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Diagonal spatial neglect

Victor W Mark, Kenneth M Heilman

Abstract

***Objective*—To determine whether stroke patients with diagonal neglect on cancellation may show diagonal neglect on line bisection, and hence to indicate whether diagonal neglect may be related solely to the type of test used or whether instead it may reflect a fundamental spatial disorder.**

***Methods*—Nine patients with subacute right hemispheric stroke who neglected targets primarily in the near left direction on line cancellation bisected diagonal lines of two opposing orientations: near left to far right and far left to near right. The errors were assessed to determine whether line orientation significantly affected bisection error.**

***Results*—Eight patients had significant bisection errors. One of these showed no effect of line orientation on error, consistent with lateral neglect. The remaining seven patients had a line orientation effect, indicating a net diagonal spatial bias. For the group, cancellation errors were significantly correlated with the line orientation effect on bisection errors.**

***Conclusions*—A significant diagonal bias on two tests of spatial attention may appear in stroke patients, although the directions of the biases may differ within individual patients. None the less, diagonal neglect may be a fundamental spatial attentional disturbance of right hemispheric stroke. Greater severity of stroke deficit as indicated by cancellation error score may be associated with a greater degree of diagonal neglect on line bisection.**

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Department of Neuroscience, University of North Dakota School of Medicine, Neuropsychiatric Research Institute, and Neurology Service, Veterans Affairs Medical Center, Fargo, ND, USA
V W Mark

Department of Neurology, University of Florida College of Medicine, and Neurology Service, Veterans Affairs Medical Center, Gainesville, FL, USA
K M Heilman

Correspondence to:
Dr Victor W Mark, Department of Neuroscience, UND Medical Education Center, 1919 Elm Street North, Fargo, ND 58102, USA.

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Patients with acquired unilateral hemispheric injuries often demonstrate a lateral spatial behavioural bias (unilateral neglect) both on standard neurological assessments and on daily living activities.[1–3] Recent reports have shown that some stroke patients may have spatial biases in other, orthogonally contrasting directions, either parallel to the intersection of the transverse and midsagittal planes (radial neglect)[4–9] or parallel to the body's truncal axis (altitudinal neglect).[10 11] Some individual stroke patients have shown significant spatial biases in up to three dimensions when bisecting horizontal (parallel to the coronal-transverse plane intersection), radial, or vertical lines.[12–19]

However, few studies have specifically examined whether spatial bias may appear in two or more dimensions simultaneously, as may be anticipated in multidimensional neglect found from bisecting lines along orthogonally distinct axes. Such neglect would be diagonal—that is, requiring the spatial bias to be specified in more than one direction relative to the body's trunk. Burnett-Stuart *et al*[20] showed that when stroke patients bisected single lines in any of eight orientations on the transverse page, most showed maximal error on lines that were diagonal rather than horizontal or radial. On cancellation tests (where subjects cross out as many targets as possible that are distributed throughout the sheet), stroke patients not uncommonly show primarily diagonal neglect[21 22]—that is, omissions are biased toward one corner of the page. As patients with left unilateral neglect most often start cancelling from the right upper portion of the page,[23] the failure to cancel stimuli in the lower left quadrant may be related to fatigue (for example, habituation or impersistence). However, we have recently shown that patients with right hemispheric stroke with near left neglect on a cancellation task may retain this bias when the cancellation sequence is controlled for fatigue effects.[24] If the diagonal neglect as demonstrated on the cancellation task is not related to fatigue but rather reflects the underlying spatial pattern of neglect, we would expect to see diagonal neglect in other tasks that assess for neglect. Therefore, in the present study we examined whether the patients with diagonal cancellation neglect from our previous study would show significant diagonal bias when bisecting diagonal lines.

