Mechanisms Underlying Hemispatial Neglect

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If patients with left-sided hemispatial neglect bisect lines incorrectly because hemianopia or sensory hemiinattention prevents them from seeing how far the line extends to the left, a strategy that ensures their seeing the left side of the line in their normal field should improve performance. If patients have hemispatial hypokinesia, moving the line toward the normal half of body space should improve performance.

Six patients with left-sided neglect from right hemisphere infarctions were required to identify a letter at either the right or the left end of a line before bisecting that line. The task was given with the lines placed at either the right, the center, or the left of the body midline.

Performance in trials when subjects were required to look to the left before bisecting a line did not differ from when they were required to look right. Performance was significantly better when the line was placed to the right side of the body than to the left. These observations support the hypothesis that patients with hemispatial neglect have hemispatial hypokinesia. An alternative hypothesis is that these subjects had a hemispatial memory defect. Although they saw the left side of the line in their normal field, they were incapable of forming a stable trace and performed as if they did not see the left side of the line.

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Unilateral spatial neglect is one of the most dramatic behavioral disorders in patients with hemispheric dysfunction. Although several authors [3, 13] have attributed the original description of this disorder to Holmes [19], he actually reported 6 patients with disturbed visual orientation from bilateral lesions. It was Riddoch [26] who reported 2 patients with undisturbed central vision who had visual disorientation limited to homonymous half-fields. Brain [6] also described 3 patients with normal visual acuity who had visual disorientation limited to homonymous half-fields. He attributed this disorder to inattention to the left half of external space and thought it was similar to the amnesia for the left half of the body that may follow a lesion of the right parietal lobe. Paterson and Zangwill [25], McFie and colleagues [23], and Denny-Brown and Banker [10] demonstrated that patients with unilateral inattention (hemispatial agnosia) not only had visual disorientation limited to a half-field but also omitted material on one side of drawings, failed to eat from one side of their plate, and failed to dress half of their body.

The mechanism underlying the defective behavior in hemispatial neglect has not been elucidated, but several hypotheses can be advanced to explain this behavioral abnormality. (1) *Deafferentation:* Patients with hemispatial neglect often are hemianopic and therefore do not see one half of space. For example, when asked to bisect a line, they quarter it because they see only half of the line. (2) *Sensory inattention:* McFie et al [23] noted that some of their patients with hemispatial neglect were not hemianopic. Rosenberger [27] tested patients' visual discrimination of bisected lines and found that hemianopic patients performed no differently from nonhemianopic patients. DeRenzi and associates [11] found that the hemispatial neglect was not limited to the visual modality. Brain [6] proposed that the mechanism underlying hemispatial neglect is attentional. (3) *Hemispatial hypokinesia:* Watson et al [31] trained animals to move an extremity contralateral to a stimulus. A unilateral hemispheric lesion was then placed to induce unilateral neglect. Animals with neglect were unilaterally hypokinetic when retested on this familiar task. When stimulated on the neglected side, which was contralateral to the lesion, they performed normally with the arm ipsilateral to the lesion. When stimulated on the nonneglected side (ipsilateral to the lesion), however, they failed to use the extremity opposite the lesion despite normal strength.

We have proposed [17] that patients with hemispatial neglect fail at line bisection and other similar tasks (e.g., drawing, crossing out lines) because the hypokinesia associated with neglect is not limited to the contralateral extremity but is a hypokinesia for any act that must be performed in the neglected hemispatial field.

