Improving left hemispatial neglect using virtual reality

U. Castiello, DSc; D. Lusher, BA; C. Burton, PhD; S. Glover, PhD; and P. Disler, MD

Abstract—*Background:* In hemispatial neglect, space can be dissociated on the basis of "near" peripersonal vs "far" extrapersonal space. The clinical manifestations of neglect can be modified by having patients use a tool to explore "far" extrapersonal space. An explanation for this is that the use of a stick produced an extension of body space resulting in a remapping of "far" space as "near" space. *Objectives:* To determine whether the remapping of space can be generalized to the amelioration of the "affected" vs the "nonaffected" space, rather than being confined to the selective amelioration of "far" vs "near" neglect; and to determine whether tool use is a necessary condition for the remapping of space. *Methods:* Using virtual reality, the authors asked six hemispatial neglect patients to reach and grasp a real object while simultaneously observing the grasping of a virtual object located within a virtual environment by a virtual hand. The virtual hand was commanded in real time by their real hand. *Results:* After a period of adaptation, hemispatial neglect patients coded the visual stimuli within the neglected space in an identical fashion as those presented within the preserved portions of space. *Conclusions:* It is possible to re-create links between the affected and the nonaffected space. Wielding a tool is not a necessary condition in reopening neglected space.

NEUROLOGY 2004;62:1958–1962

In patients with visual hemispatial neglect, "near" peripersonal and "far" extrapersonal space are neurologically dissociable,[1-3] where "near" space is defined as that within reaching distance and "far" space is beyond. For example, a patient with visual hemispatial neglect in a line-bisection task carried out within the near space did not deviate when the lines were located in the far space and line bisection was carried out with a light pen.[1] The opposite dissociation in which hemispatial neglect is evident in far but not near space has also been reported.[2,3]

When only one of these portions of space is damaged, the border between far and near space could be modulated through the use of a tool to explore the affected hemifield.[4-8] A patient with neglect of near space was shown to demonstrate neglect in far space when actions were made using a long stick. In that case, the impaired representation of space was extended across a larger distance by use of the tool.[4] Others have also demonstrated that the use of a tool was also associated with worse neglect.[8] A conflicting study of a patient with neglect of far right and near left space[6] showed that neglect was reduced when the patient held a ruler that appeared to extend his more intact representation of (near right) space across longer distances.[6] Tool use can specifically extend visual space, thus modulating the spatial representation.

However, new neurophysiologic evidence suggests that space remapping can also be induced when no tool is used. For example, it has been demonstrated that body part representations might be extended within a virtual space.[9] Monkeys were trained to recognize the image of their limb in a virtual environment to guide the same limb within the real environment. Once the monkey acquired this skill, the visual receptive field of multimodal cells was enlarged to include the screen image of the hand. It is possible that a mechanism exists that allows a match between visual input from the virtual hand within the far space and the efferent signals controlling the real hand acting within the near space, even in absence of any tool.

We tested the hypothesis that space remapping might not be specific to the "near" vs "far" dichotomy but could also be extended to the more general dichotomy of "affected" vs "not affected" space. In addition, we studied whether "virtual"-induced space remapping could be used to ameliorate visual neglect in humans without the necessity of using a tool. We tested whether this kind of virtual reality (VR) manipulation can improve the visual representation of space deficits observed in hemispatial neglect patients.

Subjects and methods. The study was approved by the Ethics Committee of the North Western Health Care Network. Informed consent was obtained from all subjects.

Subjects. Six patients with left-sided visual neglect following right hemisphere stroke were assessed (table) in addition to six neurologically healthy control subjects. The patients with neglect were classified on the basis of neurologic assessment, behavioral observation, and standard clinical tests (see the table). All patients were right handed and had normal or corrected-to-normal vision with no signs of dementia, severe gaze palsy, or previous neurologic illness. All lesions were confirmed by CT scans. Lesions were plotted (figure 1) using the templates of Damasio and Damasio.[10] One-way analysis of variance (ANOVA) revealed that

---

From the Department of Psychology (Drs. Castiello and Glover), Royal Holloway, University of London, Surrey, UK; and Department of Psychology (D. Lusher), University of Melbourne, and Melbourne Extended Care and Rehabilitation Services (Drs. Burton and Disler), Australia.

