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Ipsilesional perceptual deficits in hemispatial neglect: Case reports

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ABSTRACT

Hemispatial neglect, usually after right hemisphere lesions, is characterized by contralesional deficits in attention and perception. However, little is known about impairments of perceptual processing in the ipsilesional region of visual space (the right visual field for right hemisphere lesions). In two right hemisphere neglect patients, we used a metacontrast masking paradigm to characterize systematic spatial and temporal visual processing deficits in the ipsilesional right visual field. The presence of a visual mask caused the neglect patients to miss targets in ipsilesional space, even when a mask was presented as long as 1.5 sec after the target and in a different spatial position. These prolonged and spatially extended masking effects were not measured in age-matched healthy controls or in two control patients with hemianopsia but without neglect. The results show that perceptual processing is distorted and delayed in a region of the visual field that has been thought to be unaffected – the ipsilesional hemifield in patients with neglect.

1. Introduction

Hemispatial neglect is most often observed in stroke patients with right hemisphere inferior parietal or superior temporal lesions (Karnath, Berger, Küker, & Rorden, 2004; Karnath, Ferber, & Himmelbach, 2001; Lunven & Bartolomeo, 2017; Mort et al., 2003). The disorder is characterized by a profound deficit in perception on the side of space opposite the lesion (Driver & Mattingley, 1998; Rafal, 1994). For example, neglect patients may fail to notice people on their left, may eat food only from the right halves of their plates, and may fail to shave or put make up on the left half of their faces.

In addition to failing to represent information from contralesional space, in some cases the contralesional halves of objects are neglected even when the entire figure is within ipsilesional space (Driver, Baylis, & Rafal, 1992; see also; Marshall & Halligan, 1988). This suggests that the deficits in

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perception arise after figure-ground segmentation and object-centered representations have been formed in the brain.

A key role of attention in neglect is suggested by studies showing failures in patients with lesions to the temporoparietal junction to disengage attention from ipsilesional space towards contralesional space (Friedrich, Egly, Rafal, & Beck, 1998; Posner, Walker, Friedrich, & Rafal, 1984), even for targets appearing within the ipsilesional hemifield (Ladavas, 1990; Ladavas, Del Pesce, & Provinciali, 1989). In contrast with impaired contralesional attention, attention to ipsilesional space may actually be enhanced (D'Erme, Robertson, Bartolomeo, Daniele, & Gainotti, 1992; Ladavas, 1990; Ladavas, Petronio, & Umilta, 1990). This may result from disinhibition of the dominant left hemisphere after right hemisphere damage (Cohen, Romero, Servan-Schreiber, & Farah, 1994; Kinsbourne, 1977, 1993). Evidence for this hemispheric rivalry account of neglect also comes from studies using transcranial magnetic stimulation (TMS) to transiently disrupt processing in right parietal cortex (Blankenburg et al., 2008; Seyal, Ro, & Rafal, 1995; Szczepanski & Kastner, 2013).

Alternately, if the right hemisphere is responsible for attending to both halves of space, but the left hemisphere is responsible for attention only towards the right side of space, right hemisphere lesions would be more likely to cause neglect (Heilman & Valenstein, 1979; Heilman & Van Den Abell, 1979, 1980). Furthermore, attentional deficits may also be apparent in the ipsilesional hemifield after right hemisphere lesions (Vuilleumier & Rafal, 2000), and there may also be deficits in temporal attention in neglect (Husain, Shapiro, Martin, & Kennard, 1997).

These hemispheric asymmetry accounts of neglect suggest that perceptual processing might be affected in visual space on the same side as the brain lesion (ipsilesional), contrary to the common idea in the field that ipsilesional space is unaffected. To test this idea, in the current study we assessed the spatial and temporal processing differences in contralesional and ipsilesional space in patients with neglect using a metacontrast masking paradigm, in which a briefly presented target stimulus is presented at varying latencies prior to a metacontrast mask. In neurologically healthy subjects, when the target stimulus is presented at the same position prior to a surrounding metacontrast mask by approximately 30 msec, the target stimulus is frequently missed and only the metacontrast mask is perceived (Breitmeyer, 1984; Breitmeyer & Ogmen, 2000; Ogmen, Breitmeyer, & Melvin, 2003). It has been hypothesized that this masking results from an interruption of feedforward processing of the target stimulus by the feedback processing of the mask in visual cortex (Enns, 2004; Ro, Breitmeyer, Burton, Singhal, & Lane, 2003). Importantly, studies have previously shown that the magnitude and duration of metacontrast masking in normal subjects is affected by endogenously oriented attention (Boyer & Ro, 2007; Ramachandran & Cobb, 1995). By manipulating where in space and when in time these target and masking stimuli were presented, we assessed how neglect affects metacontrast masking in both the contralesional as well as the ipsilesional hemifields of two patients with neglect.

For comparison, we also measured the spatial and temporal extent of metacontrast masking using the identical paradigm in a group of neurologically healthy age-matched control subjects. One potential difficulty in studies of neglect is separating behavioral deficits caused by disorders of attention from purely sensory deficits resulting from damage to visual cortex. To control for this possibility, we also tested two patients with visual field deficit after damage to occipital cortex (hemianopsia but without neglect).

2. Materials and methods

2.1. *Participants*

Two patients with dense hemispatial neglect and hemianopsia and two patients with hemianopsia without neglect, all after right hemisphere lesions, participated in this study (Fig. 1). Unlike the hemianopsia patients, the two patients with neglect had severe neglect in daily activities, on shape (Mesulam, 1985) and/or line cancellation tasks (Albert, 1973), and they bisected lines further to the right of midline (see Table 1), as is often the case in patients with neglect (Halligan & Marshall, 1988). They also failed to represent the left half of objects in drawings (Fig. 1).

