Preserved leftward movement in left unilateral spatial neglect due to frontal lesions

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Abstract

Three patients with left unilateral spatial neglect after predominantly frontal lobe lesions were asked to extend a horizontal line leftwards to double its original length. In this line extension task, they readily executed movements in or towards the contralesional left space. They performed the task in the left and right hemispaces as well as in the midline. The mean extension lengths did not differ significantly among these three spatial conditions. These results suggest that directional hypokinesia takes little part in left unilateral spatial neglect due to frontal lobe lesions. It is considered that the patients could execute leftward movements as the task oriented their attention sufficiently to the left. Two of the three patients, like reported cases with frontal neglect, showed a typical exploratory deficit for the left space in the line cancellation test. Such a deficit found in the traditional tasks, however, does not mean the presence of directional hypokinesia. All three patients showed visual extinction on double simultaneous stimulation. An attentional mechanism seems to play a predominant part in unilateral spatial neglect due to frontal lesions.

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Unilateral spatial neglect is the failure of brain damaged patients to attend to and explore stimuli presented in the space contralateral to their lesions.[1 2] Neglect in humans usually occurs after right hemispheric lesions that involve the parietal lobe,[1–4] whereas in monkeys, it is a classical finding that neglect is produced by frontal lobe lesions.[5 6] Since the report of Heilman and Valenstein,[7] however, frontal lobe lesions have also been known to cause unilateral spatial neglect in humans,[3 8 9] although frontal neglect is infrequent compared with parietal neglect.[4 7]

Recent theories of unilateral spatial neglect consider that neglect is a complex deficit with multiple components, such as attentional, exploratory-motor, and representational disorders.[1 2] According to Mesulam's cortical network theory for directed attention,[10 11] the frontal region centred around the frontal eye field provides a mechanism for scanning and exploring. Because the regions contributing to directed attention are tightly interconnected, frontal lesions may produce multicomponent neglect in which exploratory motor deficit is relatively stressed. Several studies[12–15] reported that exploratory motor deficit or directional hypokinesia[12–14 16–19] (failure to execute movements fully in or towards the contralesional space) predominates in unilateral spatial neglect after lesions that involve the frontal lobe as well as the parietal lobe. A few patients with restricted frontal lesions[20–22] showed exploratory neglect without other obvious signs of neglect.

Recently, Ishiai *et al*[23] examined patients with neglect and with right parietal lobe lesions by means of a line extension task and showed that directional hypokinesia takes little part in left unilateral spatial neglect. The patients accurately extended a line leftwards to double its original length, whatever the severity of neglect found in the line bisection test. They were considered to execute movements in or towards the contralesional space as the task oriented their attention sufficiently to the left. The present study applied the line extension task to three patients with unilateral spatial neglect due to predominantly frontal lobe lesions to test if they had directional hypokinesia and failed to perform the line extension task.

