Recovering Space in Unilateral Neglect: A Neurological Dissociation Revealed by Virtual Reality

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Abstract

■ Neglect patients often show deficits in responding to targets in the contralesional side of space. Past studies were able to ameliorate these deficits through manipulation of visual input. Here, the neural bases of the recovery of space following virtual reality (VR) training in neglect patients were investigated. Neglect patients were trained to respond to targets in the left side of space that appeared in the central or in the right side of space in a VR system. It was found that only patients with lesions that spared the inferior parietal/superior temporal regions were able to benefit from the VR training. It was concluded that these regions play a crucial role in the recovery of space that underlies the improvement of neglect patients when trained with VR. The implications of these results for determining the neural bases of a higher order attentional and/or spatial representation and for treating patients with unilateral neglect are discussed. ■

INTRODUCTION

Unilateral neglect is a common consequence of damage to the right hemisphere in humans (Bisiach & Vallar, 1988). The syndrome of neglect is characterized by a failure to respond to stimuli in the contralesional half of space, with patients often behaving as if these stimuli do not exist. Although neglect is most commonly seen after damage involving the right inferior parietal lobe near the temporoparietal junction, it may also occur after damage to the frontal lobes, temporal lobes, or subcortical structures (Bisiach & Vallar, 1988). Real-life implications of neglect can be devastating, with patients failing to eat food on the left side of the plate, only dressing the right half of their bodies, and often being unaware of half of their world.

Understanding the functional and neurological bases of unilateral neglect has been an imposing task. Numerous studies of unilateral neglect have focused on its effects on orienting attention (e.g., Behrmann, Ebert, & Black, 2004; Tipper & Behrman, 1996; Behrmann & Moscovitch, 1994; Farah, Brunn, Wong, Wallace, & Carpenter, 1990; Ladavas, 1987); indeed, it appears clear that neglect involves a strong attentional component (Driver & Vuilleumier, 2001; Kinsbourne, 1987; Bisiach, Luzzatti, & Perani, 1979). However, neglect has also been shown to have effects on spatial representation (Ladavas, 2002; Caramazza & Hillis, 1990) and motor performance (Mattingley, Husain, Rorden, Kennard, & Driver, 1998; Karnath, Dick, & Konczak, 1997; Mattingley, Phillips, & Bradshaw, 1994). In summary, neglect has been associated with different regions of anatomy and with a collection of different deficits. Our present aim is to determine whether the region injured in neglect influences the temporary recovery of this syndrome.

Improving Unilateral Neglect

Although neglect may be long-lasting in patients with right hemisphere damage, several promising advances have been made in its treatment. These methods generally involve the manipulation of attention and internal spatial representations with the aim of encouraging patients to respond to stimuli in the previously neglected hemifield (for a review, see Pisella & Mattingley, 2004).

Early attempts to improve neglect involved caloric stimulation of the ear (cf. Adair, Na, Schwartz, & Heilman, 2003; Rubens, 1985). When the left ear is irrigated with cold water, or when the right ear is irrigated with warm water, the vestibular system is affected such that the representation of left–right, which is normally influenced by gravity, is shifted. This results in an automatic tendency to orient to the neglected side of space as long as caloric stimulation is taking place.

Others have used vibration of neck proprioceptive receptors as a means of inducing spatial shift (Rode & Perenin, 1994; Geminiani & Bottini, 1992; Cappa, Sterzi, Vallar, & Bisiach, 1987). For example, Rode and Perenin (1994) found that stimulation of the left side of the neck

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in neglect patients resulted in an improvement in their ability to orient to stimuli in the previously neglected visual field. This improvement presumably resulted from a shift in the egocentric encoding of body midline toward the neglected hemispace.

More recent attempts to ameliorate neglect have involved laterally shifting visual input, using either prismatic distortion (Frassinetti, Angeli, Meneghello, Avanzi, & Ladavas, 2002; Rode, Rossetti, & Boisson, 2001; Rossetti et al., 1998) or virtual reality (VR; Castiello, Lusher, Burton, Glover, & Disler, 2004). For example, in Rossetti et al. (1998), neglect patients wore prism goggles that displaced the visual field 10° to the right, resulting to patients visually perceiving objects to be situated 10° to the right of their actual location. Prisms also had the effect of distorting the spatial location of patients' arms such that, when moving their arm toward a target perceived to be directly along their midline, for example, patients were actually moving the arm to the left of a target in the left visual field. By this manipulation, Rossetti et al. were able to dramatically improve the performance of patients when pointing to, and perceiving target in, the previously neglected left visual field. Furthermore, these studies have observed that the improvement lasted days (Rossetti et al., 1998) or even weeks (Frassinetti et al., 2002) after prisms had been removed and normal vision had been restored.

We recently applied a similar principle to the treatment of neglect using VR (Castiello et al., 2004). In our study, neglect patients were presented with a virtual object that could appear in the left visual field, the right visual field, or along the midline. The real object could be either in the same or in a different location as the virtual object. We found that neglect patients who had previously been unable to reach to grasp targets in the left hemispace were able to do so when the target appeared along the midline or to the right in virtual space. Similar to studies using prismatic distortion techniques, this recovery of space extended to the time when normal vision had been restored.

