Neglect of radial and vertical space: importance of the retinotopic reference frame

J C Adair, D J Williamson, D H Jacobs, D L Na, K M Heilman

Abstract
Neglect from bilateral brain injury can disrupt responses along space defined by the vertical and radial axes. The spatial reference frames for vertical and radial neglect remain largely undefined, however. The viewer centred system, for example, consists of retinocentric and cephalocentric/corporacentric frames. In the present study, different viewer centred reference frames were dissociated in a patient with combined far radial superior vertical neglect through performance of radial line bisections above and below eye level. To separate reference frames for vertical space, bisections were performed while the patient was lying sideways. Results suggest that this patient's neglect respected a retinotopic viewer centred reference frame.

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Key words; neglect; retinotopic; reference

Patients with neglect fail to detect, respond, or orient to novel stimuli despite normal mental sensory and motor function. Spatial neglect refers to impaired stimulus-response interactions in one part of space while these interactions in other regions remain relatively intact. Spatial neglect primarily involves the detection (attention) of or action-exploration (intention) toward objects in the part of space contralateral to a hemispheric lesion, most often accompanying lesions in the right hemisphere.

Recent studies suggest that neglect can also occur along radial and vertical dimensions. Whereas biparietal injury can cause neglect for near and inferior space, bilateral temporop-occipital injury is associated with neglect of far and superior space. Thus the brain seems to contain local networks that allocate and manipulate attention across multiple spatial dimensions such that the dorsal parieto-occipital system mediates processing in near and inferior space whereas the ventral temporop-occipital system subserves far and superior space.

Space is not inherently divided into near-far and superior-inferior portions. Therefore, spatial location is defined by reference to external stimuli (object centred and environment centred) or to the organism itself (viewer centred). The viewer centred system may, in turn, comprise a group of distinct reference frames, including retinocentric (visual field), cephalocentric (head/trunk), or corporacentric (body) coordinates.

Radial neglect may be retinocentric, cephalocentric, or corporacentric. When bisecting radially oriented lines below eye level, normal subjects place their mark slightly beyond the true centre. This bias suggests that normal subjects are relatively inattentive to (a) the space nearest the body or head in a cephalocentric/corporacentric reference frame or (b) the segment of the line that falls on the superior part of the retina. Geldmacher and Heilman recently showed that the retinotopic and corporacentric/cephalocentric reference frames may be dissociated for radial line bisection.

The present study describes a patient with radial and altitudinal neglect. We sought to establish the frame to which this patient's radial and vertical neglect was referenced. The patient's performance on vertical and radial line bisections suggested that neglect primarily respected the viewer centred reference frame. Using Geldmacher and Heilman's approach, the patient's performance could be further specified within the viewer centred coordinate system. The purpose of this study was to learn whether radial neglect respected a retinotopic rather than a cephalocentric/corporacentric reference.

Case report
A 67 year old woman sought evaluation for impaired vision. Her problems began in December 1993 when she noted the abrupt onset of light headedness and disturbance of sight. Symptoms resolved rapidly, so she deferred medical evaluation until the symptoms recurred one month later, accompanied by left arm clumsiness and unsteady gait. Cranial MRI at this time demonstrated enhancing occipital lesions interpreted as areas of infarction (fig 1). She was transferred to Shands Hospital when visual function declined precipitously in February 1994. On admission, her primary complaints related to visual impairment. She professed difficulty following the moving images of her television, attributing this to "a problem with [her] glasses". Additionally, she failed to
recognise visitors until they spoke. Other complaints included unsteady gait and memory disturbance. The patient was alert and cooperative. She was completely oriented and related a complete history with minimal assistance. Her speech was fluent and grammatical and comprehension was intact. She performed simple calculations accurately. She had anterograde amnesia for verbal material, recalling none of three objects after three minutes of distraction. An elemental neurological examination disclosed mild pyramidal distribution weakness of the left extremities. Her reflexes were more brisk on the left than right; her plantar response was plantar bilaterally. Perception of tactile stimuli was normal in the distal extremities with no extinction of bilateral double simultaneous stimuli. Her gait was broadly based, and rapid alternating movements with her left arm were slightly dysmetric.