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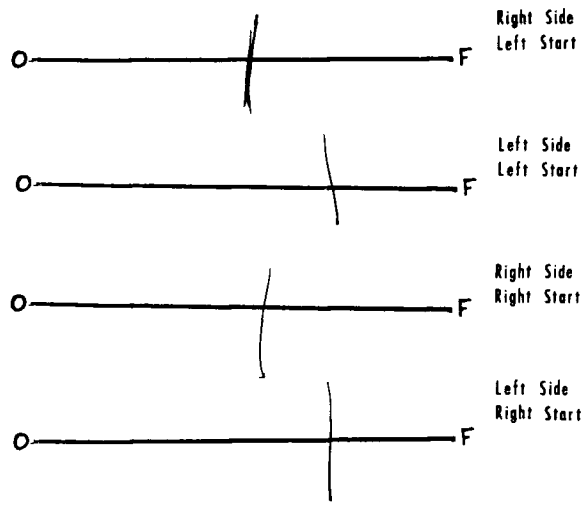
To determine which of the aforementioned hypotheses was correct, we used a modified line bisection task. Before bisecting a line, the patient had to read a letter on either the right or the left end of the line ("starting point"). A patient with left-sided neglect from a right hemisphere lesion will tend to bisect a line to the right of midline. If patients with left-sided neglect bisect lines incorrectly because hemianopia or hemiinattention prevents them from seeing how far the line extends to the left, a strategy to ensure that they see the left side should improve performance. Visual fixation on the letter to the left will displace the line into the patient's normal visual field out of his hemianopic or inattentive field. If faulty bisection is the result of hemispatial hypokinesia, the patient's performance would not be affected by this strategy. It is important to realize that the patient's hemispatial field is not the same as his visual field. The hemispatial field refers to the space to one side of the midline of the body. If the test line is placed directly in front of the patient, changes in direction of gaze will displace the line to one or the other side of the patient's visual field but will not affect its position relative to the midline of his body. When the patient gazes to the right, therefore, a portion of his right hemispatial field falls in his left visual field.

To test the hypothesis that neglect is caused by hemispatial hypokinesia, the same line bisection task was given in two additional conditions: with the lines placed either to the left or to the right of the patient. If the patient with left-sided neglect has hemispatial hypokinesia, we would expect his performance to be better when the lines are placed to his right than when they are to his left. If both an attentional disturbance and hemispatial hypokinesia are present, we would expect an interaction between starting point and line position, performance being poorest when the starting point is on the right and the line is placed to the patient's left.

Patients and Methods

The subjects were 6 men who showed extinction to simultaneous visual and somesthetic stimuli. Their mean age was 60.5 years. Two were hemianopic and 5 had left hemiplegia. None of the patients at the time of testing had head or eye deviation. We were able to review radioisotope brain scans of 2 patients and a computer tomogram of 1. One patient had a lesion restricted to the parietal lobe and 1 had a frontoparietal lesion. The third had a large frontotemporoparietal lesion. All 6 were diagnosed as having a cerebral infarction in the distribution of the right middle cerebral artery.

The 6 subjects were tested with the line bisection task. In this task, which was done seated, the patient was asked to bisect a visually presented, horizontally oriented line (Figure). The lines were 2 mm wide and were placed on



Line bisection in four different conditions performed by a patient with left-sided unilateral neglect.

21.5 × 28 cm cards. Each block of tests comprised 8 trials. On each trial a different length of line was used (22.5, 10, 15, 14, 21, 6.5, 16, and 24 cm); however, the lines and order of presentation were the same in each block. Each subject was given twelve blocks of tests in three groups of four blocks (96 trials). In the first four blocks (32 trials), the card was placed left of midline so that the right edge was in line with the middle of the patient's body. In the second four blocks of trials, cards were placed to the patient's right so that the left edge of the card was in line with the middle of the patient's body; and in the third four blocks of trials, cards were placed so that the middle of the card was in line with the middle of the patient's body. Every line had a letter at each end (see the Figure). These letters were 2 mm thick and about 7 mm in width and height. For half of the blocks the patient was instructed to look to the left of the line, tell the examiner the letter he saw, and then bisect the line. For the remainder of the blocks the patient was asked to look to the right of the line and identify the letter before bisecting the line.

Trials were scored only if the subject correctly identified the letter. Each trial was scored by measuring the distance in millimeters between the actual midline and the patient's intersecting line. If the patient bisected the line to the left of midline, the number of millimeters was given a negative score; if the lines were bisected to the right of midline, the number was given a positive score.