Neural Correlates of Improvement

To date, neural mechanisms underlying improvements in neglect following manipulation of visual input remain unknown. However, two points regarding the abovementioned studies using prisms or VR are worth highlighting. First, in past studies, it appeared that patients showed improvement in a variety of tasks, including motor tasks used in training (i.e., reaching and grasping, pointing), perceptual-based tasks (i.e., verbal report), and even tasks requiring the use of a different modality (e.g., Maravita et al., 2003). These facts suggest that improvement may result from a recovery of space in a higher order attentional and/or spatial representation that subserves both perception and action planning in multiple modalities. Second, in all cases, patients were allowed visual feedback of the moving limb, and this feedback was distorted in the same manner as information regarding the target. Specifically, when the target position was distorted to appear to the right of its true location, so, too, was the perception of the moving limb. This second point suggests an important role of online visual control in successful limb movements in neglect patients, as these patients have been shown to depend on visual reafference to monitor and to correct erroneous movements in flight (Edwards & Humphreys, 1999).

Although improvements in unilateral neglect have been reported with a number of patients with various lesions, it remains to be seen precisely what spared tissue could be responsible for the recovery of space. Based on what is known regarding spatial representation in the brain, at least two candidate regions can been proposed. First, the superior parietal lobe (SPL) in one or both hemispheres may serve as the crucial tissue subserving spatial recovery in neglect. Support for this notion comes from studies that showed that the SPL plays a role in spatial attention (Astafiev et al., 2003; Nobre et al., 1997; Corbetta, Shulman, Miezin, & Petersen, 1996) and spatial cognition (Trojano et al., 2002; Zarahn, Aguirre, & D'Esposito, 2000), and has been shown to be active during motor adaptation to prisms (Clower et al., 1996). We hereafter refer to this as the "SPL recovery" hypothesis.

A second candidate region is the spared aspect of the inferior parietal lobe (and, possibly, adjoining regions of the superior temporal lobe) in the right hemisphere. This notion is supported by the putative role of the inferior parietal/superior temporal regions in higher order spatial and/or attentional representation (Behrmann & Moscovitch, 1994; Caramazza & Hillis, 1990), multimodal integration (Driver & Vuilleumier, 2001), and action planning (Glover, 2004; Marotta, Mckeef, & Behrmann, 2003; Edwards & Humphreys, 1999; Mattingley, Husain, et al., 1998). We hereafter refer to this as the "IPL recovery" hypothesis.

Outline of the Present Study

The present study sought to determine the neural correlates of the recovery of space in patients with unilateral neglect. We performed this by identifying two sets of patients presenting with severe unilateral neglect, with each group suffering from damage to the right hemisphere (Figure 1). The two groups were matched for age, time poststroke, visual field processing, and severity of neglect (Table 1), and they differed only in the gross anatomical location of their lesions. Whereas one group suffered from extensive and overlapping lesions of the premotor cortex, motor cortex, and anterior (somatosensory) regions of the parietal lobes (the frontoparietal [FP] group; Figure 1, top), the other group suffered from extensive and overlapping damage including the posterior regions of the inferior parietal lobe and the adjoining superior temporal lobe (the temporoparietal

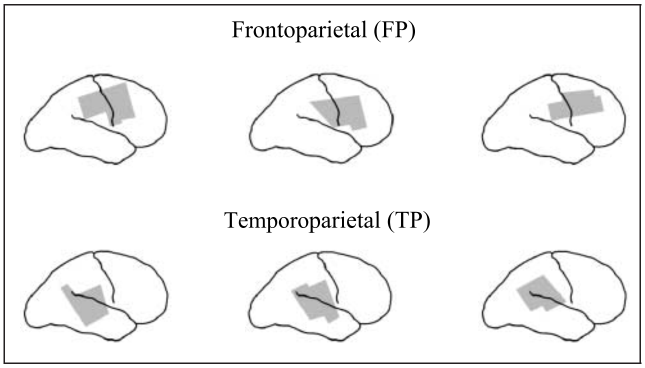

Figure 1. Reconstruction of lesion location in the FP group (top) and the TP group (bottom). (Adapted from Damasio & Damasio, 1989.)

[TP] group; Figure 1, bottom). In both groups, the SPLs were spared. For control purposes, age-matched neurologically healthy participants were also tested.

Before training with VR, FP and TP patient groups and matched controls were tested for both sensory and motor responses to targets in the left, center, or right side of space in a real environment. Following this, all three groups were trained in a grasping task using the VR technique employed by Castiello et al. (2004). In the training session, patients were seated in front of a computer monitor (Figure 2). This allowed for manipulation of the position of ''real'' and ''virtual'' targets. Subjects were presented with targets either along the midline or in the left or right hemispace, and they observed objects in virtual space that were either congruent or incongruent with the true location of the targets (Figure 3). The critical training conditions were left-incongruent trials (Figure 3F and G). On these trials, a real object was placed in the left hemispace, but appeared either directly ahead of the subjects or in the right hemispace in virtual space. This condition required subjects to move to the previously neglected left side of space while observing a target that appeared to be in non-neglected space. Before, during, and after training, participants in each group were tested for their ability to respond to targets presented in the left (neglected) visual field. Measures of perceptual performance (verbal response) and motor performance (reaching and grasping) were compared across groups.

The two hypotheses outlined above allow us to make competing predictions regarding the ability of neglect patients to remap space and thereby regain the ability to respond to leftward targets with VR training. The SPL recovery hypothesis predicts that both the TP and FP groups will retain the ability to remap space as the SPLs in all patients are intact. The IPL recovery hypothesis predicts that, as the TP group suffers damage to the IPL and surrounding areas, this group will be unable to benefit from the VR technique. The FP group, however, should retain the ability to recover space. To summarize, both the SPL and IPL hypotheses predict improvement in the FP group. However, only the SPL hypothesis predicts improvement in the TP group.