Patient JB was a 58 year old male who approximately 17 months prior to the first testing session had a large ischemic stroke involving the right frontal, parietal, temporal, and occipital cortices (Fig. 2, top). JB had severe neglect on shape cancellation as well as on line bisection tasks but not on a line cancellation task (Fig. 1A and Table 1). We also measured the extent of JB's visual field deficits by conducting a computer-based perimetry assessment (see Stimuli and procedures and Fig. 1A). At 21 months post-stroke, we also acquired from JB high resolution structural magnetic resonance imaging (MRI) scans, as well as retinotopic functional MRI (fMRI) scans, using a Philips 3 T whole body scanner. For structural imaging, we used a magnetization-prepared 180° radio-frequency pulses and rapid gradient-echo (MPRAGE) sequence optimized for gray–white matter contrast with 1-mm-thick sagittal slices and an in-plane resolution of .938 × .938 mm. Freesurfer (Dale, Fischl, & Sereno, 1999) was used to create a cortical surface reconstruction. Functional images were acquired using a gradient-recalled-echo echo-planar imaging sequence sensitive to the BOLD signal (TR = 2000 msec; TE = 30 msec; flip angle = 90°). Thirty-three axial slices were collected with a slice thickness of 3 mm and an in-plane resolution at 2.75 mm × 2.75 mm while JB viewed rotating or expanding flickering black and white checkerboards.

Patient SB was a 48 year old female who had a large right hemisphere hemorrhagic stroke approximately 6 months prior to the first of three testing session. As can be seen in Fig. 1B, the stroke involved the right frontal, parietal, temporal, and occipital cortices. SB had neglect on line cancellation and line bisection tasks (Table 1). She also had a left visual field hemianopsia as assessed with a computer-based perimetry task (see Stimuli and procedures and Fig. 1B). Although we were able to obtain copies of the clinical MRI scans acquired on a GE 1.5 T whole body scanner, we did not acquire further MRI scans because of the distortions produced by a metal plate that was inserted around her head after a craniotomy.

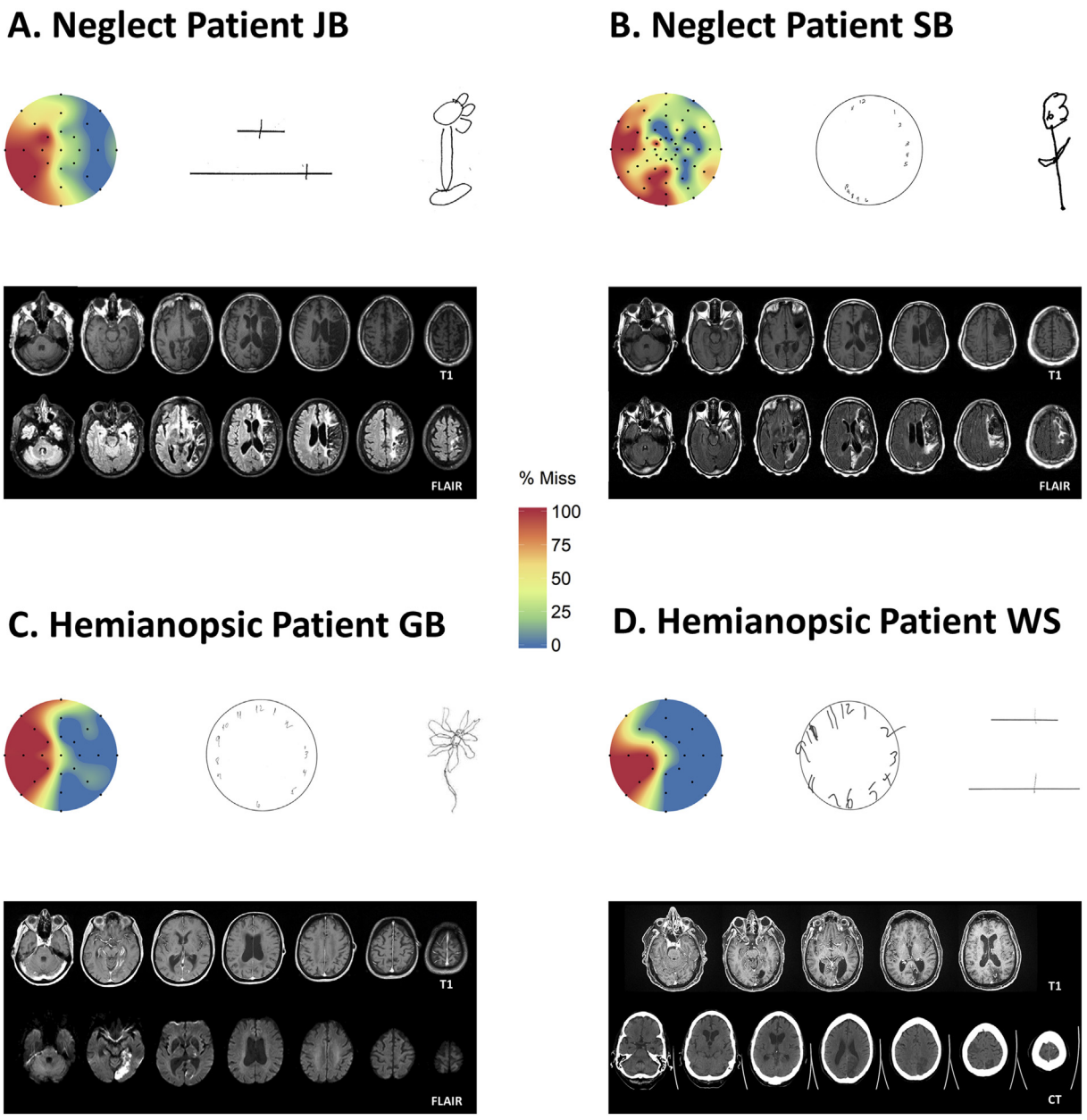

Fig. 1 – Results from a computer-based perimetry test, examples of neglect (or normal performance) on assessment tests, and MRI and CT scans showing the anatomical delineation and extent of the lesions for each patient. For all images, the left hemisphere is on the left side.