Supported by a grant from the National Health and Medical Research Council (U.C.).

Received October 14, 2003. Accepted in final form January 29, 2004.

Address correspondence and reprint requests to Dr. U. Castiello, Department of Psychology, Royal Holloway, University of London, TW20 0EX, Egham, Surrey, UK; e-mail: u.castiello@rhul.ac.uk

Table. *Demographic and clinical data for the neglect patients*

Neglect patient no.	Age, y	Sex	Lesion	Visual field	Post stroke, d	Clinical tests Line bisection test, mm	Albert line test, /36	Star cancellation test, /54
1	67	F	FP	Normal	56	12.2	15	13
2	75	M	FPO	Normal	60	7.8	23	20
3	69	F	FP	Normal	64	17.3	34	24
4	71	M	FP	Normal	58	21.2	26	14
5	74	F	P	IQ	57	12.3	22	7
6	75	M	BG	Normal	66	11.6	33	27
Mean						13.7	25.5	17.5

FP = frontoparietal; FPO = frontoparietooccipital; P = parietal; IQ = inferior quadrantanopia; BG = basal ganglia.

there was no significant difference between the mean ages of groups (neglect patients: 72 years; control subject: 73 years; $F_{1,5} < 1$).

Methods. Subjects sat in front of a table and were presented with two types of objects: 1) a real object consisting of a 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 (figure 2); 2) a virtual object that was the exact replica of the real object, presented on a computer screen located at a distance of about 50 cm from the subject's eyes. Although the monitor was positioned within the "near" peripersonal space, subjects were under the illusion that the virtual hand was operating in the "far" extrapersonal space. The virtual object was scaled to give the perception of the correct size as the viewer, because of his/her height above the table, would automatically be closer to the screen than to the real object (see figure 2). Both the real and the virtual objects could be located at three different locations with respect to the subject's midline (see figure 2): central (midsagittal plane), ipsilateral (30° right of the central location), and contralateral (30° left of the central location). The experiment was carried out in three sessions within the same day: one session in the morning and two in the afternoon.

Session 1: baseline tasks. There were two types of task, "sensory" and "motor," performed within the real or virtual environment. The two tasks were similar in all respects except that for the sensory task, subjects were required to report the location in which the object appeared, whereas for the motor task, the subjects were required to reach to and grasp the object. Subjects performed 60 trials, 20 trials for each location. Subjects performed a block of 20 practice trials before performing two experimental blocks of trials for each of the sensory and motor tasks. For all tasks, the order of stimulus presentation was counterbalanced across participants.

Session 2: real/virtual task. Subjects were instructed to reach for the real object located at one of the three predefined locations within the real environment while simultaneously being able to view only a real-time (virtual) representation of the virtual hand. While moving the real hand toward the real object, the subjects saw the virtual hand moving toward the virtual object. Subjects were prevented from seeing the "real" hand and object by means of a black wooden partition (see figure 2). A "go" signal was given by the experimenter when the virtual object appeared. This condition was subdivided into two types of trial: congruous and incongruous. Congruous and incongruous trials were those in which the real and the virtual objects were either spatially congruent (figure 3, A through C) or incongruent (figure 3, D through I), respectively. Subjects performed 120 trials, 20 for each location/trial combination. The order of object presentation was counterbalanced. Crucial for the current study are the left incompatible trials (see figure 3, F and G) in which the virtual object was