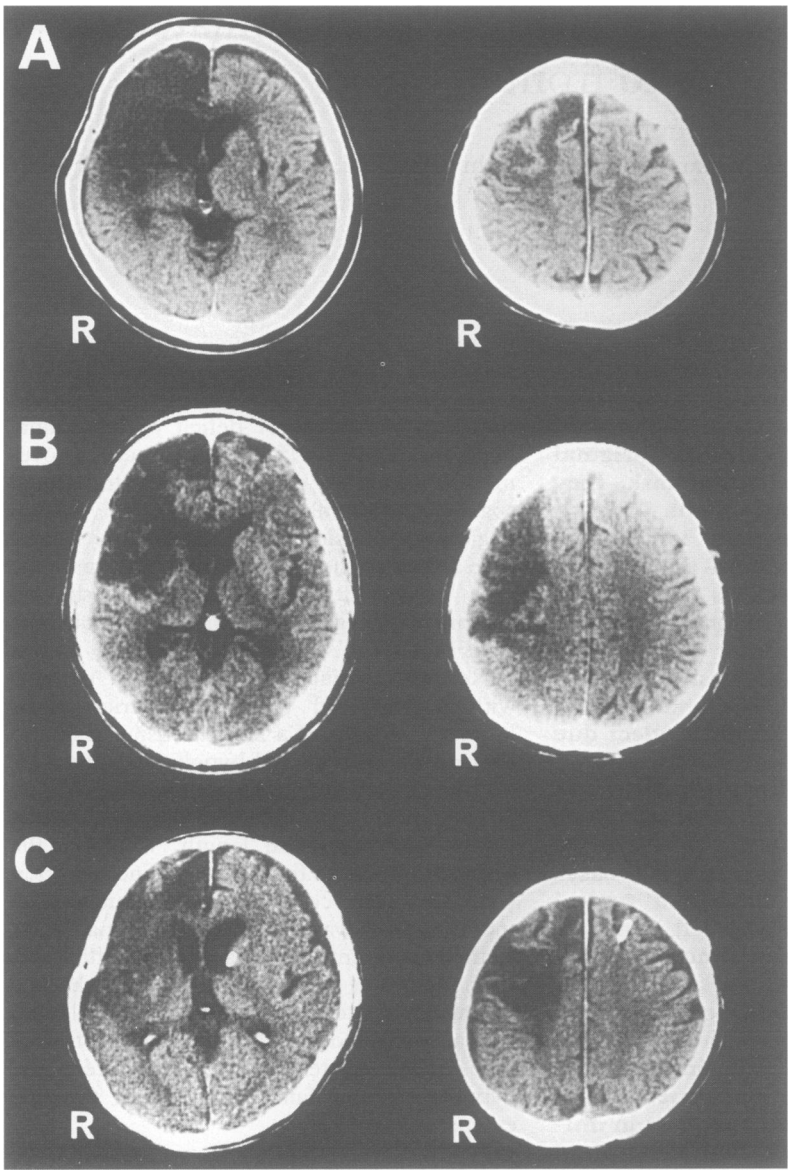
Methods

LINE BISECTION TEST

All the subjects were first given a series of line bisection tests.[23] A line 200 or 100 mm long was drawn horizontally across the centre of a piece of A4 (210 × 297 mm) paper. Three spatial conditions were examined: For the centre condition, the paper with its line was placed so that its centre lay in the sagittal midplane of the subject's trunk. For the right and left conditions respectively, the left and right edges of the paper were positioned in the sagittal midplane of the trunk. The examiner explained how to mark the centre by showing an ideal bisection of a line, then asked the subjects to bisect the lines presented in an order randomised across the three spatial conditions and the two lengths. Each subject bisected eight lines for each length in each of the three spatial conditions, thereby completing 48 trials.

LINE EXTENSION TASK

After completion of the set of line bisections, the subjects were tested for their ability to extend a line leftwards to double its original length.[23] A horizontal line 100 or 50 mm long



CT showing the predominantly frontal lesions of cases 1(A), 2(B), and 3(C). Left is on the right of the images.

was printed on a piece of A4 paper so that its left endpoint, marked with a small vertical symbol, corresponded to the centre of the paper. The subjects were asked first to put the tip of a pencil held in the right hand on the symbol. They then had to extend the line leftwards the length of the printed line. They were told not to remove the pencil from the paper before judging that the trial had been completed. The examiner explained the procedure by showing an ideal extension. The subjects then performed a practice trial, in which they were advised not to cover the line with the hand that held the pencil. Three spatial conditions were examined: For the centre condition, the paper was placed so that its centre, which corresponded to the left end of the printed line with the small vertical symbol, lay in the sagittal midplane of the subject's trunk. For the right and left conditions respectively, the left and right edges of the paper were positioned in the sagittal midplane of the trunk. Each subject performed the task in randomised order eight times for each length in each of the three spatial conditions, thereby completing 48 trials.

Case reports

All patients gave informed consent to participate in this study.