METHODS

Subjects

The subjects were six patients with left visual neglect following right hemisphere stroke (Table 1). Patients

Table 1. Demographic and Clinical Data for Neglect Patients

						Clinical Tests		
Patient No.	*Age (years)*	*Sex*	*Lesion*	*Visual Field*	*Poststroke (days)*	*Line Bisection Test (mm)*	*Albert's Line Test (/36)*	*Star Cancellation Test (/54)*
FP patients								
1	67	M	FP	Normal	56	12.2	15	13
2	69	M	FP	Normal	64	17.3	34	24
3	71	F	FP	Normal	58	21.2	26	14
Mean						16.9	25	17
TP patients								
1	77	M	TP	Normal	59	10.8	22	8
2	70	M	TP	Normal	55	13.4	36	20
3	73	F	TP	Normal	61	18.7	32	13
Mean						14.3	30	13

M = male; F = female; FP = frontoparietal; TP = temporoparietal.

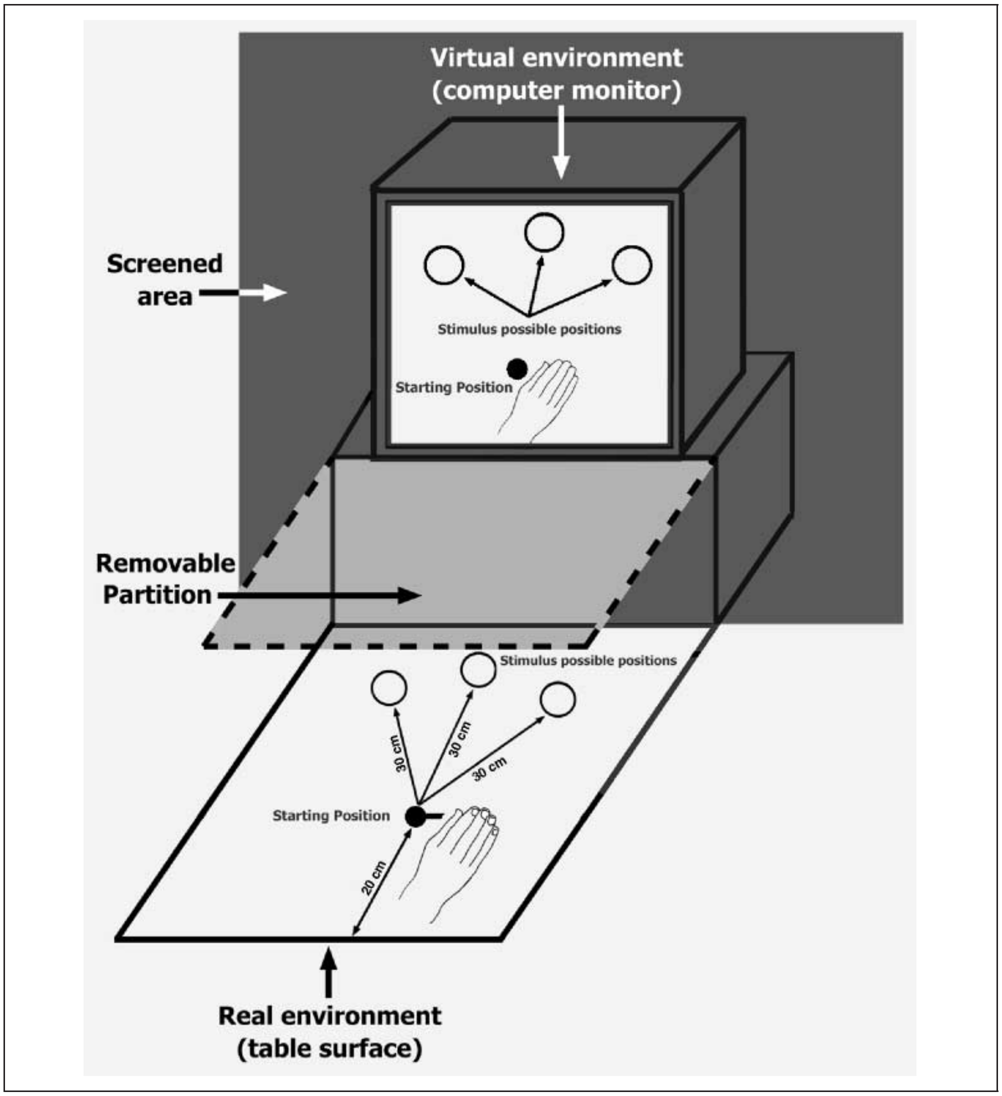

Figure 2. Schematic showing the experimental setup (see Methods for details).

were classified based on neurological assessment, behavioral observation, and standard clinical tests. All patients were right-handed and had normal or corrected-to-normal vision, with no signs of severe gaze palsy, dementia, or previous neurological illness. Lesions were confirmed by computed tomography scan. Lesions were plotted (Figure 1) using the template of Damasio and Damasio (1989). Based on lesion location, we divided the patients into a dorsal FP group and a ventral TP group.

One-way analysis of variance (ANOVA) revealed that there was no significant difference, $F(2,2) < 1$, *ns*, between the mean ages of neglect patients in the FP group (69 years), the TP group (73 years), and the controls (73 years), or in the mean days after stroke for the FP and the TP neglect patients, FP 59 days, TP 58 days, $F(1,2) < 1$, *ns*. All subjects gave informed written consent before testing began. The study was approved by the ethics committee of the North Western Health Care Network.