Standard visual acuity charts could not be used because the patient often failed to fixate the target stimuli. She consistently indicated the orientation of lines of 1 mm width and 10 mm length at 2–5 m (roughly 20/50 acuity), however, and optokinetic nystagmus was elicitable using 1 mm stripes at 40 cm (roughly 20/40). Her spontaneous eye movements were restricted, although her pursuit of slowly moving targets was normal. Although visual field testing to confrontation demonstrated perception of single stimuli in all fields, she consistently extinguished stimuli from the upper visual quadrants with double simultaneous stimulation across the horizontal meridian. The patient’s analysis of complex pictures was fragmentary as she could detect isolated elements but failed to describe their relation (simultanagnosia). When locating items visually, she searched inefficiently with inaccurate saccades. When grasping targets in the visual periphery, she variably fell short or extended beyond the object (optic ataxia). By contrast, movements directed toward her own body parts remained intact. The patient also showed mild visual object agnosia, often failing to identify visually presented objects. Conversely, she recognised objects by their characteristic sounds (for example, keys) and readily identified tactually presented items. The patient had colour anomia, successfully identifying only 12 of 24 coloured stimuli. When given a colour name, however, she selected the appropriately coloured square from an array in 24 of 24 trials and answered colour imagery questions flawlessly.

Methods
CONTROL SUBJECTS
Neurologically normal right handed volunteers ranging in age from 56 to 65 acted as control subjects (n = 7). None of the subjects reported a history of neurological or psychiatric disease.

PROCEDURE 1: ESTABLISHING SPATIAL BOUNDARIES OF NEGLECT
The location of the patient’s lesion, as well as her performance on vertical double simultaneous visual stimulation tasks, suggested that she might show neglect of multiple spatial dimensions, similar to the patient of Shelton et al. Thus we evaluated line bisection performance in three different spatial axes (fig 2). The patient and control subjects bisection lines while sitting at a table. Stimuli were positioned in a manner that placed the line’s centre about 30 cm from the body. Lines were 3 mm thick and 24 cm long, centred on 22 × 28 cm paper. Lines were presented horizontally, vertically, and radially. In the horizontal condition, the line was placed on the table with the centre aligned with the patient’s midsagittal plane. In the vertical condition, the line was fixed to a rigid surface with transparent adhesive and positioned with the centre of the line at the patient’s eye level. In the radial condition, the line was placed on the table below eye level in the midsagittal plane. Trials for each line orientation were divided into three blocks of five trials; the order of presentation for each block was varied randomly.

PROCEDURE 2: ESTABLISHING SPATIAL REFERENCE FRAMES OF NEGLECT
When an upright subject bisects vertical lines, bisection error can be related to the subject’s
Figure 3 Diagram of radial line projection on to retina. Depending on gaze direction (above or below), the same segment of line (proximal or distal) falls on opposite parts of the retina (superior or inferior).

Within the viewer centred reference frame, radial neglect can be more specifically defined as either retinotopic or cephalocentric/corporacentric. To dissociate these alternative frames of reference, radial bisections were performed with subjects gazing upward at lines above their head and gazing downward at lines below eye level. The dissociation occurs because the optical properties of the ocular lens result in image inversion on the retina. Ishiai et al showed that subjects foveate the midregion of lines they bisect. Accordingly, when attempting to bisect a radially oriented line below eye level, the line’s distal aspect falls on the inferior retina whereas the line’s proximal extent falls on the superior retina (fig 3). When viewing the same line above eye level, the distal part of the line now projects to the superior retina whereas the proximal part projects inferiorly. Therefore, if radial neglect is induced by cephalocentric/corporacentric inattention, one would expect bisection error in the same direction regardless of gaze; however, if neglect is induced by relative inattention to the portion of the line falling on the superior retina (retinotopic), one would expect bisection error in opposite directions with upward and downward gaze. The patient and control subjects completed 15 trials in each gaze condition.

**Results**

**SPATIAL BOUNDARIES OF NEGLECT**

Table 1 shows that in the horizontal condition, the magnitude of the patient’s rightward errors was greater than the magnitude of her leftward errors. There was, however, no significant difference in the number of times she erred to the left or right (expected proportion = 0·5, observed proportion = 0·47, P = 0·14). For the vertical condition, by contrast, both the magnitude (mean error = −11·9 mm) and frequency of errors (expected = 0·5, observed = 0·93, P < 0.00001) favoured inferior space. Likewise, in the radial condition, the magnitude (mean error = −13·6 mm) and frequency of errors (expected = 0·5, observed = 0·93, P = 0·00001) favoured the proximal half of the line. Her errors in the vertical and radial conditions were opposite in direction and significantly greater in magnitude than the bisection bias of control subjects. These findings suggest that she neglected superior and far peripersonal space. Her target cancellation performance was consistent with this interpretation.