Results

All subjects correctly identified the letters at the ends of the lines; therefore all trials were scored. When the starting point was to the left of the line (toward the neglected side), the 6 subjects bisected the line to the right of center by a mean of 8.11 ± 1.78 mm (SE). When the starting point was to the right of the line (toward the nonneglected side), the 6 subjects bisected the line to the right of center by a mean of 9.28 ± 1.65 mm. When the card was to the left of the

Results of Analysis of Variance Applied to Line Bisecting Test in 6 Patients with Hemispatial Neglect

Source	Degrees of Freedom	Sum of Squares	F Value	p Value
Patient	5	2,736.53	9.94	0.0001
Position	2	1,214.54	11.03	0.0001
Starting point	1	24.50	0.44	0.5073
Position × starting point	2	135.08	1.23	0.3004
Error	61	3,359.09	...	...
Corrected total	71	7,469.74	$r^2 = 0.55$	

patient (in the neglected hemispatial field), the 6 subjects bisected the line to the right of center by a mean of 14.02 ± 2.23 mm. When the card was placed at the patient's midline, they bisected the line to the right of center by 8.04 ± 1.74 mm; and when the card was placed to the right of center, they bisected the line 4.03 ± 1.83 mm to the right of center. The results of an analysis of variance are presented in the Table. There are no significant differences between the two starting points and no significant interaction between position and starting point. The position of the card, however, was significant.

To determine where the differences between the three card positions were significant, a Duncan multiple comparison procedure was used. When the card was placed to the left, the subjects bisected the line more to the right than when the card was in the center or right position ($p < 0.05$). When the card was placed to the right, the patients tended to bisect the lines less to the right than when the card was placed in the center ($p < 0.10$). The right position was compared with the center position for each patient using Wilcoxon's matched pair signed-rank test [5]. The results of these nonparametric tests demonstrated that 3 patients performed significantly better ($p < 0.01$) when the card was in the right position than in the center. These were also the 3 subjects whose performance on this task was poorest.

Discussion

Our study demonstrates that when patients with unilateral spatial neglect have imposed on them a strategy to ensure that they have seen the full extent of a line in their hemianopic or inattentive field, their performance not only remains abnormal, it does not even improve. This observation is inconsistent with the hypothesis that the line is incorrectly bisected because it is not seen. The observation that performance varied with the line position and not the starting point is consistent with the hemispatial hypokinesia hypothesis.

We and our co-workers [16, 30] proposed that the unilateral neglect syndrome is a defect in the orienting response (an attention-arousal defect) caused by disruption of a corticolimbic-reticular loop. This loop is similar to that proposed by Sokolov [29]. The cortex is responsible for the highest level of stimulus analysis (i.e., novel versus nonnovel, significant versus nonsignificant), and the reticular system is responsible for mediating arousal. Although there is interhemispheric communication, each hemisphere contains its own corticoreticular loop, and a hemispheric lesion can cause an asymmetrical defect in the orienting response.

Unlike other reaction patterns, the orienting reflex is preparatory rather than consummatory [22]. Increased arousal can lower sensory thresholds, but, perhaps even more important, it prepares an organism (or a hemisphere) for action. Lesions that induce unilateral neglect produce an asymmetrical reduction of arousal, and the hypoaroused hemisphere cannot prepare for action and therefore is hypokinetic. Patients who have neglect may be hemiplegic because of pyramidal tract lesions; however, occasionally one sees a patient who has unilateral poverty of movement (hypokinesia) who is not weak and whose cerebral lesion is outside the traditional motor areas (e.g., in the inferior parietal lobe). Some support for our hypothesis comes from the works of Mountcastle and associates [24] and Lynch et al [21], who have shown, by single-cell recording of the inferior parietal lobe in monkeys, that certain cells appear to have an attentional function and act as if they are alerted in anticipation of a movement about to be effected. Ablation of this area in monkeys [14] produces neglect. Hemispatial neglect in man is also most frequently seen with lesions of the inferior parietal lobe [6, 9].

We propose that unilateral hypokinesia in the extremities is not limited to the extremity contralateral to the lesion but is a hypokinesia to any stimulus that comes to the hypoaroused hemisphere. We also propose that each hemisphere is responsible not only for mediating distal movements of the contralateral extremity and processing contralateral sensory input, but also for mediating behavior in the contralateral

spatial field independent of which extremity is used. This hemispatial hypokinesia may not be limited to the extremities but may also include eye movements.

The fact that our subjects continued to bisect lines to the right of center, even in the right position, suggests that there is a gradient across the midline and that each hemisphere also exerts an influence in ipsilateral space, which perhaps decreases as one moves laterally.

