Retinotopic modulation of space misrepresentation in unilateral neglect: evidence from quadrantanopia

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A patient with right sided brain damage suffered contralesional neglect, inferior quadrantanopia (with 0° sparing in the left eye and 13° sparing in the right), and a visual field restriction (to 15°) in the upper contralesional quadrant of the left eye. In binocular vision, the patient showed underestimation of the horizontal size of contralesional line segments unless cued to localise their end points. When asked to reproduce, in monocular vision, 10° and 20° distances between two attentionally cued end points lying on the frontal vertical plane, the patient showed relative contralesional overextension and ipsilesional underextension along the directions falling within the blind sectors of the neglected space. No asymmetry was present along the directions falling within the seeing sectors of the same space. These findings suggest precise retinotopic modulation of space misrepresentation in unilateral neglect.

Neglect patients fail to attend to stimuli in the space contralateral to their unilateral brain damage. Visual neglect is considered to depend on the disruption of multimodal representations of space integrating visual, proprioceptive, and vestibular inputs in one hemisphere, most often the right. It can occur independently of visual field defects caused by damage to retinotopic representations of space in primary visual pathways (that is, hemianopia). Conversely, hemianopia is not necessarily accompanied by neglect. It has been shown that relative underestimation of horizontal distances in the contralesional space, and corresponding overestimation of equivalent ones in the ipsilesional space, can be associated with neglect. This pattern of anisometry seems severe in patients suffering both neglect and hemianopia, mild in some neglect patients with posterior lesions and no visual field defects, and absent in the large majority of patients with neglect and no hemianopia.

Patients with pure hemianopia suffer the reverse pattern of horizontal space misrepresentation—that is, contralesional overestimation and ipsilesional underestimation. In this report, we show that apparent space anisometry along the directions of the frontal vertical plane falling within the spared retinotopic areas of the neglected space can be resolved by attentional cueing, while anisometry along the directions falling within the blind retinotopic areas is not resolved by cueing.

CASE REPORT

We studied a 76 year old right handed woman. On August 2001 she suffered a right frontal-temporal-parietal stroke (see computed tomography of her brain in fig 1) resulting in left hemiplegia. Two and a half months later, at the time of testing, intellectual function was within the normal range, with no memory or language impairment. Goldman perimetry before and after our study revealed contralesional inferior quadrantanopia (with 0° sparing in the left eye and 13° sparing in the right eye) and a visual field restriction (to 15°) in the upper quadrant of the left eye (fig 2). A structured clinical interview disclosed total unawareness of visual field defects, in both monocular and binocular vision.

Mild contralesional neglect was found. In the line bisection test, the averaged ipsilesional deviation on three trials (line length, 20 cm) was 97 mm. In the letter cancellation test, the patient performed a right to left row by row inspection of the
array with no vertical bias in the spatial distribution of omissions (42/53 cancelled items on the left, 51/51 on the right). However, in other tasks with scattered items the neglect showed a diagonal gradient. In the line cancellation test, the patient omitted only one item in the bottom left corner of the page (10/11 on the left, 10/10 on the right). In the copy of a scattered array of 10 crosses presented on an A4 sheet of paper, the patient omitted three items located in the bottom left corner of the model. Similarly, in the Wundt–Jastrow illusion test, the illusion was always missed (0/10) when the two fans were oriented leftward-downward, missed only once when the fans were leftward-upward or rightward-upward, and never missed when the fans were rightward-downward.

**Landmark task**

In two sessions, run a week apart, the patient made a visual forced choice (uncued size comparison) about the length of the segments of 12 centrally bisected horizontal lines and of 10 lines bisected 0.5, 1, 1.5, 2, or 2.5 cm to the left or right of the true centre. The centre of lines was aligned with the mid-sagittal plane of the body. All lines were 20 cm long and subtended approximately 20° of the visual field, so that they could fall within the spared retinotopic sector of the horizontal meridian. In each session, the task was readministered immediately afterwards and the patient was required by the examiner to look at and localise the end points of the lines at the beginning of each trial (cued size comparison). Both tasks were performed in free vision. On each trial the patient had to point (verbally and manually) at the subjectively shorter (session 1) or longer segment (session 2).

**Visual end point setting**

With this task, we evaluated space misperception along the horizontal, vertical, −45°, and +45° meridians of the visual field. The patient reproduced, on eight trials, 10° and 20° distances between a central reference and a target presented in one hemispace by monocularly setting (with the head restrained) another target in the diametrically opposed direction and hemispace. The side and amplitude of reproduction varied in a fixed random sequence. The central reference was aligned with the centre of the orbit of the seeing eye, and the head with the midsagittal plane of the body. Unlighted light emitting diodes (2×2 mm) were used as end point targets (green and red) and as a central reference (yellow). Targets were moved by the experimenter along a black bar that could be rotated on a black vertical panel. The patient verbally guided the moving target, which was initially positioned close to the central reference. Unlimited time was allowed for setting the position of the moving target. As with cued size comparisons, in this task any asymmetry in reproduction can be attributed to genuine space misperception and not to defective attentional inspection, because the patient was required to look at and check the position of targets and of the central reference at each step of each trial.