**SPATIAL REFERENCE FRAMES OF NEGLECT**

When laying on either side, the patient bisected viewer centred vertical lines below the true centre (table 2). The mean error was greater when she lay on her left side (−18·7 mm (SD 23·9)) than when she lay on her right (−2·5 mm (SD 16·4)). The patient more consistently bisected lines below true centre when on the left side (expected = 0·5, observed = 0·7, P = 0·037) than on the right (expected = 0·5, observed = 0·45, P = 0·16). As she held the marker in her right hand under both conditions, this difference may reflect restriction of arm movement when laying on her right side. Alternatively, the difference may reflect an interaction between viewer centred neglect of inferior space and environment centred neglect of right space. The superimposition of environment centred rightward bias would exaggerate viewer centred inferior bias when laying on the left side but attenuate viewer centred inferior bias when on the right. In any event, her performance in both recumbent positions suggests that neglect of the upper segment of lines is based predominantly upon the viewer centred perspective.

As discussed, the viewer centred reference system consists of retinotopic and corporacentric/cephalocentric components. The patient’s bisection error, in both radial and vertical axes, could be explained by inattention to stimuli that project to the inferior half of the environment.
retina. Performance on radial bisection above and below eye level supports this assertion: direction of gaze significantly influenced performance (table 2). During downward gaze, the patient consistently misbisection radial lines proximal to the midpoint. When gazign upward, her bisection error reversed, falling consistently beyond the centre (expected = 0.5, observed = 0.76, P = 0.003). Controls tended to bisection slightly distal to the midpoint for radial lines in the inferior location and slightly proximal to the midpoint for radial lines in the superior location, thus replicating the findings of Geldmacher and Heilman. The patient’s radial bisection error was opposite in direction and significantly greater in magnitude than that of control subjects. Hence, her performance was not compatible with cephalocentric/corporacentric neglect. Rather, radial (and perhaps vertical) bisection errors seem to depend on spatial coordinates defined by the retinotopic frame of reference.

Table 2: Spatial reference frames of neglect

<table>
<thead>
<tr>
<th></th>
<th>Left lateral</th>
<th>Right lateral</th>
<th>Radial (below eye level)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient mean (SD)</td>
<td>-18.7</td>
<td>-2.5</td>
<td>+10.5</td>
</tr>
<tr>
<td>Control</td>
<td>+0.2</td>
<td>+0.5</td>
<td></td>
</tr>
<tr>
<td>Control 95% CI</td>
<td>-3.81-4.55</td>
<td>-3.81-4.12</td>
<td>-4.52-3.46</td>
</tr>
</tbody>
</table>

* Denotes error to the right, above, and beyond true centre in mm; data represent mean of 15 trials in each condition; 95% CI = 95% confidence interval.

Discussion

The patient showed neglect for stimuli in superior vertical and far radial space. Associated deficits included visual agnosia, colour dysnomia, and visually guided reaching. Her signs and symptoms suggested dysfunction in visual association areas that comprise the ventral pathway, an anatomical localisation that was confirmed by MRI. Therefore, she closely resembled the patient described previously by Shelton et al. By contrast, other recent accounts of patients with neglect of radial and vertical space suggest that injury to parieto-occipital regions comprising the dorsal visual pathway produced neglect for inferior vertical and near radial space. Thus spatial neglect can impede perception and exploration of space along multiple spatial axes.

Before accepting the patient’s behaviour as altitudinal radial neglect, other explanations must be considered. Impaired visuospatial judgment might reflect damage to primary visual areas. The patient was not cortically blind, however, nor could we establish the presence of altitudinal hemianopia. More importantly, the patient reported single stimuli presented to the upper visual fields, supporting the integrity of the geniculocalcarine pathway. Extinction of visual stimuli when presented simultaneously with inferiorly located stimuli provided further evidence that attentional factors produced defective performance. As she showed elements of Balint syndrome, performance on cancellation and bisection tasks might reflect misreading due to optic ataxia. The patient’s errors showed systematic directional bias, however, suggesting that attentional factors were operative. Whether inattention might restrict the spatial domain of optic ataxia remains, to our knowledge, an unanswered question. In any case, the patient’s visual and perceptual deficits alone seem insufficient to explain defective performance on line bisection and target cancellation.