Table 1 – Patient performance (misses and mean percentage of errors) on neglect assessments.

Patient	Line Cancellation		Shape Cancellation		Perimetry		Bisection
	Left	Right	Left	Right	Left	Right	Rightward
JB (N)	0/8	0/9	7/13	0/6	87.7%	8.1%	6.8%
SB (N)	3/8	1/9	1/8	0/6	67.7%	23.7%	4.2%
GB (H)	0/8	0/9	1/11	1/13	98.9%	3.3%	2.4%
WS (H)	0/8	0/9	1/5	0/3	79.8%	.0%	3.5%

N = Neglect; H = Hemianopsia.

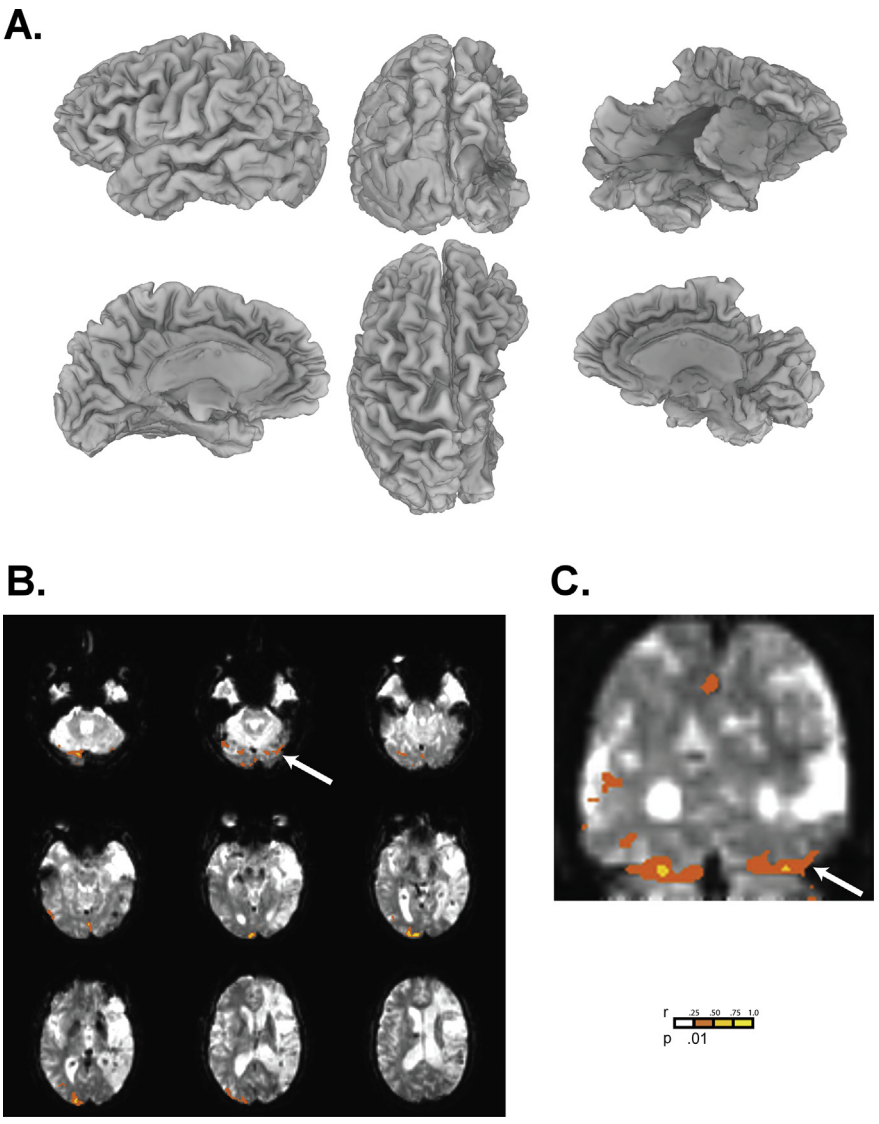

Fig. 2 – Anatomy and neural responses to visual stimulation in patient JB. A) Three-dimensional pial surface reconstruction of patient JB's brain from a high-resolution MPRAGE MRI scan. Top (from left to right): Lateral view of the left hemisphere; posterior view of the cortex; lateral view of the right hemisphere. Bottom (from left to right): Medial view of the left hemisphere; superior view of the cortex; medial view of the right hemisphere. B) Sequences of axial brain images from most inferior (top left) to most superior (bottom right). Spacing between successive images of 6 mm. Color shows significant responses to visual stimuli consisting of flashing black and white checkerboards (either rotating or expanding). Arrows highlight ipsilesional activation in ventral temporal and occipital cortex. C) Coronal slice at location of white arrow showing ipsilesional and contralesional activation. Left is left in all images.

The mean age of the two patients with neglect was 53 years of age. To rule out any effects of age, an additional ten healthy age-matched control subjects with a mean age of 53.4 years (range: 42–69) and normal or corrected-to-normal vision participated in this experiment after informed consent. The age-matched healthy control subjects and two hemianopsia without neglect patients were recruited from the New York City metropolitan area.