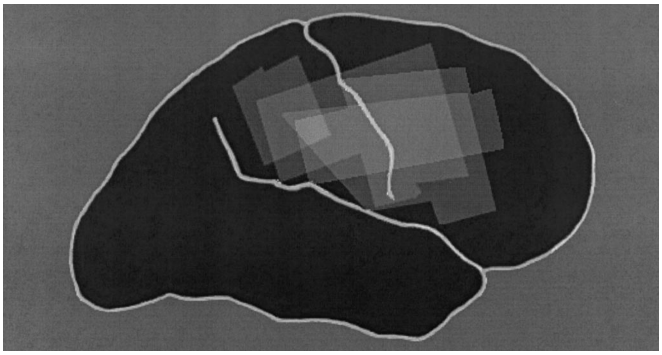

Figure 1. A depiction of the sites of the cortical lesions identified from CT scans for five (of six) of the patients (the lesion of the patient with subcortical damage is not represented).

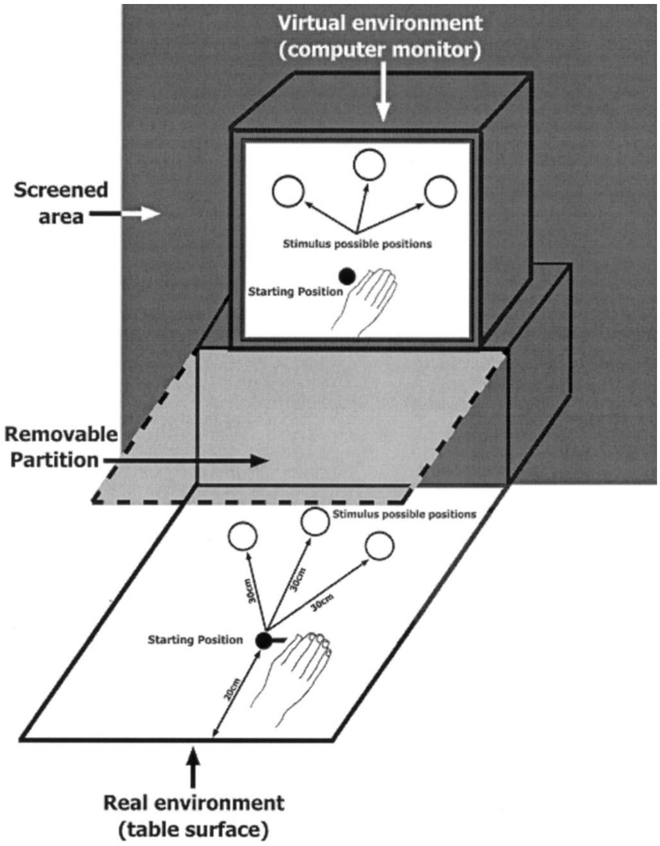

Figure 2. Schematic of the experimental setup.

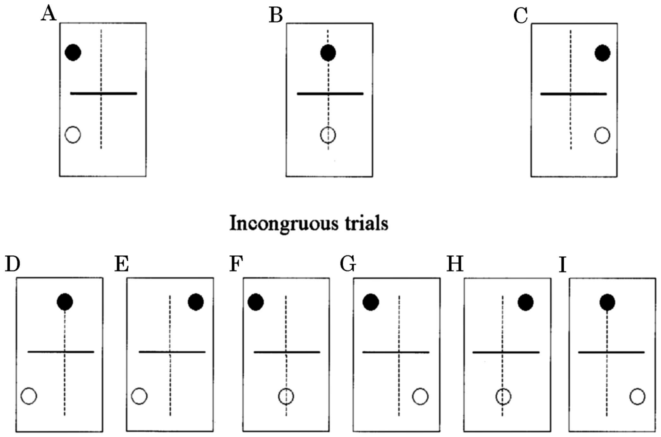

Figure 3. Diagrammatic representation for the virtual (black circles) and the real (white circles) object location for congruous (A to C) and incongruous (D to I) trials.