CASE 1

A 63 year old right handed woman had a stroke on 19 December 1989. The present examination was performed nine months after the onset. At this time, CT showed an infarction that involved almost all the right frontal lobe and its subcortical structures, as well as the anterior part of the right temporal lobe (figure, A). The patient had a left hemiplegia and a left sided moderate sensory loss. There was no visual field defect on confrontation testing. She exhibited left sided visual extinction, however, on bilateral simultaneous stimulation. Typical left unilateral spatial neglect was found on neuropsychological examination. She omitted left sided 15 of 30 lines in the line cancellation test[24 25] and copied only the right half of a figure of a daisy.[1 26] In the line bisection test[26 27] with lines 200 mm long, she placed the mark about 15 mm to the right of the true midpoint.

CASE 2

A 59 year old right handed man suddenly developed a left hemiplegia and a left sided moderate sensory loss on 22 July 1990. The present examination was undertaken a month after onset. CT at this time revealed an infarction that involved almost all the right dorsolateral frontal lobe and its subcortical structures, as well as the insula (figure, B). The lesion extended to the postcentral gyrus. The patient had no visual field defect but showed visual extinction, omitting about 50% of the left sided targets on bilateral simultaneous stimulation. Typical left unilateral spatial neglect was found on neuropsychological examination. He copied only the right half of a daisy and omitted left sided 15 of 30 lines in the line cancellation test. When bisecting 200 mm lines, he placed the mark about 10 mm to the right of the true midpoint.

CASE 3

A 66 year old right handed man was admitted to hospital with a sudden headache on 16 August 1992. CT and angiography showed the rupture of an aneurysm of the anterior communicating artery. An operation on the aneurysm was performed next day and an apparent left hemiparesis appeared six days later. The present examination was performed seven months after the operation. At this time, CT showed an infarction that involved almost all the right frontal lobe and its subcortical structures, as well as the anterior half of the right temporal lobe (figure, C). The patient had no visual field defect but showed left sided visual extinction on bilateral simultaneous stimulation. Mild left unilateral spatial neglect was found on neuropsychological examination. He copied all the petals of a

Table 1 Deviations from true midpoint in the line bisection test

Case	Spatial condition			Kruskal-Wallis test	Post hoc comparisons		
	Left	*Centre*	*Right*		*L v C*	*C v R*	*L v R*
				200 mm line			
1	18·5 (7·4)	13·8 (5·8)	0·5 (7·3)	$p < 0.001$	NS	$p < 0.01$	$p < 0.01$
2	8·0 (5·5)	9·8 (4·8)	1·6 (4·8)	$p < 0.025$	NS	$p < 0.01$	$p < 0.05$
3	30·1 (3·9)	20·6 (7·8)	−4·8 (9·5)	$p < 0.001$	NS	$p < 0.01$	$p < 0.01$
				100 mm line			
1	5·3 (4·1)	2·9 (3·6)	−2·7 (4·3)	$p < 0.025$	NS	$p < 0.05$	$p < 0.01$
2	3·5 (1·7)	1·9 (1·0)	−2·6 (2·1)	$p < 0.001$	NS	$p < 0.01$	$p < 0.01$
3	15·6 (2·9)	5·6 (3·3)	−4·9 (5·2)	$p < 0.001$	$p < 0.05$	$p < 0.05$	$p < 0.01$

Values are means (SD).

daisy but omitted its left leaf. Although the copying of a daisy was examined only once, the omission of the easily recognisable left leaf (40 mm long and 16 mm wide) was considered to show the presence of neglect. Thirty age matched control subjects never omitted this part of the figure. He placed the mark about 20 mm to the right of the true midpoint when bisecting 200 mm lines. In the line cancellation test, however, he marked all the lines.