Method

We screened subacute patients with right hemispheric stroke with a single standard line cancellation test[25] (40 black lines, 25×2 mm, in pseudorandom orientations on a horizontal 216×279 mm sheet about 150 mm from the subject, placed symmetrically across the subject's midsagittal plane). As with the experimental tasks below, subjects were not permitted to shift the stimulus page or their seats, but eye and head movements were not constrained. We continued in the study only patients who failed to cancel at least two lines on the page and whose omissions lay mainly in the near and left directions combined. The nine patients who qualified were six men and three women, ages 46–61 (mean 54), all right handed. Patients were tested from 13–52 days after stroke (mean 30 days). An unselected group of elderly neurologically healthy adults (four men, five women, ages 64–79, mean 68) served as control subjects. All were right handed except

Lesion location and cancellation and line bisection results

Patient No	*Cerebral lesion*	*Cancellation omissions (%)*	*Mean line bisection errors (mm)†*		*Mean error difference (positive lines− negative lines)*
			Positive lines	*Negative lines*	
1	TPO infarct	39	113.3	96.8	16.5*
2	BG haem	21	84.4	31.5	52.9*
3	FP infarct	7	−6.4	−1.1	−5.3*
4	FTP haem	4	−3.1	2.3	−5.4
5	TPO infarct	32	110.8	65.2	45.6*
6	P infarct	6	70.2	83.5	−13.3*
7	FTP haem	7	−4.4	−5.5	1.1
8	FP infarct	15	−0.6	9.0	−9.6*
9	T SAH	25	−16.3	20.1	−36.4*
Patient group averages		16	38.4	33.9	4.5*
Control group averages		0	−0.5	−0.9	0.4

*$p<0.05$ Significant line orientation effect (matched pair *t* test, one tailed).
†Values are to the right of true midpoint unless preceded by a − sign.
BG=basal ganglia; haem=haemorrhage; F=frontal; P= parietal; O=occipital; T=temporal; SAH=subarachnoid haemorrhage.

one with mixed hand preference who performed the tasks with his right hand. All study subjects gave signed informed consent. As the control subjects omitted no targets on standard line cancellation, they were judged not to have cancellation neglect and were not given the experimental cancellation task (below).

When preparing the bisection task we had no previous data relating cancellation neglect to error size on diagonal line bisection. We wished to maximise our likelihood of measuring error differences between lines of contrasting orientations. Because after brain injury bisection error on horizontal lines increases with line length,[26] our stimuli exploited the largest available paper size that could be utilised by an available photocopier. Thus we used lines that were 400 mm long and 3 mm wide, centred on paper that was 432 mm long and 279 mm wide. Although the page sizes thus considerably differed between the cancellation and bisection tasks, these differences were irrelevant to the purpose of our study, which was to compare directional bias across different tasks irrespective of stimulus or page size.

Two sets of lines were presented of mirror-opposite orientations. One set of lines extended from near or lower left to far or upper right and hence had a positive slope; we call these positive lines. The other set extended from far or upper left to near or lower right; we call these negative lines. As the lines were collinear with diagonally opposite page corners and were inclined about 33° to the page's long axis, we considered that the lines differed sufficiently from horizontal or radial lines to be noticeably "diagonal."

Twenty lines of each orientation were presented to each subject. Subjects were instructed to bisect each line with a pencil using the right hand, after which the examiner immediately replaced the page with a new unmarked page. Subjects were required to return their hands to their sides before bisecting the next line. To deter subjects from marking the centre of the page irrespective of line orientation, during the task we also had them bisect 200 mm diagonal lines that were centred in each of the page's quadrants (half of the 400 mm lines), one on each page. Each block of stimuli thus consisted of six lines: two long diagonal lines, oppositely oriented and centred on the page, and four short off centre diagonal lines, each located in a unique quadrant. In each block the lines were randomly ordered. Twenty blocks were given to each patient, for a total of 120 pages at one sitting. Bisections were measured as the distance along the line from its veridical midpoint, with errors to the right assigned a + sign and errors to the left a - sign. We measured the mean error differences between long lines of opposing orientations. Because line orientation and location were confounded in trials that used the short lines, we do not review their results here.