The two groups of patients with neglect were well matched for degree of neglect (see Table 1). For example, on the star cancellation test, the FP patients found a mean of only 17 of 54 targets (range, 12.2–21.2), all on the right side of the sheet. Similarly, the TP patients found a mean of 13 of 54 targets (range, 8–20), again all on the right side of the sheet.

Apparatus

Subjects sat by a table and faced the apparatus, as depicted in Figure 2. The apparatus consisted of a monitor placed on top of a hollow box into which the subjects could reach. The computer screen was located approximately 50 cm from the subject's eyes. Vision of the reaching limb within the box was occluded by a black partition between the reaching limb and the eyes. Targets for grasping consisted of either (1) a real object (white polystyrene sphere, 8 cm in diameter) resting on the table at a distance of 30 cm from a starting position located 20 cm in front of the subject, or (2) a virtual object presented on the computer screen. The virtual

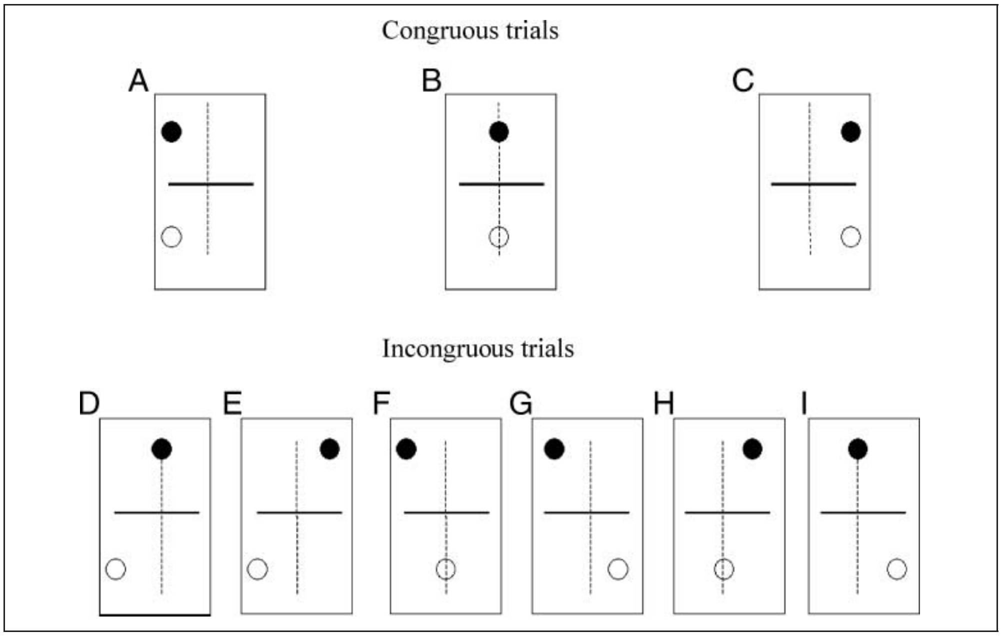

Figure 3. (A–I) Schematic of various trial types in the training task. Virtual targets are shown as black circles; real targets are shown as white circles. The top three panels represent congruent trials in which the locations of real and virtual targets matched. The bottom six panels represent incongruent trials in which the locations of real and virtual targets did not match. The crucial left-incongruent trials are the two leftmost trials in the bottom row.

object was a replica of the real object; its size was manipulated such that it had the same appearance as the target object for each given distance.

Procedure

Subjects sat by the table and reached to grasp either the real or the virtual object. According to Figure 2, the real and virtual objects could be located either centrally (midsagittal plane) or 30° to the left or to the right of midline. The experiment was carried out in three sessions within the same day, one in the morning and two in the afternoon.

Session 1: Baseline Task

Subjects performed one of two types of task within either the real or the virtual environment. An object (or its virtual counterpart) was presented in one of three positions (midline or ±30° laterally); in the "sensory" task, subjects were required to report the location in which the object appeared (left, right, or center). In the "motor" task, subjects had to reach out and grasp the object. Each participant performed four blocks, one of each combination of real/virtual and sensory/motor. The baseline task consisted of 10 trials at each location in each of four blocks. The total number of trials in the baseline task was thus 120. Experimental tasks were preceded by a block of 20 randomly determined practice trials. Stimulus presentation was counterbalanced across participants.

Session 2: Training Task

Subjects were required to reach for the real object located at one of three locations within the real environment while simultaneously viewing the real-time virtual representation of the hand. While moving toward the real object, subjects observed the virtual hand moving toward the virtual object. Vision of the real hand was occluded by a wooden partition (Figure 2). Thus, subjects never saw their own hand moving in this condition, only the virtual hand. At the onset of each trial, subjects saw the virtual hand at the center starting position. When the virtual target appeared, a "go" signal was given by the experimenter. This task consisted of two types of trial: (1) congruent trials in which the real and virtual objects were spatially congruent (Figure 3, top), or (2) incongruent trials in which the real and virtual objects occupied different spatial locations (Figure 3, bottom). Subjects performed 240 trials, 20 per location/trial combination. The order of object presentation was counterbalanced. Crucial to the present study were the left-incongruent trials (Figure 3, F and G) in which the target was located to the left within the virtual environment, whereas the real object appeared to the right or middle.