Results

LINE BISECTION TEST

The distance between the true midpoint and the mark showing the subjective midpoint was measured to the closest millimetre and expressed as positive if the mark deviated to the right. Table 1 shows the mean deviations from the true midpoint and the statistical results concerning the spatial effect for each patient. All the three cases placed the mark to the right of the true midpoint in the left and centre conditions for both the 200 and 100 mm lines. The mean deviations found in these bisections were significantly greater than those of the 10 age matched normal controls in our previous study.[23] The mean deviations of the normal controls for the 200 mm lines were 1·1 (SD 2·1) mm, 1·3 (2·4) mm, and 2·1 (3·2) mm for the left, centre, and right conditions respectively, and those for the 100 mm lines were 0·4 (SD 1·5) mm, 0·5 (1·4) mm, and 0·6 (1·3) mm. When bisecting 200 mm lines in the right condition, cases 1 and 2 marked near the true midpoint and case 3 marked to the left of it. When bisecting 100 mm lines in the right condition, all the three cases marked slightly to the left of the true midpoint. The mean deviations were significantly different among the three spatial conditions for each of the two lengths for each case (Kruskal-Wallis test). Post hoc comparisons (non-parametric equivalent of Williams' test[28]) showed that the mean deviations were significantly greater for the centre than for the right condition and for the left than for the right condition.

LINE EXTENSION TASK

The length of the overextension was calculated by subtracting the ideal extension (100 or 50 mm) from the length of subject's extension measured to the closest millimetre. When the extension was less than the ideal length, the calculated value was treated as a negative overextension. Table 2 shows the mean overextensions and the statistical results concerning the spatial effect for each patient. The mean overextensions were all positive for each spatial condition for each line length. In our previous study,[23] the mean overextensions of the 100 mm lines of the 10 normal controls were 0·6 (SD 4·0) mm, 1·8 (4·0) mm, and 2·5 (4·3) mm for the left, centre, and right conditions respectively. Those of the 50 mm lines were 2·2 (SD 6·2) mm, 2·2 (6·1) mm, and 2·8 (4·9) mm. The three cases of the present study extended the 100 mm lines significantly longer (about 10 mm) than the normal controls except when cases 2 and 3 extended the lines almost accurately in the centre and right conditions respectively. In the extension of 50 mm lines, the mean overextension for each spatial condition was within the mean ±2 SDs of the normal controls. The effect of the three spatial conditions was not significant for each length for each case (Kruskal-Wallis test).

Discussion

The three patients showed left unilateral spatial neglect after predominantly frontal lobe lesions. Their lesions extended to the postcentral gyrus or the subcortical structures, but

Table 2 Overextensions in the line extension task

Case	Spatial condition			Kruskal-Wallis test	Post hoc comparisons		
	Left	*Centre*	*Right*		*L v C*	*C v R*	*L v R*
				100 mm line			
1	12·8 (4·6)	12·9 (3·7)	12·5 (3·2)	NS	NS	NS	NS
2	13·0 (13·4)	3·5 (7·9)	11·8 (8·6)	NS	NS	NS	NS
3	11·7 (10·9)	13·4 (7·9)	9·8 (10·3)	NS	NS	NS	NS
				50 mm line			
1	2·5 (1·9)	0·1 (4·1)	4·0 (8·3)	NS	NS	NS	NS
2	4·8 (8·6)	11·6 (12·6)	5·1 (7·5)	NS	NS	NS	NS
3	6·1 (6·4)	6·0 (5·9)	8·3 (8·9)	NS	NS	NS	NS

Values are means (SD).

not to the parietal region around the inferior parietal lobule, where lesions are known to cause unilateral spatial neglect.[1-4] They readily executed leftward movements in the line extension task, in which they had to extend a line leftwards to double its original length. There was no significant difference in the length of line extension among the left, centre, and right conditions, although the line bisection errors were affected by these spatial conditions, as Heilman *et al*[17] reported. These results suggest that an exploratory motor component[10 11 15 20 22] or directional hypokinesia[12-14 17-19 21] takes little part in left unilateral spatial neglect due to frontal lesions. As we did not record reaction times, our results do not exclude the type of directional hypokinesia reported by Heilman *et al*[18]—namely, prolonged reaction times for leftward movements. We found that the three patients started to extend the lines leftwards, however, immediately after presentation of the test sheets.