Patient GB was an 81 year old female who had a right posterior cerebral artery infarct approximately 5 months prior to the first of two testing sessions. Fig. 1C shows this patient's lesion in the right occipital and temporal cortices from a 1.5 T clinical MRI scan. Unlike patients JB and SB who had hemispatial neglect, patient GB showed no signs of neglect on shape and line cancellation tasks and had only a small amount of line bisection errors (Table 1). The extent of GB's visual field deficits was also assessed using a computer-based perimetry assessment (see Stimuli and procedures and Fig. 1C).

Patient WS was a 71 year old male who had a right posterior cerebral artery infarct approximately 14 months prior to the testing session. Fig. 1D shows WS's lesion in the right occipital cortex in a 1.5 T clinical MRI scan and a CT scan. As with GB, and unlike the neglect patients, WS showed no signs of neglect on shape and line cancellation tasks and had only a small magnitude of line bisection errors. WS's visual field

deficits, as assessed using a computer-based perimetry assessment (see Stimuli and procedures), are illustrated in Fig. 1D.

2.2. Apparatus

For all subjects, we used an IBM ThinkPad laptop computer with a 35.8 cm LCD monitor. The monitor was positioned at a viewing distance of approximately 57 cm and the frame rate of the monitor was set at 60 Hz for all subjects except for patient JB, for whom the frame rate was set at 50 Hz (note that we coded the software so that this different frame rate only affected two SOAs: 66.7 msec was changed to 60 msec and 116.7 msec was set to 120 msec). Custom software written in C was used to control stimulus presentation.

2.3. Stimuli and procedures

To map the visual fields of each patient, we used a modified perimetry task in which a single visual stimulus was presented at varying positions in the visual field from fixation. Note that this perimetry test to assess the visual fields may have also been influenced by the left visual field attentional deficit in neglect. On each trial, a black fixation cross measuring .2° in visual angle was presented at the center of the computer monitor on a white background. After a 500 msec fixation interval, a small black square measuring .25° was presented in the periphery for 50 msec. The patients' task was to respond on each trial whether or not the target square was seen. For all patients except SB, the target randomly appeared at one of eight evenly spaced polar directions at one of three eccentricities from fixation (3°, 6°, or 9°). Each visual field position was probed 10 times, for a total of 240 trials for patients JB and GB, and 9 times, for a total of 216 trials for patient WS. For patient SB, the target could appear at one of twelve evenly spaced polar directions at one of five eccentricities from fixation (2°, 4°, 6°, 8°, or 10°), and each visual field position was probed 10 times, for a total of 600 trials.

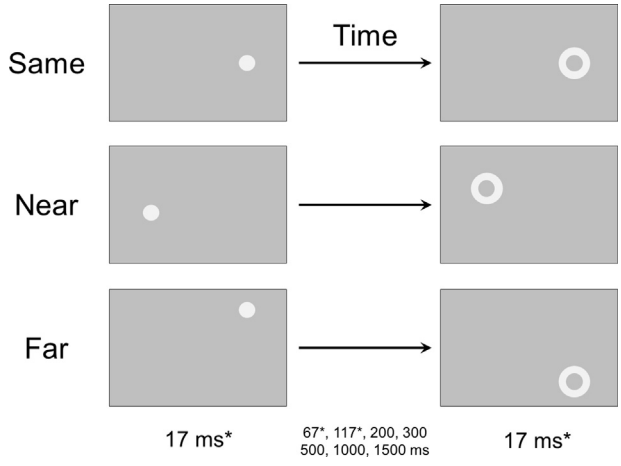

Fig. 3 – The stimuli and timing used to assess the spatial and temporal extent of metacontrast masking in the left and right visual fields. On each trial, a target disk was briefly presented and was followed at varying SOAs by a metacontrast mask that appeared on the same side. The target disk and metacontrast mask were both presented in either the same position, near, or far from one another. *The stimuli presentation times were 20 ms and the latencies between the disk and mask onset were 60 msec and 120 msec for patient JB.

For the metacontrast masking task, the visual stimuli were light gray on a dark gray background and consisted of a fixation point, a target disk, and a surrounding annulus that served as the metacontrast mask (see Fig. 3). The diameter of the fixation point subtended .1° of visual angle, the target disk subtended .5°, and the metacontrast mask subtended 1°. At the start of each trial, a fixation point was first presented for 500 msec followed by the presentation of a 1000 Hz pure frequency tone for 200 msec, which further signaled the start of each trial. Following an 800 msec interval after the offset of the tone, during which only the fixation point was presented, a target disk was then presented for 16.7 msec (or 20 msec for patient JB). The stimulus onset asynchrony (SOA) between target disk and metacontrast mask was either 67, 117, 200, 300, 500, 1,000, or 1,500 msec (or 60, 120, 200, 300, 500, 1,000, or 1,500 for patient JB). The mask briefly appeared after the interstimulus interval and remained on the screen for 16.7 msec (or for 20 msec for patient JB). These types of stimuli and timing parameters are often used to assess metacontrast masking functions, which typically follow a U-shaped function (Breitmeyer & Ogmen, 2000). However, because the shortest SOA was already 60 msec long, we anticipated measuring only an increasing level of performance and fitted psychometric functions to each participants' performance data.

The target disk and metacontrast mask both appeared on either the left or on the right side of fixation at one of three spatial separations from one another. In the same conditions, both the target disk and the metacontrast mask appeared 5° to the left or the right of fixation. In the near conditions, the target and mask were vertically displaced from one another with a center-to-center distance of 1.5°. In the far conditions, the target and mask were vertically displaced by 3°. In the near and far conditions, the disk appeared below the mask on half of the trials whereas the disk appeared above the mask on the other half of the trials.

For each trial of the metacontrast masking experiment, participants reported whether they saw the disk alone, the mask alone, both the disk and the mask, or nothing. The neurologically healthy control subjects responded on each trial using the keyboard, whereas the patients responded verbally on each trial, and their responses were entered into the computer by the experimenter.