Session 3: Posttraining Sensory Task

Subjects were required to perform the sensory task in virtual and real conditions as in Session 1 to measure the effect of manipulation on the performance of the sensory task. Session 3 commenced between 1 and 2 hr following the cessation of the training session.

Virtual Reality

A data glove (Virtual Realities; Fifth Dimension Technologies, Irvine, CA, USA) allowed the subjects to control the virtual hand that moved in real time within a computer-generated environment. The sampling rate was 200 Hz. All devices were operated via PC. We were able to resolve issues of real–virtue compatibility that may arise when the glove is worn by different subjects with differently sized hands.

Movement Recording

Reaching movements were recorded using the Flock of Birds system (Ascension Technology, Burlington, VT). A magnetic sensor was placed on the wrist of the reaching hand. Recordings of marker position were taken at 100 Hz and were stored in a computer for analysis offline. Following testing, movement trajectories were computed from the stored data.

Data Analysis

Accuracy was analyzed in the sensory and motor tasks (Sessions 1 and 3). Performance in the sensory task was considered correct when subjects successfully reported the location in which the object appeared within 4 sec of its presentation. A correct movement was considered as one in which the subject completed a successful reach and grasp, closing the hand around the target within 4 sec of its appearance.

We also analyzed the trajectories of complete movements. We used hand path curvature (HPC) as an index of the degree of directional error in action planning. Spatial resampling was carried out to produce hand paths, which each contained 100 equally spaced spatial segments, thereby allowing comparisons between movements. Spatial resampling did not change the shape of any individual hand path and did not result in normalization of movement amplitude. Hand paths were also translated spatially so that movements to different target locations within the workspace could be compared. This procedure resulted in a set of hand paths aligned along a single axis. This procedure is similar to that used by Haggard and Richardson (1996) to compare reaches with different start and end points within the workspace. The HPC index consisted of the ratio between the magnitude of the maximum lateral deviation achieved at any point during the movement (mm) and the straight line joining the kinematically determined start and end positions of the movement (mm). Note that the HPC index produces a measure of HPC (1) that is independent of movement amplitude, and, (2) in which all values, regardless of whether the hand path curved leftward or rightward, are positive.

RESULTS

Baseline Tasks

For baseline tasks, the percentage of trials in which the object was successfully detected (sensory task) and in which the reaching movement was successfully carried out (motor tasks) were analyzed using ANOVA. The between-subjects factor was Group (FP, TP, controls). The within-subjects factors were Type of Task (sensory, motor), Environment (real, virtual), and Location (left, middle, right). For this analysis, the interaction Group × Location was significant, $F(1,2) = 43.21, p < .0001$. This interaction revealed that neglect patients had a very low percentage of successful trials when the stimulus appeared at the left location, whereas the control subjects had a high percentage of successful trials irrespective of object location. This pattern was found for both the sensory and the motor tasks (Figure 4) performed within the real or the virtual environment. Lack of significant interactions between the main factors Type of Task and Environment and the other variables signifies that this pattern was found for both the sensory and the motor tasks performed within the real or the virtual environment. Both FP and TP patients showed a clear inability to respond to leftward targets in both the baseline sensory task and the baseline motor task. These results confirmed the presence of similar severe unilateral neglect in both groups of patients before training with VR.

Training Task

During the training task, subjects were exposed to spatially congruous and spatially incongruous trials (Figure 3). ANOVA was carried out to test the effect of left-incongruous trials (Figure 3F and G) on the performance for left-congruous trials (Figure 3A) and for center-incongruous and right-incongruous trials (Figure 3D and E). In these latter types of trial, a movement toward the real stimulus located on the left was required. For this analysis, the data for left-congruous trials and for center-incongruous and right-incongruous trials were divided based on occurrence (before or after) relative to left-incongruous trials. Although the exact

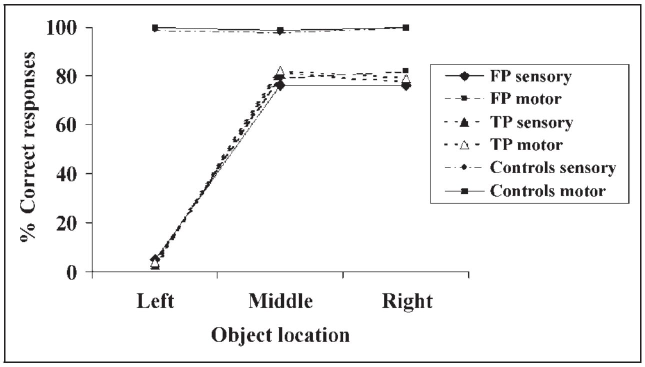

Figure 4. Performance of patients and controls in baseline perceptual and motor response task in the real environment only. The percentage of correct responses is plotted as a function of Group, Location, and Type of Task.