Absence of directional hypokinesia has been reported in neglect due to predominantly parietal lesions[23 29] but not in frontal neglect. In our line extension task, the patients seemed to look continually at the left extreme of the line during the process of leftward extension, as fixation usually centres on the pencil tip during manual drawing.[23 30] Selection of a motor plan should automatically produce a shift of attention towards the spatial sector in which the action will be executed.[31] We thus consider that the patients could execute movements in or towards the contralesional space as the line extension task oriented their attention sufficiently to the left.

In the studies with traditional diagnostic tasks for neglect, several authors[15 20-22] have emphasised an exploratory motor component or directional hypokinesia in unilateral spatial neglect due to frontal lesions. The patients of Daffner *et al*[20] and Bottini *et al*,[21] and patient 2 of Liu *et al*[22] showed severe exploratory neglect without other obvious signs of neglect. Binder *et al*[15] found that the combination of abnormal cancellation and normal line bisection was always associated with a frontal or basal ganglia localisation. We also found that two of the three patients with frontal lesions (cases 1 and 2) neglected the left hemispace typically in the line cancellation test but bisected the lines with small rightward errors. Case 3, however, who also had a large frontal lesion, marked all the lines in the line cancellation test, whereas his rightward bisection errors were greater than those of cases 1 and 2. Such a dissociation in performances in these two tasks has been reported in patients with lesions that involved the parietal lobe[32] but not in patients with predominantly frontal lesions. Despite the variability of neglect manifestations, however, all the three patients readily executed leftward movements in the line extension task. These findings suggest that the traditional diagnostic tasks cannot distinguish among the components of mechanisms underlying unilateral spatial neglect. Not only unilateral spatial neglect itself but also insufficient motivation for tasks[25] may affect performances in exploration tasks, such as the cancellation test. Our cases 1 and 2 showed improvement of left unilateral spatial neglect in the line cancellation test when motivated with the use of numbering of lines instead of simple crossing out.

Some experimental studies[13 14 33] tried to differentiate an exploratory motor component from an attentional component by decoupling the direction of a visual stimulus and the direction of hand or eye movement. The task of Bisiach *et al*[13] was a modified line bisection task with an apparatus with pulleys. The task of Tegnér *et al*[14] was a line cancellation task with a looking glass. These groups of authors suggested that the motor component or directional hypokinesia is more pronounced in patients with lesions involving the frontal lobe. The lesions of their patients were large, however, and involved the parietal lobe as well as the frontal lobe. The patient of Butter *et al*[33] had a frontal infarction with only a slight extension to the postcentral gyrus. After left sided inattention abated, the patient showed directional hypokinesia of eye movement only when a stimulus on the right required a leftward eye movement. Although the deficits found in these crossed motor tasks seem to be explained by directional hypokinesia, other factors may affect the performances of patients with frontal lesions. The crossed motor tasks are difficult in that when patients desired to move the pointer for bisection[13] or the hand image through mirror view[14] to the right (or left), they had to move the hand oppositely to the left (or right). Some of the patients of Tegnér *et al*[14] showed difficulties for hand movements towards either side in the mirror view condition. Frontal patients have difficulty in following rules[34] and tend to continue their automatic action regardless of the instructions that they have just received.[35] In the line extension task, the site and direction of motor execution correspond to those of attention as in the other typical tests for neglect, such as the line cancellation test,[24 25] the line bisection test,[26 27] and the copying of figures.[1 26] We therefore consider that absence of directional hypokinesia shown in the line extension task is convincing. The present study did not examine the three patients with the tasks of Bisiach *et al*[13] and Tegnér *et al*.[14] Further studies that contrast performances in these tasks and the line extension task should contribute to our understanding of the mechanisms of unilateral spatial neglect due to frontal lesions.