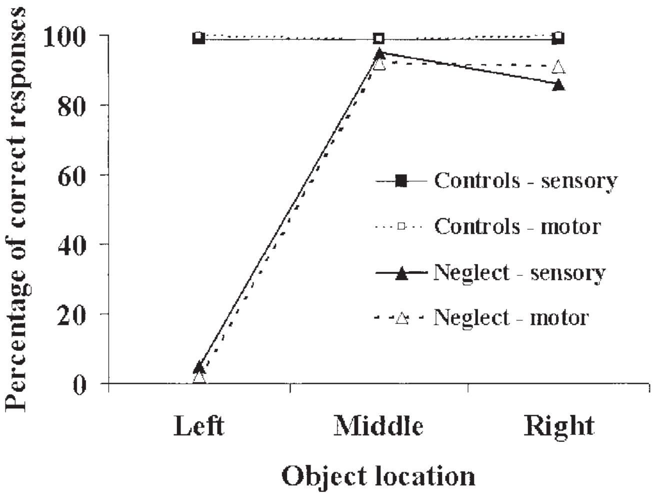

Figure 4. Graphic representation of the group × type of task × location interaction.

located to the left within the virtual environment and the real object appeared to the right or in the middle in the real environment. In this condition, subjects moved their real hand toward the real object located in the center or on the right, but they could see the virtual hand grasping the object located on the left. The question of interest here was whether exposure to such a manipulation could provide an efficient way of forging new links between the preserved space (where the real hand was acting) and the neglected space (where the virtual hand was acting). If this new linking is possible, then the effects of this manipulation should be evident when participants are required to direct the real hand toward the neglected side.

Session 3: sensory task. Subjects were instructed to perform the "sensory" task as in session 1. This measured the effect of the manipulation adopted in session 2 on performance of the sensory task.

VR technique. The use of VR allowed us to systematically manipulate the location of the virtual object within the virtual environment with respect to the location of the real object within the real environment. A data glove (Virtual Realities; Fifth Dimension Technologies, Irvine, CA) allowed the subjects to control a virtual hand that could be moved in real time within a computer-generated environment such that the virtual hand was able to visually interact with the virtual object. We were able to satisfactorily resolve issues of accuracy and equivalency commonly associated with gloves of this type (i.e., the comparability of data recorded when the glove has been worn by different subjects with different hand sizes). The sampling rate was 200 Hz. All the devices were connected to a PC using RS-232 serial ports.

Criteria for accuracy. This report is concerned with accuracy data. Performance of the sensory task was considered "correct" when subjects reported the location in which the object appeared within 4 seconds of its presentation. Performance of the motor task was considered "correct" when participants closed their fingers around the object, the object changed color (from white to red), and a sound was presented. A movement was considered as "incorrect" when either 1) the subject did not start the movement when the object was presented or 2) the subject briefly started the movement toward or away from the presented object, but after 50 frames (500 milliseconds), the movement was halted.

Results. For the baseline session (session 1), the percentages 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 (neglect, 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 ($F_{1,5} = 58.13$, $p < 0.0001$). 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 group subjects had a high percentage of successful trials irrespective of object location (figure 4). The lack of significant interactions between the main factor type of task and environment with the other variables signifies that this pattern was found for both the sensory and the motor task performed within the real or the virtual environment.

In the second session, subjects were exposed to the spatially congruous and spatially incongruous trials. An ANOVA was carried out to test the effect of the left-incongruous trials (see figure 3, F and G) on the performance for the left-congruous trials (see figure 3, A) and the center-incongruous and right-incongruous trials (see figure 3, D and E). In these latter two types of trials, 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 the left-incongruous trials. Though the exact 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 (neglect, controls) and the within-subjects factors were type of trial (congruous, incongruous), occurrence (before vs after), and location (left, middle, right). The interaction between group and occurrence was significant ($F_{1,5} = 14.32$, $p < 0.0001$). This interaction revealed that the neglect patients showed a significant increase in the percentage of correct left responses after having experienced the left-incongruous trials (figure 5). For the control group, the percentage of correct responses was above 90% for both congruous and incongruous trials, regardless of when they experienced the invalid left trials. The 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.

