratory strategies. On the other hand, unawareness of visual field deficits is frequently associated with spatial neglect (e.g., Bisiach et al. 1986; Vallar et al. 1991), preventing such compensations. Therefore, visual field deficits associated with neglect not only fail to reduce the ipsilesional bias (Kerkhoff 1993), but may indeed exacerbate neglect under conditions, such as line bisection, in which the utilisation of a complete retinotopic representation of the visual field is required.

The dissociation between line bisection and cancellation performances of patients with left neglect may be interpreted specifying the reference frames involved

in each task. The Müller-Lyer illusory effects arise primarily at a retinotopic level of representation. This is suggested by the behavioural observation that in both normal subjects and right-brain-damaged patients with left neglect the spatial position of the stimulus with reference to the mid-sagittal plane does not modulate the size of the illusion (Vallar et al. 2000). The present findings that occipital damage disrupts the illusory effects are in line with this conclusion. Such a retinotopic impairment adds to the disorder of an egocentric reference frame, exacerbating the rightward displacement of the subjective mid-point of the segment. In line with this hypothesis, in the present study right-brain-damaged patients with a greater rightward error in line bisection had not only a left visual field deficit and occipital damage (see Binder et al. 1992; Doricchi and Angelelli 1999), but also exhibited no illusory effects. This provides direct evidence for a contribution of retinotopic reference frames to the task of setting the mid-point of a horizontal line. This retinotopic information should be made available to higher-order spatial egocentric frames, whose role in line bisection has long been known: The position of the stimulus affects the bisection error of patients with neglect (Heilman and Valenstein 1979; Bisiach and Vallar 2000), but not, as noted earlier, the Müller-Lyer illusion (Vallar et al. 2000).

The hypothesis that the lack of a complete retinotopic representation of the stimulus increases the ipsilesional error in line bisection may also account for the differential effects of line length in the two groups. As Fig. 2 shows, with shorter (8-cm) lines the rightward error was comparable in all neglect patients. With longer lines, an increase in the rightward error was shown in all patients (the well-known effect of line length: Bisiach et al. 1983; Riddoch and Humphreys 1983; Halligan and Marshall 1988; Marshall and Halligan 1989; Mozer et al. 1997), but this was much greater when a visual field deficit was present (see D'Erme et al. 1987, for early evidence). Under conditions in which exploration of the line is biased towards the right side, in patients with visual field deficits the proportion of the line which does not undergo early visual processing would increase with line length. This would result in retinotopic representations of longer lines more truncated on their left side. On such representations of line length, shortened by visual field deficits, an egocentric rightward bias applies, ending up in a bisection error greater than that committed by neglect patients with no visual field deficits. The conclusion that retinotopic information feeds to an egocentric level of representation, where the computations necessary for a mid-point judgement are performed, is compatible with recent evidence showing activations in the premotor frontal and posterior parietal cortex, but not in the occipital lobe (Vallar et al. 1999; Galati et al. 2000).

The comparable severity of neglect in the two groups of patients, as assessed by cancellation and reading tasks, independent of the presence of visual field deficits (see Doricchi and Angelelli 1999, for a similar observation), indicates that the role of a retinotopic representa-

tion is comparatively minor. An accurate line bisection is likely to require a global appreciation of the extent of the stimulus, which is a unitary object. By contrast, cancellation and reading tasks may be in principle performed using a piecemeal approach, allowed by the multiple-object nature of the stimulus. Under these conditions, the detrimental role of a contralesional visual field deficit may be less relevant, with the spared retinotopic input providing sufficient information for the processing of a sequence of individual objects relatively small in size, such as letters or scattered lines.

In neglect patients without hemianopia, the size of the illusory effect was larger on the contralesional left side, compared with the right side. This suggests that processing of visual illusions such as the Brentano-Müller-Lyer is not only independent of spatial representational and focal attention systems (impaired in neglect), but these same processes may exert, under normal conditions, a modulation effect, which may reduce the size of the illusion. The view that spatial attention may inhibit some perceptual effects is consistent with a recent observation by Chatterjee et al. (2000), who asked two patients with left neglect to judge the relative heaviness of pairs of weights placed in the two hands. They found that contextual effects of previous weights induced a leftward bias in their judgement. Chatterjee et al. concluded that in neglect patients contextual effects, which are normally mitigated by attention, may have a greater influence on the formation of representations of the left, neglected, side, resulting in a paradoxical leftward bias. Consistent with this interpretation, brain-damaged patients with hemianopia without neglect did not show any lateral bias in the illusory effects.

Finally, the present observation that in neglect patients without visual field defects the illusory effects were larger contralesionally is also compatible with developmental data showing that the magnitude of the Müller-Lyer illusion and of its Brentano form decreases with age (Predebon 1984). This age trend may reflect a developmental change in perceptual cognitive processing (Girgus et al. 1975). In patients with unilateral neglect illusory effects are greater in the contralesional side, where attentional modulation is made disproportionately weak by the unilateral brain damage. These findings suggest an interpretation of the developmental reduction of the magnitude of the Müller-Lyer illusion in terms of developmental changes in spatial directed attention.

Some years ago Halligan and Marshall (1992), on the basis of a double dissociation between impairments in line bisection and cancellation tasks, took the view that unilateral spatial neglect is a "meaningless entity." Suggestions have been repeatedly made that neglect, like many neuropsychological deficits, should be conceived as a multicomponential disorder (Barbieri and De Renzi 1989; Vallar 1998). A similar argument also applies to other dissociations within neglect, such as the observation that some patients exhibit the Müller-Lyer illusory effects in line bisection, while some others do not (Mattingley et al. 1995; Vallar et al. 2000). The present

findings qualify the now widely accepted multicomponential view of the neglect syndrome in terms of an analysis of the kinds of representation involved in each task, and of their neural correlates. More specifically, they elucidate the role of the impairment of early visual processing and retinotopic representations in shaping the pattern of preserved and impaired performance in patients with spatial unilateral neglect.

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