Observations in normal subjects support the hypothesis that each hemisphere is important for mediating behavior in the contralateral spatial field. In normal subjects, the time taken to react to a lateralized visual stimulus is determined by the anatomical connections between the receiving hemiretina and the responding hand. Ipsilateral responses, which are mediated by intrahemispheric neuronal circuits, are faster than contralateral responses, which require interhemispheric transfer [4]. For example, if a stimulus is presented to the right visual field, the response is faster with the right hand than with the left. This is no longer the case in reaction times involving choice, when the arms are crossed so that the right hand is on the left side of the body and the left hand is on the right side. In this situation, stimuli in the right visual field, for example, are responded to faster with the left hand than with the right.

This phenomenon has been termed "stimulus response compatibility" [2] and has been thought to reflect a natural tendency to respond with the hand that is already in the appropriate hemispatial field. An alternative explanation is that each hemisphere is responsible not only for moving the contralateral extremity and processing contralateral stimuli but also for mediating behavior in the contralateral hemispatial field, regardless of which extremity is being used. The right hand, for example, takes longer to respond to a right-sided stimulus when it is in the left hemispatial field than when it is in the right hemispatial field. This is because, in the former instance, bilateral hemispheric processing is required: the left hemisphere must process the visual stimulus, but the right hemisphere must contribute to the response of the right hand because it is in the left hemispatial field.

Although our results are compatible with the hemispatial hypokinesia hypothesis, there is an alternative explanation. Our group has demonstrated that patients with neglect have a unilateral auditory memory defect [18]. Samuels et al [28] tested patients with right parietal lesions and demonstrated a similar phenomenon in the visual modality, though they did not evaluate their subjects for neglect. William James [20] noted that "an object once attended will remain in the memory whilst one inattentively allowed to pass will leave no trace behind." Although our subjects saw the full extent of the line, it is possible that the side of the line in the left hemispatial field did not form a stable trace. As the subject explored the remainder of the line, he "forgot" the left side of the line and performed as if he had not seen it. As mentioned in the introduction, the hemispatial field is not the same as the visual field but refers to the space to one side of the midline of the body. If there were an attentional hemispatial memory defect, it would not be for the portion of the line in the left visual field but rather for the portion of the line on the left side of the body. Unfortunately, our experimental paradigm could not distinguish between the hemispatial hypokinesia and hemispatial inattention-memory hypotheses; however, if one accepts the latter hypothesis, it is difficult to explain why patients draw half a daisy.

Most early investigators reported that hemispatial neglect occurred after right hemisphere lesions [6, 25]; however, Battersby et al [3] thought that the incidence of hemispatial neglect from right hemisphere lesions was spuriously high because severely aphasic patients could not be tested. When Battersby and associates corrected for nontestable aphasics, they found that the incidence of hemispatial neglect from right-sided lesions was no different from that occurring with left hemisphere lesions. Albert [1], using a crossing-out task, found that although the incidence of visuospatial neglect was only slightly higher with right hemisphere than with left hemisphere lesions, the former produced a more profound defect. Costa [8], Faglioni [12], Gainotti [13], Colombo [7] and their associates, as well as others, have demonstrated a similar asymmetry. If neglect is caused by a defect in arousal, this behavioral asymmetry implies that there is a hemispheric asymmetry in arousal mechanisms.

We propose that each hemisphere can mediate its own attention-arousal response and that the right hemisphere can mediate this response for the left hemisphere better than the left hemisphere can mediate an attention-arousal response for the right hemisphere. Left hemisphere lesions would then produce less neglect than right hemisphere lesions since the right hemisphere would be capable of mediating an attention-arousal response for the left hemisphere. Right hemisphere lesions would produce a bilateral (although asymmetrical) defect because the left hemisphere would be incapable of mediating an attention-arousal response for the right hemisphere and also because left hemisphere arousal would be reduced on account of the right hemisphere damage. This hypothesis is supported by the demonstration of bilateral arousal defects in patients with right hemisphere lesions [15]. Since the inattentive hypoaroused hemisphere, according to our previous

arguments, would be incapable of preparing for action or seeing stable traces, hemispatial hypokinesia or a hemispatial inattention-memory defect would be more common and more severe with right hemisphere lesions than with those in the left hemisphere.

The results of this experiment have pragmatic implications. Because patients with neglect perform more poorly when the line is placed in the hemispatial field contralateral to their lesion, screening tests for hemispatial neglect should include testing in the spatial field contralateral to the lesion. In everyday life, the environment of these patients should be arranged so that all activity calling for their response occurs in the spatial field ipsilateral to the lesion.

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