Correlation analyses between the number of left-incongruous trials preceding both left-congruous and (center and right)–incongruous trials were performed to further explore the effect of exposure to the left-

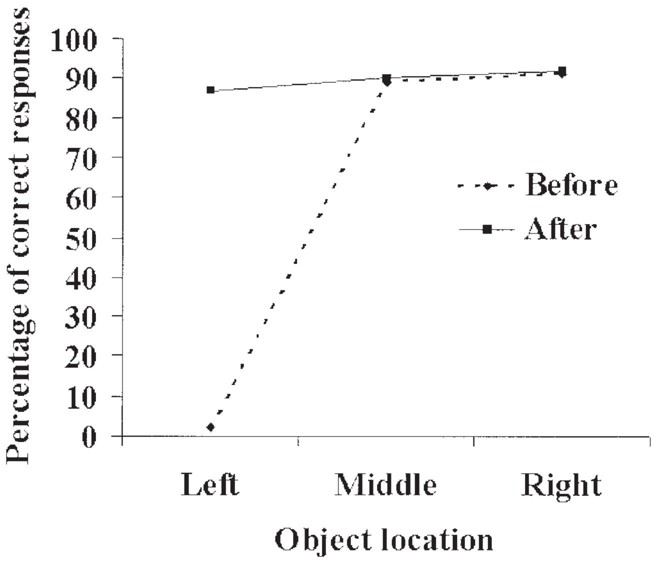

Figure 5. Graphic representation of the group × occurrence interaction. Only data from the neglect group are represented. Values for the control group were all above 90% of correct responses in all conditions.

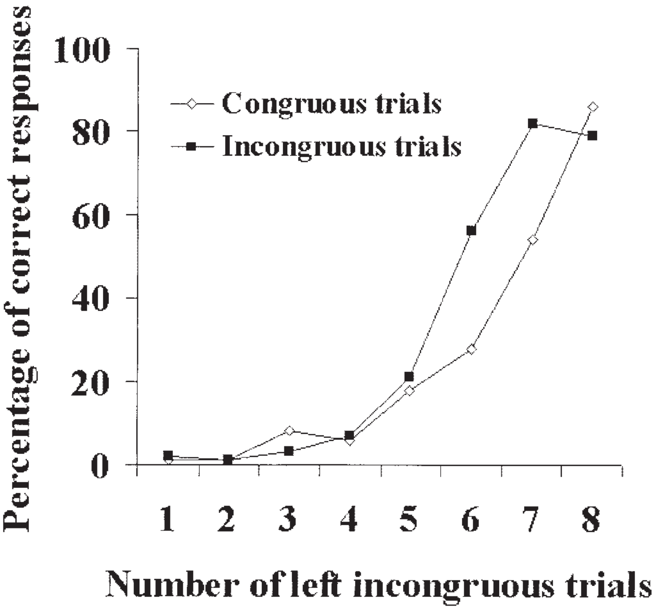

Figure 6. Graphic representation of the effects that the exposure to the left-incongruous trials had on the performance for left-congruous and right- and center-incongruous trials where a movement to the left was required.

incongruous trials on the success rate of subsequent movements toward the left space for neglect patients. The percentage of correct responses to the left for both the congruous and the incongruous trials condition increased with respect to the number of left-incongruous trials experienced by the neglect patients (figure 6). The correlation was high (congruous trials: $r = 0.76$; incongruous trials: $r = 0.78$), accounting for more than half of the variance in each case.

In a third session, patients with neglect were asked to repeat the sensory task performed in the first session within the virtual and the real space to verify that an improvement also occurred for tests that did not require a motor response. An ANOVA with session (first and third) and location (left, center, and right) as within-subjects factors was performed. Results revealed that the percentage of correct responses for the left trials was greater for the third session than for the first session ($F_{1,5} = 55.34$, $p < 0.0001$; 4 vs 80%). This suggests that exposure to left-incongruous trials also impacted the perceptual component of neglect.