number varied, all subjects experienced at least eight left-incongruous trials before the left-congruous, center-incongruous, and right-incongruous trials. Here, the between-subjects factor was Group (FP, TP, controls) and the within-subjects factors were Type of Trial (congruous, incongruous), Occurrence (before vs. after), and Location (left, middle, right). The interaction Group × Occurrence was significant, $F(1,2) = 23.18$, $p < .0001$. This interaction revealed that there was a clear dissociation in performance in training tasks in the FP and TP patients (Figure 5). During training, two patients in the FP group began to show a significant improvement in their responses to leftward targets beginning on the seventh left-incongruous trial; the third FP patient showed improvement beginning on the eighth left-incongruous trial. All FP patients had attained near-normal performance by Trial 10. In contrast, the TP group failed to show any signs of improvement even after 10 left-incongruous trials. Figure 6 shows that patients in the TP group hardly moved at all toward the leftward target whenever it appeared on the left in virtual space, and they failed to attain the leftward target even when it appeared in the central location in virtual space. On these trials, the patients initially began to move and stopped or did not move at all. That is, poor performance on these trials was not due to movements that simply took longer than the trial duration, but was rather due to movements that were halted very early and never continued. As is evident from Figure 6, patients' behaviors may also have indicated difficulty in crossing the midline. For the control group, the percentage of correct responses was very near the ceiling for both congruous and incongruous trials, regardless of when they experienced the left-incongruous trials. Lack of interaction between the main factor Type of Trial and the other measures signifies that the increase in percentage of correct left trials was similar for both congruous and incongruous trials.

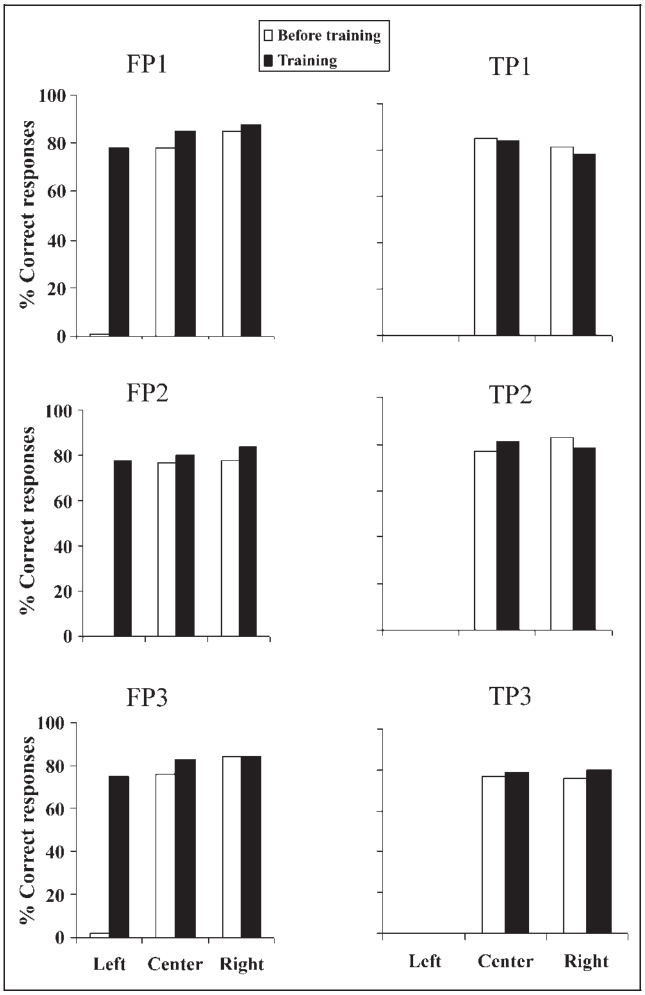

Figure 5. Performance in the motor task before and after training. Correct responses to targets that are presented on the left, in the center, and on the right are plotted in baseline (empty rectangles) and posttraining (filled rectangles) sessions for individual patients in the FP (left) and TP (right) groups.

Figure 6 also shows characteristically curved trajectories of neglect patients. Measures of HPC showed that the degree of curvature in both groups increased as a function of target position, with more leftward targets being associated with greater HPC (Table 2). Indeed, the greatest HPC scores were observed for the FP group in movements to targets in the (previously neglected) left visual field. This supports the reported relation between unilateral neglect and directional errors in action planning (Glover, 2004; Edwards & Humphreys, 1999).

Posttraining Sensory Task

To verify that an improvement also occurred for tests that did not require a motor response, in the third session, FP and TP patients were asked to repeat the sensory task performed in the first session within the real space. This took place 1–2 hr after the training session. An ANOVA with Group (FP, TP) as between-subjects factor and with Session (first, third) and Location (left, center, right) as within-subjects factors was performed. The three-way interaction Group × Session × Location, $F(1,2) = 24.12$, $p < .001$, revealed that the percentage of correct responses for the left trials was significantly greater for the third session than for the first session only for the FP group, $F(1,2) = 24.12$, $p < .001$, 5% vs. 83%. No improvement was noticed for the TP group (4% vs. 5%). This suggests that exposure to left-incongruous trials also had an effect on the perceptual component of neglect, but only for the FP group (Figure 7).

DISCUSSION

The present study addressed the issue of the neurological bases of space recovery in unilateral neglect. Using a VR paradigm, we created a situation in which neglect

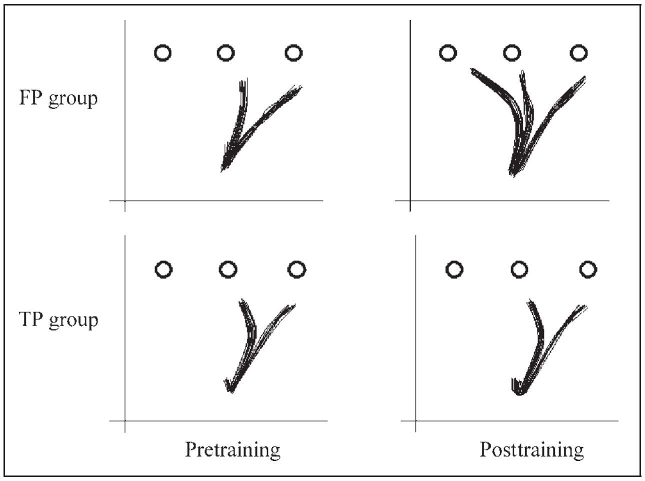

Figure 6. Hand path trajectories of the FP group (top) and the TP group (bottom) in reaches to targets in the three locations before (left) and following (right) training. Note that the trajectories fall short of the targets because the marker was placed on the wrist. The very short trajectories in the TP group represent responses to targets on the left.