2.4. Experimental design and statistical analysis

Participants ran a practice block to get accustomed to the metacontrast masking task, but trials from this block were not included in the statistical analyses. Following the practice block, sequential blocks of 70 trials were run until five blocks were completed by the neurologically healthy participants in one testing session. Data collection on the patients continued in each session until they expressed fatigue or could no longer perform the task. Patient JB completed 5 blocks of the

Table 2 – Percentage of target detections for each patient and the age-matched controls on the metacontrast masking task.

Patient	Position	Left							Right						
		67	117	200	300	500	1000	1500	67	117	200	300	500	1000	1500
JB (N)	Same	.0	.0	.0	.0	.0	.0	.0	.0	20.0	20.0	20.0	40.0	40.0	100.0
	Near	.0	.0	18.2	.0	.0	10.0	.0	.0	.0	30.0	27.3	90.9	54.5	80.0
	Far	.0	.0	.0	.0	.0	9.1	30.0	.0	.0	30.0	40.0	63.6	45.5	70.0
SB (N)	Same	4.2	13.0	8.3	9.1	.0	.0	.0	8.3	.0	4.2	8.7	.0	.0	45.5
	Near	8.3	16.0	4.3	8.3	8.3	41.7	4.2	47.8	8.3	54.2	12.5	62.5	25.0	45.8
	Far	12.5	75.0	16.7	54.2	4.2	60.9	28.0	58.3	4.2	47.8	20.8	50.0	13.0	75.0
GB (H)	Same	.0	.0	.0	.0	.0	.0	.0	.0	.0	50.0	88.9	50.0	77.8	100.0
	Near	.0	.0	.0	.0	.0	.0	.0	.0	23.5	83.3	88.9	52.9	94.1	88.2
	Far	.0	.0	.0	.0	.0	.0	.0	11.8	25.0	88.9	88.9	44.4	88.2	82.4
WS (H)	Same	.0	.0	.0	.0	.0	.0	.0	20.0	60.0	100.0	100.0	100.0	100.0	100.0
	Near	.0	.0	.0	.0	.0	.0	.0	80.0	90.0	100.0	90.0	100.0	100.0	90.0
	Far	.0	.0	.0	.0	.0	.0	.0	60.0	100.0	100.0	90.0	100.0	100.0	100.0
Controls	Same	46.0	88.5	92.0	100.0	96.0	100.0	100.0	50.0	74.0	84.0	96.0	96.0	100.0	98.0
	Near	69.0	86.0	95.0	98.0	98.0	99.0	96.9	72.0	86.0	94.0	97.0	97.0	100.0	99.0
	Far	80.0	91.0	95.0	100.0	99.0	100.0	100.0	83.0	93.0	97.0	97.0	99.0	99.0	100.0

N = Neglect; H = Hemianopsia.

metacontrast masking task over two separate testing sessions on different days whereas patient SB completed 14 blocks of the metacontrast masking task over three testing sessions on different days. Patient GB completed 9 blocks of the masking task over two testing sessions on separate days and patient WS completed 5 blocks of the masking task in one testing session.[1]

For each of the patients, separate three-way ANOVAs were conducted with side of stimuli, spatial separation, and SOA as the within subject variables and trials coded as the random factor. χ^2 analyses were used for comparisons between conditions for each of the patients. Psychometric masking curves were derived by fitting with a logit function the percentage of trials across the SOAs in which the subject correctly reported seeing both the target disk and the metacontrast mask. This sigmoidal rather than a u-shaped function was used because the experimental design did not include any target-to-mask SOAs shorter than 60 msec. Within this range of SOAs, masking effectiveness increases monotonically with SOA.

For the neurologically healthy, age-matched control subjects, psychometric masking curves were derived from the percentage of trials across the SOAs in which the subject correctly reported seeing both the target disk and the metacontrast mask. We then extracted the 75% detection rate latency from the psychometric functions of each subject and conducted a two-way within-subjects analysis of variance (ANOVA) on these latencies with side of stimuli (left or right) and spatial separation of target and mask (same, near, or far) as the two within-subject factors and subject as the random factor.

[1] As indicated by an anonymous reviewer, one limitation of this study is the unequal number of blocks completed by each patient, which was a consequence of patient availability and fatigue. However, an analysis using only the data from the first five blocks from each patient yielded statistical results that were highly similar. Therefore, the complete datasets from each patient are included in the main analyses and the differences in the degrees of freedom are a result of the different number of blocks and error trials (e.g., failure to respond) between patients.

To compare performance between the age-matched control subjects and the neglect and hemianopsic patients, we conducted significance tests on the differences in performance between each patient with that of the controls (Crawford & Howell, 1998). The *p*-values were adjusted for each patient using a false-discovery rate (FDR) correction for multiple comparisons (Benjamini & Hochberg, 1995).

3. Results

3.1. *Neuroimaging and perimetry*

Both neglect patients had extensive right hemisphere lesions from middle cerebral artery (MCA) strokes that spanned the frontal, parietal, occipital and temporal lobes (Fig. 1). Patients GB and WS also had right hemisphere lesions but from posterior cerebral artery (PCA) strokes that affected the occipital and temporal lobes. The cortical surface model of patient JB revealed extensive damage to dorsal occipital cortex, but relative sparing of ventral occipital and temporal cortex (Fig. 2). This sparing corresponds to JB's better visual detection abilities in the left upper visual field compared to the left lower visual field in the perimetry test (Fig. 1A). BOLD fMRI measures of the response to visual mapping stimuli showed robust activity in ventral occipital temporal regions of the lesioned right hemisphere (Fig. 2B,C). Although we were unable to acquire high resolution structural and functional MRI scans in patient SB, her clinical MRI scans showed that there was also some sparing of right ventral occipital cortex, as with patient JB, which also corresponds to her increased ability to see some unilateral visual targets in the upper left visual field compared to her lower left visual field (Fig. 1B).