Discussion. We examined the effect of VR manipulation in patients with left neglect. After being exposed to a certain number of trials in which the virtual object was located to the left within the virtual environment and the real object appeared to the right or in the middle in the real environment (i.e., left-incongruous trials), all the neglect patients were subsequently able to reach toward objects located to the portion of space of which they were previously unaware (i.e., the left hemifield). These results show an active process stimulated by VR resulting in the recalibration of visuomotor coordination and the ability to act on the organization of high levels of spatial representation such as those usually impaired in patients with visual neglect.

Although our VR manipulation may be similar to the prism adaptation technique used to rehabilitate visual neglect,[11,12] a crucial difference exists. Whereas with the prism adaptation technique, the patients adapted to an exaggerated sensorimotor bias to the right hemifield, here the patients adapted to the mismatch between the affected and the unaffected space. Therefore, it may not be appropriate to interpret the current results in relation to prism adaptation studies.

Rather, we interpret these results in the light of recent data from neuropsychology and electrophysiology. Recent neuropsychological studies have shown that similar space-remapping processes may occur in the brains of human patients when preserved and impaired portions of space are connected by means of tools.[4-8] For example, detection of visual targets in the left far space was improved when patients with severe neglect held a tool.[6] Here we extended this to show that it is not necessary for a tool to be used. The novelty of this result is that it was obtained by creating a coincidence of the movement of the real hand and the hand's virtual image, allowing us to "train" the patient to use the virtual image to guide the real hand in neglected space. This would presumably result in the formation of specific neural circuitry governing a unique mode of visuoproprioceptive integration.

Having shown that tool wielding is not necessary for improvement of performance in patients with neglect raises the question of whether our VR technique takes advantage of different mechanisms than tool wielding. In both cases, the critical factor appears to be the creation of a link between the affected and the unaffected portions of space. The underlying mechanisms of the physical extension of action space effected by tool use and the virtual extension of action space effected by our VR technique deserve further investigation.

Other researchers have used mirrors[13] and television monitors[14] with features in common with the virtual apparatus used in this study. In those studies, direct viewing of the exploring hand was prevented and congruent vs incongruent test conditions were administered. In one study,[14] patients with hemispatial neglect were asked to perform line bisection and cancellation tasks while viewing stimuli on closed circuit television under two conditions: 1) a "direct" condition that made the direction of hand movement on the workspace congruent with that on the monitor and 2) an "indirect" condition in which movement in the workspace was in the opposite direction of that seen on the monitor. These results indicated that in indirect conditions, patients were able to explore the space neglected in the direct condition. Here, we add to this by showing that space remapping does not require the patient to perceive his/her own hand within the virtual environment, but rather it is sufficient to have real-time control of the effector.

An important question is whether the improvement in the patients who took part in the current study is transient or sustained. Various rehabilitation procedures using single applications of a variety of methods (caloric stimulation, neck vibration, optokinetic stimulation) have resulted in improvements lasting only a few minutes. Conversely, prism adaptation techniques can lead to improvements ranging from 2 hours to 5 weeks.[11,12] The patients of this study were given a pause ranging from 1 to 2 hours between the crucial second VR session and the final session in which the adaptation effects were still evident. Thus, we can be quite confident that the period of improvement produced by our VR manipulation lasted at least as long as the shortest period reported following prism adaptation and longer than the few minutes reported using other techniques. This suggests that VR techniques can potentially lead to long-lasting improvements in neglect patients, although the exact length of the amelioration will require further investigation.