patients were able to respond to targets in the previously neglected left visual field by simulating the target's appearance in the central region of space. We observed that patients with FP lesions (the FP group) sparing the posterior inferior parietal and superior temporal regions acquired the ability to respond to the left visual field. Furthermore, this improvement lasted for at least 1–2 hr (the time between the cessation of the training session and the commencement of the posttraining session). The 1- to 2-hr span between the training and the posttraining tasks suggests that the improvement lasted longer than that previously found using caloric stimulation (e.g., Rubens, 1985) or vibration of the neck (e.g., Cappa et al., 1987), and at least as long as the shortest periods tested following the use of prism (e.g., Rossetti et al., 1998) and VR (Castiello et al., 2004) techniques. However, this benefit did not accrue to patients with damage involving the posterior IPL and the superior temporal lobe (the TP group). We now discuss these results in terms of the putative functions of areas of the posterior half of the brain.

Table 2. Comparison of HPCs as a Function of Group and Target Location in the Posttraining Reaching-and-Grasping Task

Target Location	*Controls*	*FP*	*TP*
Left	0.059	0.325	NA
Center	0.056	0.174	0.174
Right	0.059	0.089	0.091

NA = not applicable.

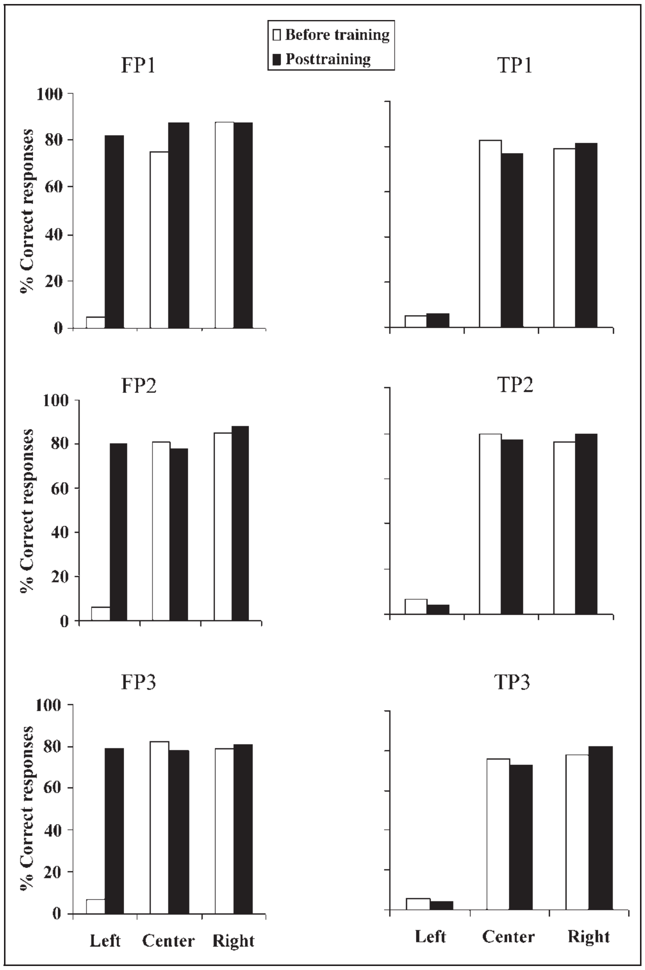

Figure 7. Performance in the posttraining sensory task. Conventions are as in Figure 4.

To address this issue, it is worthwhile to consider the processes required in the recovery of space and to examine the regions of the brain that might subserve these processes. Bearing in mind that recovery of space can also occur after vestibular and somatosensory stimulation, the most likely candidate would be a region that represents space in a multimodal fashion. At least two such areas are known to exist in the human brain, namely, the prefrontal cortex and the posterior parietal cortex. Yet, only the latter area was affected in any of the patients studied here.

The inferior parietal lobes in humans acquire multimodal information from all of visual, somatosensory, and auditory senses, and have been hypothesized to represent a region of higher order spatial representation (Pavani, Ladavas, & Driver, 2003; Driver & Vuilleumier, 2001). This region thus seems uniquely poised to perform a major role in the function of recovering space. Note also that, in both present and past studies, the recovery of space effected through a motor task has transferred rather easily to other more sensory-based tasks (e.g., verbal response). This supports the contention that the recovery of space is at an attentional or a representational level, rather than at a purely motor or a purely perceptual level.

We suggest that the regions damaged in the TP group may play a crucial function in the specification of target for an upcoming action in conjunction with attentional processes. In neglect, attention is typically diverted to the ipsilesional visual field, and stimuli in the neglected field are ignored as targets for action. When these same stimuli are made to appear in central space, however, the attentional premotor requirement of target selection is enabled, allowing the stimuli to be coded as the target of an upcoming action. However, when the inferior parietal/superior temporal regions are damaged, the result is an inability to recruit a motor plan for acting in the left side of space, despite the fact that the stimulus is now present in central vision.