Each patient completed one screening test but 18 experimental cancellation pages.[24] As the number of experimental cancellation trials approximated the number of long diagonal lines of one or the other orientation, we used the experimental cancellation task results to assess the severity of cancellation neglect. Our cancellation task required patients to cancel lines by working first within either the near (lower) or the far (upper) half of the page and then changing to the other part after they indicated they had completed the initial half of the page. The half page that was not being cancelled was concealed by a sheet of black opaque paper. The order of half page completion was controlled so that it alternated with each successive page.

Patients were tested on all of the above tasks within a 5 day period each. The experimental cancellation and the bisection tasks were given no more than 2 days apart for any patient.

Results

The table indicates the patients' lesion locations and cumulative percentage cancellation omissions. Most of the patients had over 5% omissions and thus maintained the conventional criterion for unilateral spatial neglect that is based on evaluations of healthy subjects.[27–29] However, patient 4 had 4% omissions, fewer than two omissions for every 40 lines, and therefore he did not exceed the 5% error cut off. None the less, patient 4 omitted three lines on one page, with two in the near left quadrant. Furthermore, whereas he usually omitted no more than two lines a page, omissions were biased to the near left quadrant. Thus patient 4 was consistent with the other patients in showing directionally biased neglect (below), albeit modestly.

Figure 1 shows the patients' "neglect centres" on cancellation. The neglect centre for each patient was determined by assigning x and y coordinates to the centres of all omitted stimuli and then averaging all of the x coordinates and all of the y coordinates. The average (x, y) coordinate was assumed to represent the geographic centre of all omitted lines. Its location relative to the page centre was assumed to indicate the overall directional bias of neglect.[21] The neglect direction for the patients combined is shown by the inscribed angle, the apex of which is at page centre. As shown, all of the patients, individually as well as combined, had near left neglect.

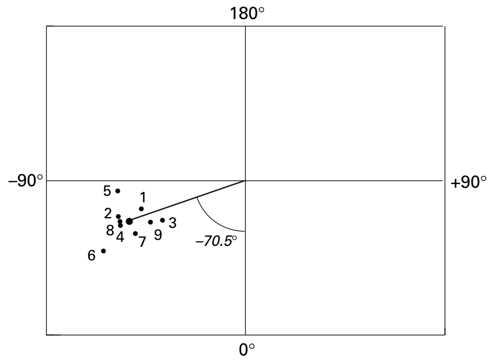

Figure 1 Neglect centres for individual patients (small dots) and for patient group average (large dot) plotted relative to the cancellation page centre Numbers correspond to patient numbers in the table. Angle indicates the polar direction of the patient group neglect centre from the page centre, with 0° to indicate direction toward the patient, 180° away from the patient, -90° toward the patient's left, and +90° toward the patient's right (see Mark and Monson[21]).

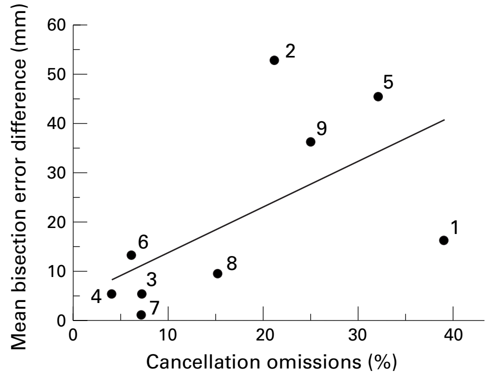

Figure 2 Correlation of orientation specific mean line bisection differences (absolute values) v percentage cancellation omissions for each patient. Numbers correspond to those of patients (table). Regression line: y = 0.927x+4.614.

The table also provides the mean line bisection errors according to line orientation and differences between orientation specific means for all subjects. The control subject means did not significantly differ from zero and did not show a line orientation effect (*t*s>0.6, df=179, ps>0.14). The patients' error means therefore were compared against zero rather than the control values. As a group, the patients' bisection markings on either positive or negative lines significantly differed from zero (*t*s>9.4, df=179, p<0.0001). Individually, all patients' bisections significantly differed from zero except patient 3 on negative lines, patient 4 on both types of line, and patient 8 on positive lines (*t*s<0.51, df=19, ps>0.3). All patients had significant line orientation effects on bisection error except patients 4 and 7.