3.2. *Task performance: Neglect patients*

Unsurprisingly, as a result of their neglect and hemianopsia, neglect patients JB and SB failed to correctly detect the target disk and the metacontrast mask on the majority of trials when

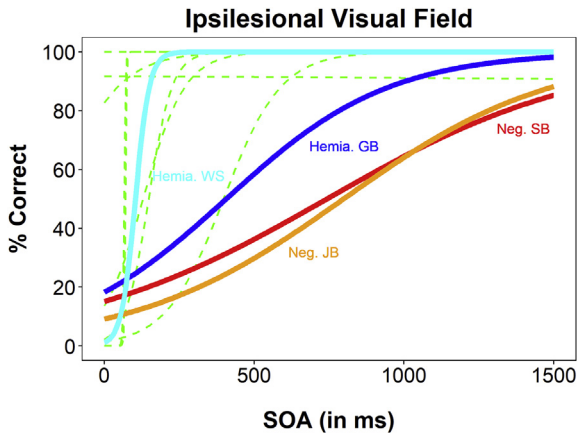

Fig. 4 – Psychometric metacontrast masking functions for the same position condition for each neglect patient (thick solid lines in orange for JB and red for SB), hemianopsic patients (thick solid lines in blue for GB and cyan for WS), and age-matched control subjects (thin dashed green lines).

the stimuli were presented in their left, contralesional hemifield (Table 2). Surprisingly, both patients also had difficulty performing the task in their ipsilesional (presumable normal) hemifield (Table 2 and Fig. 4). Even at SOAs as long as 1,000 msec and 1,500 msec between the target and mask, both patients continued to miss some of the targets in their right visual fields.

Performance was significantly worse in the left as compared to the right visual field ($F_{1,317} = 100.17$, $p < .001$ for JB and $F_{1,953} = 150.02$, $p < .001$ for SB), and there was a significant main effect of SOA, with poorer performance at the shorter SOAs ($F_{6,317} = 14.92$, $p < .001$ for JB and $F_{6,953} = 25.10$, $p < .001$ for SB). The side × SOA interaction was also significant ($F_{6,317} = 10.16$, $p < .001$ for JB and $F_{6,953} = 10.56$, $p < .001$ for SB). For SB only, the side × spatial separation × SOA three-way interaction was significant ($F_{12,953} = 2.18$, $p = .011$). The other interactions and the main effect of spatial separation between the target and the mask were not significant.

To further illustrate the ipsilesional perceptual deficits in these neglect patients, we also conducted χ^2 tests with FDR corrections for multiple comparisons on the p-values to compare target and mask detection performance at each of the earlier SOAs with the 1,500 msec SOA. Since the main effect of spatial separation was not significant for either patient, these analyses were conducted on the data without this factor. Unlike the neurologically healthy control subjects, who detected the majority of the targets after an SOA 67 msec, both patient JB and patient SB continued to make errors in the ipsilesional hemifield on the majority of the trials. Target and mask detection was significantly worse at all SOAs less than 500 msec when compared to performance at the 1,500 msec SOA for patient JB (all χ^2s > 12.48, all ps < .002, FDR corrected) and significantly worse at all SOAs less than 300 msec compared to correct performance at 1,500 msec for patient SB (all χ^2s > 18.32, all ps < .001, FDR corrected). In fact, both patients continued to make a substantial percentage of errors at SOAs equal to or longer than 500 msec, including at the longest 1,500 msec SOA. Patient JB detected both the target and the mask on only 64.9% of the trials for SOAs equal to or greater than 500 msec SOA and patient SB detected both the target and the mask on only 58.8% of these longer SOA trials.

In addition to comparing the percentage of correct responses across the different conditions, we further analyzed the performance data to gain a better understanding of the perceptual processing deficits in these neglect patients. For patient JB, the target disk was missed on 89.8% of the error trials whereas the mask was missed on the other 10.2% of the error trials. Patient SB did not perceive the target disk on 89.6% of the error trials; the mask was not detected on the other 10.4% of error trials. These results indicate that the patients with neglect had a prolonged metacontrast masking function and that this masking was effective over larger regions of space compared to neurologically healthy control subjects.

3.3. *Task performance: Healthy control subjects*

The latencies for 75% detction performance for the neurologically healthy control subjects were similar for the left and right visual fields (Table 2 and Fig. 4), and the main effect for side of presentation was not statistically significant ($F < 1$). However, there was a significant main effect of spatial separation between the target disk and the metacontrast mask ($F_{1,9} = 15.00$, $p < .005$), with later (i.e., longer lasting) metacontrast masking when the disk was presented at the same position as the mask as compared to when the disk and the mask were presented far from one another ($t_9 = 3.87$, $p = .011$, two-tailed and FDR corrected). The interactions between side of presentation and spatial position did not approach statistical significance.

We further analyzed the error trials to assess whether subjects were missing the target stimulus or the mask when only one stimulus was perceived. In line with the metacontrast masking literature, when a stimulus was missed, it was the target disk on the majority of the error trials (88.3%) rather than the metacontrast mask (11.7%). When the mask was missed, it was often because subjects responded to seeing the disk prior to the appearance of the mask (the SOAs were 1,000 or 1,500 msec on 50.0% of these error trials). Therefore, when the spatial positions of the target and mask were near or the same and the timing between the two stimuli was sufficiently short, backwards masking was sufficiently measured using these stimuli.