Some other interpretations of our results are also possible. For one, it may be argued that patients in the TP group simply lacked the ability to make leftward movements owing to a more basic motor deficit. This idea might gain support from the fact that both groups of patients showed rightward errors in initial movement heading that became more pronounced when the target was further to the left of the rightmost target. However, elementary motor disturbances following damage to the TP region have never been reported, and we would thus be reticent to attribute our results to a basic problem in making leftward movements in these patients.

A second alternative explanation might be that damage to cells in the IPL region of the TP group remotely affected the functioning of cells in the SPL as a consequence of intimate connectivity of these two regions (Pandya & Yeterian, 1985; Seltzer & Pandya, 1984). This, in turn, may have impaired the SPL in what might be its normal function. Indeed, it is well known that naturally occurring brain damage can have effects on brain areas outside of the lesion (Kolb & Whishaw, 2003). However, if one accepts this contention, then it becomes difficult to explain why damage to the premotor cortex in the FP group did not also lead to such a disruption, given that it also possesses strong connections with the SPL (Passingham, 1993). Furthermore, both groups of patients showed intact online monitoring and control of their movements once initiated—a function ascribed to the SPL (Glover, 2003, 2004; Grea et al., 2002; Rossetti & Pisella, 2002; Pisella et al., 2000)—suggesting that at least one major function of the SPL remained intact. Thus, we are disposed to dismiss this argument.

A reviewer suggested a third possible alternative based on distributed processing. On this account, the IPL may indeed play a significant role in the recovery of space, but it may do so in conjunction with other areas of the brain, possibly including the SPL. As many functions in the brain (including attention and spatial representation) are believed to rely on widely distributed neural networks, this notion is inherently plausible. The IPL may be necessary, but not sufficient, for the recovery of space observed in the present study. Furthermore, given that our results suggest that the IPL is a crucial component of the network involved in the recovery of space and that the SPL is not, we would speculate that neglect associated with a lesion confined to the IPL would benefit from our training technique, whereas neglect associated with a lesion confined to the SPL would not benefit from our training technique.

The results of the present study suggest that attempts to treat unilateral neglect may be more beneficial to those patients whose lesions spare the posterior IPL and possibly the superior aspects of the temporal lobe. However, some concerns may be expressed with this interpretation. For one, it may be argued that the relatively small number of patients tested in each group makes it difficult to draw strong conclusions. Nonetheless, individual data show that performance was consistently good for the FP group and was consistently poor for the TP group in responding to left-side targets following training.

A second concern with this claim relates to the findings of previous studies involving attempts to improve unilateral neglect using prism adaptation (Frassinetti et al., 2002; Rode et al., 2001; Rossetti et al., 1998). In those studies, which involved a similar shift in the perception of space as we engendered with our VR paradigm, some patients with TP lesions showed improvements following training. Of those studies, precise localization was only reported in Frassinetti et al. (2002); however, in that case, two of three patients whose lesions included the IPL improved following training with prisms. One reason for the discrepancies across studies may have been related to the type of motor tasks involved (pointing in the prism studies vs. reaching and grasping in the present study) or to some unknown differences between the prism and VR techniques. It would be beneficial to test our findings using larger samples of neglect patients and to examine patients with varying lesion locations, using different techniques, to further clarify these issues.

The question may also be raised as to why training only led to improvement for leftward targets and not for targets presented in the center or the right side of space. We suggest that the improvement in the former case resulted from the requirement to make movements to the previously neglected left side of space. Conversely, movements to the center or the right side of space were not novel occurrences and, thus, did not affect the ability to respond to these targets.

A final thought regarding the notion that the IPL is important in the recovery of space concerns recent work by Corbetta et al. (1996), which suggested different roles for the superior parietal–frontal regions vs. the ventral parietal–frontal regions (Kincade, Abrams, Astafiev, Shulman, & Corbetta, 2005; Serences et al., 2005). In functional magnetic resonance imaging studies, these authors have shown that bilateral superior parietal and dorsal areas of the frontal lobes appear to play a strong role in attention allocation and response preparation. In contrast, the right IPL and the ventral areas of the frontal lobes appear to play a more executive ''circuit-breaker'' role. Specifically, the ventral parietal–frontal system appears to be involved in detecting new salient visual stimuli and in directing the dorsal parietal–frontal system to switch attention to them. These findings suggest that the right IPL may play an executive role in many processes, not just in the recovery of space.

The results of the present study suggest that space recovery techniques such as VR may lead to at a least temporary relief for patients suffering from unilateral neglect. However, the usefulness of these techniques may depend, at least in part, on the integrity of structures in the inferior parietal/superior temporal lobes of the right hemisphere, which may play a critical role in higher order attentional and/or spatial representation. As the present study represents the first attempt to localize the areas responsible for the recovery of space, any conclusions reached must be viewed with caution. Future studies using techniques such as VR and prism adaptation will undoubtedly be needed to shed more light on both the treatment of neglect and the neural substrates responsible for its efficacy.

Conclusions

We tested the ability of patients with unilateral neglect to recover space with the aid of VR. Whereas FP patients showed a dramatic improvement in both motor and perceptual performance following training with VR, TP patients did not benefit from the same training. These results suggest that the recovery of space required for the recalibration of motor and perceptual responses to a neglected visual field may depend on the integrity of a multimodal attentional and/or spatial representation region in and around the right inferior parietal lobe.

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