The patient group made significantly greater right errors on positive versus negative lines (*t*=1.75, p=0.04), consistent with net near left neglect. Of the seven patients with significant bisection error and line orientation effect, three (1, 2, and 5) showed mean bisection values consistent with near left neglect. However, several subjects' performances varied from the means. Patient 7 had significant left bisection error on both lines without line orientation effect, consistent with right lateral neglect. Three patients seem to have far left neglect. Patient 6 erred to the right on both kinds of lines, but more so on negative lines. The mean errors of patient 8 on positive lines were close to 0, whereas on negative lines they were considerably to the right. Patient 9 showed, on average, a decidedly left (near) error on positive lines and a significantly greater right (near) error on negative lines, also consistent with net far left neglect. Patient 3 on average erred to the left on both lines, but significantly only on positive lines, consistent with far right neglect.

In general, the severity of neglect in our experimental group was heterogeneous, with the patients differing in both error frequency on the cancellation test and error magnitude on the line bisection test, as shown in the table. Inspection of the table, however, suggests that the patients with greatest cancellation errors also had the greatest line orientation effects on bisection error. To evaluate this relation, we plotted orientation based differences in bisection error against percentage cancellation omissions (fig 2). We used the absolute value of bisection error differences rather than the signed values shown in the table, as the patients had mixed directional biases. The results suggest that greater neglect on cancellation is associated with greater line orientation effect on bisection (*r*=0.61, one tailed p=0.04).

Discussion

Diagonal neglect has been primarily found on the cancellation task. However, case reports of brain injury have indicated diagonal neglect on reading,[30] diagonal execution on writing or drawing,[31–34] and quadrantic visual extinction on double simultaneous stimulation.[35 36] In a prior study using the cancellation task we showed that diagonal neglect did not seem to be induced by fatigue.[24] If diagonal neglect in the cancellation task reflects the spatial pattern of neglect, then we should see more severe neglect on diagonal lines that go from near left to far right than on diagonal lines that are oriented in the opposite direction. We found that the diagonal line bisection task confirmed the results that we obtained from cancellation tasks. As a group our patients' bisection errors were greater with lines that went from lower (near) left to upper (far) right than they did when they bisected diagonal lines that went in the opposite direction.

Because we did not note how many stroke patients failed to show diagonal neglect on the screening cancellation examination, we cannot indicate its general incidence. However, corner based spatial bias on cancellation or other two dimensional search tasks have often been reported or depicted in the literature.[21] Because bisection tasks nearly always present horizontal lines, diagonal bias on bisection has been evaluated rarely, the report by Burnett-Stuart *et al*[20] and its preliminary communication[37] being the only other studies of its occurrence in cerebral injury.

Thus although we cannot report the frequency of diagonal neglect in stroke, our readily finding such neglect among our patients suggests that diagonal neglect may be considerably underreported. In addition, the investigational convention for reporting spatial errors strictly in lateral, radial, or vertical directions will underestimate the diversity of directional spatial bias in cerebral injury.

Two of our patients (3 and 8) had no net neglect on lines of one orientation, suggesting that the oppositely oriented lines were exquisitely sensitive to diagonal bias. In contrast, subjects 1, 2, 5, 6, and 9 had significant neglect on both kinds of lines, but significantly more so on lines of one orientation. These findings suggest that lines of other orientations that were not included might have demonstrated greater or intermediate bisection error, consistent with earlier reports[20 37] that found that bisection error may systematically vary with line orientation.