Our results may relate to the activity of bimodal neurons found within the intraparietal cortex.[9] It has been proposed[9] that some intraparietal neurons coding the hand can be altered in accordance with psychological modifications of the body schema. For example, when a monkey is trained to recognize the image of its hand on a video monitor, the visual receptive field of these bimodal neurons was projected onto the video screen so as to code the image of the hand as an extension of the self. The very same neurons that seemed to code the image of the hand in normal conditions also responded to the image in the video monitor. It is possible that a novel visual coordinate system was created during the training to achieve efficient movement referring only to the image on the monitor.

We suggest that following our VR manipulation, analogous neural structures may have enlarged their visual receptive fields to include the virtual hand. This then made the response to visual stimuli near the virtual hand strong, even when this was displaced into the visual field contralateral to the lesion. The integration of the virtual projection of the hand on the monitor with proprioceptive afference from the hand moving toward portions of space that were perceivably intact might have facilitated action in the neglected space. Proprioception and vision of the virtual arm may become synthesized into a new coherent link between the preserved and the neglected space that could be used to direct the action toward neglected space. This hypothesis is tentative, given that five of our six patients had evidence of parietal lobe involvement and it is unclear whether neural reorganization can take place within damaged cortical tissue. It is possible that the proposed remapping of spatial representations may depend on the activity of parietal networks located in the undamaged hemisphere. Subcortical structures such as the cerebellum may also play a role. As with other rehabilitation techniques such as prism adaptation, the cerebellum may be involved in higher-order processing.[15]

Acknowledgment

The authors thank Drs. Francesco Pavani and Angelo Maravita for their comments on the manuscript.

References

1. Halligan PW, Marshall JC. Left neglect for near but not for far space in man. Nature 1991;350:498–500.
2. Cowey A, Small M, Ellis S. Left visuospatial neglect can be worse in far than in near space. Neuropsychologia 1994;32:1059–1066.
3. Vuilleumier P, Valenza N, Mayer E, et al. Near and far visual space in unilateral neglect. Ann Neurol 1998;43:406–410.
4. Berti A, Frassinetti F. When far becomes near: remapping of space by tool use. J Cogn Neurosci 2000;12:415–420.
5. Farné A, Ládavas E. Dynamic size-change of hand peripersonal space following tool use. Neuroreport 2000;11:1645–1649.
6. Ackroyd K, Riddoch JM, Humphreys GW, Nightingale S, Townsend R. Widening the sphere of influence: using a tool to extend extrapersonal visual space in a patient with severe neglect. Neurocase 2002;8:1–12.
7. Maravita A, Clarke K, Husain M, Driver J. Active tool use with the contralesional hand can reduce cross-modal extinction of touch on that hand. Neurocase 2002;8:411–416.
8. Pegna AJ, Petit L, Caldara-Schnetzer AS, et al. So near yet so far: neglect in far or near space depends on tool use. Ann Neurol 2001;50:820–822.
9. Iriki A, Tanaka M, Obayashi S, Iwamura Y. Self-images in the video monitor coded by monkey intraparietal neurons. Neurosci Res 2001;40:163–173.
10. Damasio H, Damasio AR. Lesion analysis in neuropsychology. New York: Oxford University Press, 1989.
11. Rossetti Y, Rode G, Pisella L, et al. Prism adaptation to a rightward optical deviation rehabilitates left hemispatial neglect. Nature 1998; 395:166–169.
12. Frassinetti F, Angeli V, Meneghello F, et al. Long-lasting amelioration of visuospatial neglect by prism adaptation. Brain 2002;125:608–623.
13. Tegner R, Levander M. Through a looking glass: a new technique to demonstrate directional hypokinesia in unilateral neglect. Brain 1991; 114:943–951.
14. Na NL, Adair JC, Williamson JG, et al. Dissociation of sensory-attentional from motor-intentional neglect. J Neurol Neurosurg Psychiatry 1998;64:331–338.
15. Schmahmann JD. Dysmetria of thought: clinical consequences of cerebellar dysfunction on cognition and affect. Trends Cogn Sci 1998;2:362–371.