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**Figure 2** Visual perimeters of the left and right eye (test stimulus: size III, intensity 4e). 10° (top) and 20° (bottom) averaged distances (with SD in parentheses), reproduced along the frontal vertical plane, are reported at the corresponding end sides of each meridian. Significant asymmetries of reproduction between the opposite sides of the same meridian are marked with a symbol at the top end of the corresponding meridian. *p < 0.01; †p = 0.03; t test.
RESULTS
Landmark task
In the uncued condition, the patient invariably judged that the left, contralesional, segment of centrally bisected lines was shorter (12/12, session 1) or that the right, ipselesional, segment was longer (12/12, session 2). In the cued condition, no lateral bias was present in session 1 (5/12 left shorter: binomial test, NS) and a bias opposite to that of the uncued condition was present in session 2 (that is, 10/12 left longer: binomial test, p = 0.02). In the uncued condition, the contralesional segments of lines bisected 0.5 or 1 cm to the right of the true centre were still perceived as being shorter, but in the cued condition the segments of all asymmetrically bisected lines were perceived flawlessly in both sessions.

Visual end point setting
Averaged reproduced distances and the results of statistical comparisons (t test) between corresponding distances on the two sides of each meridian are reported in fig 2. No asymmetry was observed along the horizontal and vertical meridians. With the left eye, relative contralesional overextension (that is, underestimation) and ipselesional underextension (that is, overestimation) were found both when 10° and 20° distances were reproduced along the +45° meridian, falling on the entirely blind lower quadrant, and also when 20° distances were reproduced along the −45° meridian, where there was sparing of only 15° of the contralesional upper visual field. Along this latter meridian, no asymmetry was present for 10° distances falling inside the spared retinotopic space. With the right eye, along the +45° meridian relative contralesional overextension was found for 20° distances (falling outside the spared contralesional retinotopic portion of the meridian) but not for 10° distances (falling inside the spared portion). No asymmetry was observed along the entirely spared −45° meridian.

DISCUSSION
The dissociations observed in our patient bring out some relevant points. First, asymmetry of reproduction was observed within the blind retinotopic space of both the upper and the lower contralesional quadrant, whereas no asymmetry was present within the spared retinotopic space of the same quadrant. This shows that asymmetry was not merely caused by variations in neglect severity between the upper and lower contralesional space, as could have been suggested by the presence of a diagonal component in the neglect of the patient. The broader implication of this specific finding is that space misrepresentation in unilateral neglect cannot simply be accounted for by variations in neglect severity among different patients (we also note that our patient suffered mild neglect). Taken together, underestimation of contralesional horizontal size in attentionally uncued size comparison, no lateral (or even a reversed) bias in cued size comparison, and symmetric cued end point setting along the spared retinotopic space provide an explanation for previous contrasting findings in neglect patients without field defects reported both by the same and different investigators. In those studies, contralesional underestimation was found in uncued size comparison but was not found in visual and visuomotor cued end point setting tasks.4,8 Our case study shows that underestimation of contralesional horizontal size can be the result of defective contralesional attention unless task instructions explicitly cue the end points of the segments to be compared.7 The general asymmetrical reproduction along the +45° diagonal and the omissions of items in the lower contralesional space shown by our patient also suggest the need to investigate the possible role of inferior quadrantopia in the pathogenesis of diagonal neglect.11,12

Our data favour the hypothesis that space anisometry in unilateral neglect depends on concomitant damage to visual retinotopic representations of the neglected space. We have proposed that dysmetric performance is a result of the inability to remap the blind retinotopic space in a higher order frame of reference, where visual, proprioceptive, vestibular, and efference copy signals linked to eye–head scanning are integrated. When intact, these multimodal cues could provide metrically correct memories of spatial positions falling in the blind hemifield by using multimodal information gathered from the inspection of the same positions with the seeing hemifield. Accordingly, we interpreted relative contralesional overextension as deriving from the metrically dysregulated effort of shifting away the contralesional blind hemifield and bring the subjective end point position into the seeing ipselesional field. Conversely, ipselesional underextension was seen as being caused by hypometric scanning toward the subjective ipselesional end point position so as not to lose either the central reference or the end point position into the blind field moving ipselesionally. Future studies should directly test these hypotheses by monitoring eye movements. Bisioh et al stressed that the ipselesional bias shown by neglect patients can be interpreted as originating from anisometric representation of the horizontal space only when it is matched by relative contralesional overextension in size or distance reproduction. In fact, contralesional overextension excludes alternative explanations such as ipselesional attentional deviation, defective attentional disengagement from the ipselesional space, or contralesional hypokinesia. Our observations show that purely perceptual tasks—in which horizontal items with uncued end points are used as test stimuli—cannot disentangle the pathological effects linked to reduced contralesional attention from those linked to space misrepresentation. This could interfere with the accurate evaluation of the spatial metric abilities shown by neglect patients when forced to analyse the otherwise spontaneously neglected space. This may have implications for diagnosis and rehabilitation.

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