3.4. *Task performance: Hemianopsic patients*

Because of their hemianopsia, patients GB and WS were unable to detect any of the targets and masks in their left visual fields (Table 2). However, when the target and the mask appeared in their right visual fields, both patients had difficulty perceiving the target disk at the short SOAs but not at the long ones, especially for targets that appeared in the same position as the mask (Table 2 and Fig. 4, right). Thus, there was a significant main effect of side of target ($F_{1,557} = 150.02$, $p < .001$ for GB and $F_{1,308} = 2{,}317.42$, $p < .001$ for WS), a significant main effect of SOA ($F_{6,557} = 25.10$, $p < .001$ for GB and $F_{1,308} = 8.28$, $p < .001$ for WS), a significant side by SOA interaction ($F_{6,557} = 10.56$, $p < .001$ for GB and $F_{6,308} = 8.28$, $p < .001$

for WS), and a significant side by spatial separation by SOA interaction ($F_{12,557} = 2.18$, $p = .011$ for GB and $F_{12,308} = 2.08$, $p = .018$ for WS). For WS, there was also a significant spatial separation by SOA interaction ($F_{12,308} = 2.08$, $p = .018$), demonstrating larger masking effects for the same spatial position at early SOAs, but this interaction was not significant for patient GB. The main effect of position and the side by spatial separation interactions did not approach significance for either of the patients.

χ^2 tests with FDR corrections for multiple comparisons on the p-values were used to compare target and mask detection performance in the ipsilesional hemifield at the different SOAs. Since the main effect of spatial separation was not significant, these analyses were conducted on the data without this factor. Unlike the neurologically healthy control subjects and patient WS, who detected the majority of the targets after an SOA of 67 msec, patient GB also missed substantial percentages of targets in the ipsilesional hemifield at an SOA of 117. Stimuli detection was significantly worse for GB at the 67 msec and 117 msec SOAs as compared to performance at the 1,500 msec SOA (both χ^2s > 16.0, ps < .001, FDR corrected). However, patient GB detected both the target and the mask on an average of 58.4% of the trials across the other SOAs. For WS, performance was significantly worse at only the 67 msec SOA compared to performance at the 1,500 msec SOA ($\chi^2 = 9.44$, $p = .013$, FDR corrected). WS detected both the target and the mask on an average of 95.6% of the trials at all SOAs greater than 67 msec. Whenever a stimulus was missed, the target disk was missed on 72.4% of the error trials for GB and 85.7% of the error trials for WS, whereas the mask was missed on the other 27.6% of the error trials for GB and 14.3% of the error trials for WS. For GB, this larger percentage of missed mask trials was primarily driven by performance at the 500 msec SOA, when the metacontrast mask was missed on 100% of the error trials. These missed masks at the 500 msec SOA may have been a result of GB making eye movements to the targets, which may have induced saccadic suppression.

3.5. *Single-cases vs control comparisons*

We also compared performance in the ipsilesional field for each patient with the group of neurologically healthy, age-matched control subjects, averaged across hemifields, using a modified t-test procedure that adjusts for non-normality and small sample sizes (Crawford & Howell, 1998). At the two earliest SOAs, performance was similar between each of the patients and the control subjects because target detection was equivalently impaired by the metacontrast mask (all ts > −1.81, all ps > .10, two-tailed and FDR corrected). At all other SOAs, including as long as 1,000 msec and 1,500 msec, both neglect patient JB (all ts < −2.93, all ps < .035, two-tailed and FDR corrected) and neglect patient SB (all ts < −3.03, all ps < .049, two-tailed and FDR corrected) were significantly worse at detecting targets and masks in the ipsilesional right visual field compared to the average across both hemifields in age-matched control subjects. However, in contrast to the neglect patients, performance of hemianopsic patient GB was comparable to the control subjects at all SOAs except for at the 500 msec ($t = −5.97$, $p < .001$, two-tailed and FDR corrected) and 1000 msec ($t = −6.82$, $p < .001$, two-tailed and FDR corrected) SOAs. These differences were primarily due to patient GB responding to the target prior to or during the onset of the mask. Performance of hemianopsic patient WS did not differ from the controls at any of the SOAs (all −1 > ts < 1, ps > .5).

4. Discussion

These results demonstrate systematic impairments of perceptual information processing on the side of visual space normally considered to be unaffected in neglect patients—that is, on the same side as the lesion. Unlike the neurologically healthy control subjects and the hemianopsic patients without neglect, who only missed targets when a mask was presented at the same spatial position shortly after a target, the two neglect patients missed targets in ipsilesional space even when the masks were vertically displaced by 3° and presented up to 1,500 msec after the target. These findings indicate that patients with "hemispatial" neglect may actually have whole-field distortions of attention and perception. On the contralesional side, perceptual information is entirely missed and/or neglected, leading to or resulting from failures in attention, but may nonetheless be processed unconsciously (Berti & Rizzolatti, 1992; Esterman et al., 2002; Ladavas, Paladini, & Cubelli, 1993; Marshall & Halligan, 1988; Mattingley, Bradshaw, & Bradshaw, 1995; McGlinchey-Berroth, Milberg, Verfaellie, Alexander, & Kilduff, 1993; Ro & Rafal, 1996). On the ipsilesional side, however, certain types of information, such as the metacontrast mask used in this study, may displace preceding stimuli from conscious perception for extended periods of time.