Diagonal neglect might emerge through the interaction of separate orthogonally-related spatial attentional biases (for example, a bias to attend rightward and distally). Alternatively, perhaps spatial orientation is inherently diagonal or multidimensional, and previously reported bisection neglect on horizontal, radial, or vertical lines merely reflected the intersection of the line's axis with an intrinsically multidimensional spatial mechanism and therefore was reported as lateral, radial, or altitudinal neglect. In support of the second mechanism, Robinson *et al*[38] found that visually responsive parietal association neurons in the macaque had primarily *combined* contralateral and inferior visual field responsiveness. Hence, intrinsically diagonal orientation bias may be a predominant feature of parietal neurons.

When the scores on the two different (positive and negative) diagonal lines are averaged, the mean horizontal error can be determined. Two patients with right hemispheric lesion (3 and 7) bisected both lines toward the left of centre. These patients seemed to have ipsilateral neglect. Ipsilateral neglect is often associated with frontal lesions.[39–42] Our two patients had involvement of the frontal lobes, although other patients in our study with frontal involvement did not demonstrate ipsilateral neglect. In addition, ipsilateral neglect in patients 3 and 7 appeared only on bisection, whereas on cancellation they showed contralateral neglect, similar to previous reports of frontal injury.[39 42] Ipsilateral bisection neglect after frontal injury has been related to recovery.[40 41] Our frontally lesioned patients did not demonstrate a consistent relation between chronicity of stroke and ipsilateral versus contralateral neglect, but as our sample was small and we did not have precise lesion information, we cannot evaluate the relation between ipsilateral neglect and recovery from frontal injury.

Patient 9 seemed to have far radial neglect on line bisection, although with significantly stronger far left than far right neglect. Far radial neglect is usually associated with temporal injury,[12 17 18 43] and it is pertinent that patient 9 had exclusively temporal lobe injury on neuroimaging. However, on cancellation patient 9 showed near radial neglect. Shelton *et al*[18] suggested that the inferior temporal lobe may mediate attention to far radial space. Our data are insufficient to indicate why patient 9 showed dissociated radial neglect between cancellation and bisection, contrary to Shelton *et al*'s[18] subject.

The dissociation in spatial bias between cancellation and bisection in our patients suggests that diagonal neglect cannot be strictly ascribed (if at all) to a fixed attribute such as location of the cerebral lesion. Within patient shifts of lateral biases on different tasks are not unusual, having been reported after unilateral hemispheric injury on cancellation versus line bisection[39 42 44 45] as well as among other spatial evaluations.[46–50] Similarly, Halligan and Marshall[7] found a non-significant correlation between two dimensional biases on cancellation versus horizontal and radial line bisection after right hemispheric stroke.

These findings suggest that differences in cognitive operations according to task may underlie task specific directional biases in cerebral injury. Humphreys and Riddoch[44] convincingly argued that shifts in lateral neglect on the same array within one subject were related to whether he considered targets as unrelated individual items or parts of a unified whole. Similarly, fundamental differences in cognitive approaches have been suggested to underlie task dependent dissociations in lateral neglect occurrence or severity.[51 52] Whereas lesion location itself cannot explain task related directional differences in neglect, perhaps regional cerebral activation in some stroke patients changes according to the specific spatial task, which might secondarily influence the direction of spatial bias. Some studies of normal subjects have suggested that interhemispheric differences in cerebral activation on directed spatial tasks may correlate with non-structural attributes such as personality style[53] and hormonal state.[54] Assessing diagonal or multidimensional neglect would be more sensitive for evaluating these influences than would traditional unidimensional spatial assessment.

Despite the task-related between patient and within patient directional differences, we found that stroke severity as indexed by cancellation error total was significantly correlated with the magnitude of the line orientation effect on bisection error. Thus directional dissociation does not imply dissociated neglect severity. Our findings agree with those of Mattingley *et al*,[55] who concluded after analysing their own results as well as those of Binder *et al*[39] that abnormal bisection performance is generally correlated with increased cancellation error. Although no doubt fundamentally different cognitive operations govern both tasks, these results suggest that clinically appreciable, subacute hemispheric injury causes a significant vulnerability toward pathological spatial bias, regardless of task. Our findings suggest that this bias is often diagonal.

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