Experimental manipulations of the vertical line bisection task suggest that the patient’s neglect was referenced predominantly to the viewer centred frame. For radial lines, her performance varied significantly as a function of gaze direction, suggesting that her radial neglect is specifically referenced to a retinotopic frame. Although specific conclusions cannot be made for the vertical axis, the most parsimonious explanation of her neglect in the viewer centred reference frame is that it is also retinotopic.

Whereas several investigators have shown that lateral (horizontal) neglect occurs with respect to both environment centred and viewer centred coordinate systems, few studies have examined spatial reference frames in neglect of the vertical and radial space. Mennemeier et al observed one patient with far superior and one with near inferior neglect. In tasks pitting the viewer centred frame against the environment centred frame, both patients’ errors suggested that task performance was best predicted by the environment centred frame. As radial bisections were always performed below eye level, however, our findings are not directly comparable with respect to the radial axis. Interestingly, their patient with far superior neglect, resembling our patient, tended to make viewer centred errors when bisecting vertical lines from the right lateral decubitus position.

The paradigm used by Mennemeier et al failed to alter bisection bias within the control group. The authors interpret these findings to suggest a primacy of the viewer centred frame for defining neglect in normal subjects. Thus they speculate that brain injury either induces disinhibition of the environment centred frame or interferes with development of the viewer centred frame. By contrast, the present report, as well as an earlier study, shows that looking up or down at radial lines reversed bisection bias for both the patient and control subjects. Thus, the viewer centred spatial reference frame adopted under normal circumstances can remain undisturbed for radially directed attention in patients with neglect.

In the visual cortex, two retinal surface coordinates (eccentricity from the fovea and distance above and below the horizontal meridian) topographically represent the visual fields. Retinotopic organisation occurs in both the primary visual cortex and association areas. Thus the finding that certain components of visuospatial processing respect a retinotopic reference frame, as in our patient, may not seem extraordinary. All prior studies,
however, of lateral (horizontal) visuospatial neglect suggest that impaired spatial judgments depend on both viewer centred (retinal) and environment centred coordinate systems. The retinotopic reference frame, by contrast, may be relatively more important for spatial information processed by the inferior retina. Previous claims that the physiological properties of the inferior retina (and the ventral visual pathway) result in a relative processing advantage in the search for and recognition of items from the extrapersonal visual environment. As extrapersonal visual search is linked to retinotopic spatial coordinates, functional specialisations of the ventral visual system may rely more on a retinotopic reference frame. Damage to this system, resulting in abnormal information processing from the upper visual field (and far space below eye level), may therefore manifest through neglect, which primarily respects retinocentric coordinates.

Jeerakathil and Kirk modified the notion of a retinotopic reference frame for normal attentional bias. They posited an attentional bias toward the perceived top of objects based on an internal representation. Their subjects misbisected lines above true midline in the vertical condition and beyond true midline for radial lines below eye levels. Providing an alternative reference frame through directional labels, however, such as placing the label “TOP” at the environment centred lower end of the line, significantly reduced the normal bisection error. Importantly, labels did not influence the magnitude of error for radial lines bisected above eye level. These data suggest interactions between viewer centred and object centred reference frames.

Several important issues need to be considered with regard to the influence of different spatial reference frames on neglect behaviour. Are reference frames influenced in the neglect syndrome independent of sensory modality? Thus far, all studies attempting to dissociate viewer centred and environment centred frames have relied on visuospatial tasks. Perhaps some modalities (for example, auditory) rely more on environment centred frames whereas others (for example, somatosensory) depend on viewer centred coordinate systems. The complex interaction between different reference frames also remains largely unexplored. For the vertical and radial axes, Mennemeier et al suggest that the degree of interactivity may relate to lesion site: the patient with parieto-occipital injury showed relative independence between frames, whereas the patient with temporoparietal injury showed interaction between frames. Similarly, our patient’s performance on bisection tasks in a recumbent position seemed to indicate an interaction between environment centred and viewer centred reference frames.

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