Previous studies have demonstrated impairments of attentional orienting towards targets in ipsilesional space when an attentional cue was presented more ipsilesionally, thereby requiring a contralesional shift of attention within the ipsilesional hemifeld (Ladavas, 1990; Ladavas et al., 1989). The current results extend these previous findings by showing extended spatial and temporal processing deficits in the often presumed "normal" visual field in neglect patients. Studies of attention in patients with focal brain damage (Friedrich et al., 1998; Posner, Cohen, & Rafal, 1982; Posner et al., 1984; Posner, Walker, Friedrich, & Rafal, 1987; Rafal & Posner, 1987) and in neurologically normal subjects with fMRI (Astafiev et al., 2003; Beauchamp, Petit, Ellmore, Ingeholm, & Haxby, 2001; Corbetta et al., 1998; Corbetta, Miezin, Shulman, & Petersen, 1993; Corbetta, Kincade, Ollinger, McAvoy, & Shulman, 2000; Corbetta & Shulman, 2011; Nobre, Allison, & McCarthy, 1998; Nobre, Gitelman, Dias, & Mesulam, 2000) have demonstrated a network of brain areas suggested to be involved with different components of attention. Given that the neglect patients in our study showed extensive metacontrast masking over space and time, one likely mechanism that may explain this pattern of performance is an overactive attentional engagement system that causes the processing of the mask to suppress the processing of the preceding and sometimes vertically displaced targets. Note that this hyperactive engagement of processing in ipsilesional space is independent of any disengage deficits towards contralesional space,

which was not measured in this study due to the targets and masks only appearing at the same spatial position or vertically displaced. Indeed, several studies have demonstrated an ipsilateral hyperorienting of attention after parietal lesions or disruption from TMS (Blankenburg et al., 2008; D'Erme et al., 1992; Hilgetag, Theoret, & Pascual-Leone, 2001; Seyal et al., 1995; Szczepanski & Kastner, 2013). Despite these compelling lines of evidence ipsilesional hyperorienting, however, the data from the current study suggest that some other mechanism may be at play because enhanced attention should have reduced the effectiveness of the subsequent metacontrast mask, as previous studies have shown (Boyer & Ro, 2007; Ramachandran & Cobb, 1995).

An alternative explanation for the current results is that the right hemisphere is responsible for attending to both halves of space (Heilman & Valenstein, 1979; Heilman & Van Den Abell, 1979, 1980), resulting in more extensive metacontrast masking even in ipsilesional space after right hemisphere damage because of the globally reduced attention. In other words, the right hemisphere brain damage, particularly to the ventral attention network that includes the temporoparietal junction (Corbetta et al., 2000; Corbetta & Shulman, 2011; Friedrich et al., 1998), may have resulted in weakened attentional orienting responses even towards ipsilesional space. This interpretation is consistent with the results from the perimetry test, where both neglect patients sometimes failed to detect even single ipsilesional hemifield stimuli. This interpretation would also be consistent with a previous study convincingly demonstrating general non-spatial deficits in arousal in neglect (Robertson, Mattingley, Rorden, & Driver, 1998). Although more systematic studies with a larger group of patients with more focal lesions, including ones with left hemisphere lesions, and a larger group of age-matched controls will be necessary to more definitely demonstrate these ipsilesional deficits and hemispheric asymmetries, these results provide compelling evidence that certain aspects of attention may also be impaired in ipsilesional space of neglect patients.

Several studies have demonstrated extinction of contralesional stimuli, even when presentation of an ipsilesional stimulus is asynchronous (Baylis, Simon, Baylis, & Rorden, 2002; Cate & Behrmann, 2002; di Pellegrino, Basso, & Frassinetti, 1997; Guerrini, Berlucchi, Bricolo, & Aglioti, 2003; Rorden, Jelsone, Simon-Dack, Baylis, & Baylis, 2009). In the current study, it was almost always the subsequent masking stimulus that was readily detected and the preceding masked stimulus that was missed on the ipsilesional side, unlike these previous studies of asynchronous extinction, in which a subsequent contralesional stimulus could be extinguished by a preceding ipsilesional one. In this respect, the current findings also contrast with those demonstrating an extended attentional blink (Husain et al., 1997) in that the preceding target stimulus did not produce a prolonged inability to detect the later masking stimulus. These findings suggest that a general attentional impairment may explain asynchronous extinction, extended attentional blinks, and the current prolonged ipsilesional masking effects measured in neglect patients. However, our findings of extended metacontrast masking in the ipsilesional hemifield further suggests that low-level physical features may also be important in affecting the perception of previously presented stimuli. Together with other studies demonstrating differences in detection that are task dependent (e.g., Baylis, Driver, & Rafal, 1993; Vuilleumier & Rafal, 2000), the current findings suggest that the individuation of stimuli in neglect may involve interactions between low-level sensory processes and high-level regions involved with top-down control.

Interestingly, both neglect patients with right MCA territory lesions had visual field deficits and white matter damage, with some ability to detect single targets in contralesional space in the perimetry task assessing their visual fields. Structural MRI scans of both patients revealed lesions that affected dorsal but not ventral primary visual cortex and fMRI of patient JB showed ventral occipital cortex activity in the lesioned hemisphere. In addition to demonstrating ipsilesional perceptual processing deficits in neglect, our findings further suggest that MCA lesions may affect dorsal primary visual cortex more than ventral primary visual cortex. A larger and more systematic study of patients with MCA and posterior cerebral artery (PCA) lesions is required, however, to determine whether upper visual field sparing is more common after MCA lesions and the contributions of white matter lesions in these observed effects. Furthermore, although we collected large numbers of trials from each patient to estimate their psychometric functions and conduct single-case statistical analyses, future studies with more extensive neuropsychological profiles and with larger groups of patients, including right hemisphere MCA patients without neglect, will be helpful in further clarifying the exact nature of these effects.

While the term "hemineglect" implies that deficits are limited to the visual field contralateral to the lesions, we show that patients with "hemispatial" neglect have spatially and temporally extended perceptual processing deficits in the ipsilesional visual field. Because of the attenuating effects of attention on metacontrast masking, these results provide evidence of attentional impairments on the right half of space after right hemisphere lesions and suggest that the right hemisphere may be involved with orienting attention to both halves of space.

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