After a unilateral frontal eye field lesion, monkeys tend to deviate the eyes and the head towards the side of the lesion, show rare spontaneous eye movements contralateral to the lesion, and neglect stimuli in the contralateral space.[5 6] Incapacity to move towards the contralesional stimuli cannot fully explain their unilateral spatial neglect. Latto and Cowey[5] reported that these monkeys could not respond to visual stimuli presented contralateral to the lesion even when the required response was the pressing of a lever with the

preferred hand. Rizzolatti *et al*[6] reported that the presentation of contralesional threatening stimuli does not elicit emotional responses. Furthermore, after the oculomotor disturbance had disappeared, the monkeys still preferred the ipsilateral visual stimulus in the test with two stimuli in far space. In the present study, we examined all the three patients one month or more after onset. None of them showed any obvious deviation of the eyes or head towards the right. The range of eye movement was not restricted on routine neurological examination. All of them, like most of the reported cases with frontal neglect,[7 9 21 33] showed visual extinction on double simultaneous stimulation. Attentional mechanism[1] thus seems to play a predominant part also in human unilateral spatial neglect due to frontal lesions. The results of the present study suggest that the underlying mechanism is essentially the same in frontal and parietal neglect. The patient of Daffner *et al*[20] and patient 2 of Liu *et al*[22] showed exploratory motor neglect but did not, however, exhibit visual extinction. They had smaller frontal lesions than our patients whose lesions involved most of the frontal lobe. To clarify the nature of frontal neglect in humans, we need further studies on patients with frontal lesions of various sizes and sites in either acute or chronic phase.

All the three frontal patients extended 50 mm lines accurately but extended 100 mm lines about 10 mm longer than the normal controls. Ishiai *et al*[23] reported that the patients with unilateral spatial neglect due to parietal lesions accurately performed the line extension task for both line lengths (50 and 100 mm), whatever the severity of neglect found in the line bisection test. Thus we do not consider that the excessive extensions by the patients with frontal lesions resulted from unilateral spatial neglect. The excessive extension might be caused by continuous perseverance[36] or visual grasp[33 37] that was disengaged by frontal lesions, although at present, we do not know why it occurred for only the longer lines.

Patients with left unilateral spatial neglect sometimes bisect lines with greater deviations in the left hemispace than in the midline and in the midline than in the right hemispace.[17 23] Our patients with frontal lesions also showed such a spatial effect in the line bisection test. As both the patients with frontal lesions and those with parietal lesions[23] could readily execute leftward movements, directional hypokinesia cannot explain the spatial effect. This effect may result from attentional imbalance,[38] with attention biased to the right side after right hemisphere damage. The leftward deviations found in our patients' bisection in the right condition, however, seem paradoxical to this explanation. Patients with neglect with parietal lesions may also occasionally show leftward bisection errors in the right hemispace.[23 26] Ishiai *et al*[26] considered that unilateral spatial neglect cannot be excluded by the absence of rightward deviation, because they found the eye fixation pattern characteristic of unilateral spatial neglect in such bisections. They, however, analysed the eye fixation pattern only from the time of the first fixation on the stimulus line. What determines the point on the line at which patients with neglect first fixate remains unspecified.[26] Marshall and Halligan[39] interpreted the line bisection performances of patients with neglect in terms of two constructs: the size of the Weber fraction[40] (the "just noticeable difference" between two magnitudes) and the attentional direction of approach to a psychological "indifference zone", the extent of which is determined by the Weber fraction. Patients with left unilateral spatial neglect may usually adopt a right to left scan track of attention and place the mark when the scan reaches the indifference zone that is expanded consequent on cerebral damage. When asked to bisect a line in the right hemispace, however, our patients had first to search toward the right space where the line was presented, as they showed no deviation of the eyes or head when no visual stimulus was presented. According to the interpretation by Marshall and Halligan,[39] in the right condition, they may have approached from the left endpoint to the indifference zone and placed the subjective midpoint to the left of the true midpoint. Once neglect patients fixate a point on the line, they tend to persist with this point.[26] The first rightward search may thus have had a strong effect on the bisection in the right hemispace.

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