7 Left-to-right reversal of hemispatial neglect symptoms following adaptation to reversing prisms

F. D. Feloiu, J. J. Marotta, M. Vesia, S. E. Black and J. D. Crawford

Abstract

Damage to the right posterior parietal cortex may result in left visual-field deficits including hemispatial neglect and/or asymmetry in pointing accuracy (as in optic ataxia). It is unclear whether these disorders are due to deficits in retina-fixed or world/action-fixed coordinates. We trained parietal patients and age-matched controls to point at remembered visual targets while looking through left-right optical reversing prisms. If neglect remained fixed in retinal coordinates, reversing vision should reverse the baseline pointing patterns. However, if neglect was fixed in action coordinates, the prism task should not affect the baseline patterns. Remarkably, eight of the nine brain-damaged patients learned this task, compared to only six of the ten age-matched controls. Three right-parietal patients showed target neglect in pointing to the left, and this neglect reversed from the left to the right during prism training. These results suggest that parietal neglect (specific to our patients) remains fixed in visual coordinates rather than in motor coordinates.

Cortical Mechanisms of Vision, ed. M. Jenkin and L. R. Harris. Published by Cambridge University Press.

7.1 Introduction

In everyday life, we use vision to guide movements of the hand when we perform various tasks, such as reaching to and grasping a cup of coffee, driving a car, using a tool or working on a computer. In other words, we perform eye-hand coordination when carrying out these tasks. Although we do many of these things with ease, such seemingly simple behavior requires a complex transformation of visual information input into the appropriate coordinated motor responses of both the eyes and hands. The question of how and where this transformation is implemented in the brain is, to a large extent, unknown.

The posterior parietal cortex (PPC) is thought to be part of the "dorsal stream" of vision and is involved in processing spatial information and directing visually-guided actions (Andersen et al., 1997; Colby and Goldberg, 1999; Crawford et al., 2004; Goodale and Milner, 1992; Milner and Goodale, 1993; Jeannerod et al., 1995). Human neuroimaging techniques have been successfully used to identify regions within PPC that are activated during various tasks such as saccades and arm movements. In a functional magnetic resonance imaging (fMRI) study, Sereno et al. (2001) reported a bilateral region in the PPC that showed a contralateral topographic pattern of activations for memory-guided eye movements. In a subsequent event-related fMRI study, Connolly et al. (2003) identified a human analog of monkey's "parietal reach region", an area in the medial aspect of the PPC that responded preferentially when humans planned to point to, rather than to make a saccade to a remembered location. Medendorp and colleagues (Medendorp et al., 2003) found that the same PPC region showed contralateral topographic activations for both saccades and pointing and, furthermore, that this information in PPC was encoded and updated in a gaze-centered frame of reference.

However, these gaze-centered signals within PPC could represent either the visual stimulus (vision) or the movement command toward that stimulus (motor). Fernandez-Ruiz and colleagues (Fernandez-Ruiz et al., 2007) used a reversing prism pointing technique to test whether the gaze-centered signal in human PPC encodes the visual goal of the movement (that is, upstream from the vision-to-motor transformation) (Gottlieb and Goldberg, 1999) or the direction of the movement (downstream from this transformation) (Kalaska, 1996; Eskandar and Assad, 1999; Zhang and Barash, 2000). The authors trained healthy individuals to point in a MRI setup while looking through optical left-right reversing prisms. Without the prisms, the PPC activations were contralateral to both the visual goal and movement direction (since both were in the same visual field), in agreement with previous fMRI studies (Sereno et al., 2001; Medendorp et al., 2003). However, with the left-right reversing prisms, the activations remained contralateral to the visual goal, but were ipsilateral to the direction of movement. These results suggested that human PPC encodes visual target direction rather than movement direction. It is not known how this relates to visuospatial symptoms of parietal damage.

Disruptions within parietal lobe may lead to various parietal syndromes such as optic ataxia (misreaching), hemispatial neglect (failure to process or report information presented in the contralesional space), constructional apraxia (difficulty in drawing or constructing objects), gaze apraxia (inability to move the eyes voluntarily to objects of

interest) and akinetopsia (inability to perceive movement).

Based on neuropsychological data, two main functional regions can be distinguished within the PPC. Lesions to the right inferior parietal lobule and the temporal parietal junction may induce left unilateral neglect (Heilman et al., 2000; Marotta et al., 2003; Parton et al., 2004; Vallar and Perani, 1986), a neurological deficit involving perception, attention and/or performing actions within the left side of the subject's workspace. On the other hand, lesions to the superior parietal lobule and to the region including and surrounding the intraparietal sulcus may induce a deficit in visually guided movements (e.g., reaching, grasping, pointing) known as "optic ataxia" (Perenin and Vighetto, 1988).

Hemispatial neglect is a neurological disorder characterized by a failure to attend to, report, or represent information appearing in the visual field contralateral to the location of a brain lesion, in spite of sensory processing and visual acuity being intact for that field (Heilman et al., 2000). Neglect induces many functional debilitating effects in everyday life. For example, neglect patients may eat food only from the right side of their plate, ignore people who approach from the left, miss words from the left of the page when reading, or omit details on the left when copying pictures. It was suggested that perceptual and visuomotor deficits seen in neglect patients may be due to the patient's inability to form good structural representations of the entire object for use in visual perception and visuomotor control (Marotta et al., 2003).

Neglect is often associated with contralesional hemiplegia or hemiparesis (Bisiach and Vallar, 1988; Robertson and Marshall, 1993), which has been shown to be responsible for poor functional recovery and reduced ability to benefit from treatment of impaired motor functions (Katz et al., 1999; Pantano et al., 1996).

Some parietal neglect patients may have no apparent deficit for an isolated stimulus on the affected side. Their deficit only emerges when stimuli are presented on both sides simultaneously, in which case the previously detectable contralesional stimulus is now "extinguished" from awareness by the competing ipsilesional stimulus. This phenomenon is thought to reflect an attentional rather than sensory disorder (Baylis et al., 1993; Ward et al., 1994).

Studies have shown that hemispatial neglect is not exclusively due to lesions centered on the PPC. Neglect has been also shown to occur after lesions to the parahyppocampal region of the medial temporal lobe (Mort et al., 2003), temporal-parietal-occipital junction (Leibovitch et al., 1999), superior temporal gyrus (Karnath et al., 2001; Karnath et al., 2004), frontal lobe (Husain and Kennard, 1996) or putamen and caudate nucleus within basal ganglia (Karnath et al., 2004).

Many studies have approached the issue of separating "perceptual" components of neglect (patients could not perceive targets on the contralesional space, but were able to direct movements toward that space) from "motor" components of neglect (patients perceived targets on the contralesional space but were unable to direct movements to that space) by the use of opposition tasks, in which the perceptual and motor demands of the tasks were set in spatial opposition via, for example, a 90° angle mirror (Bisiach et al., 1995; Tegner and Levander, 1991) or an epidiascope (Nico, 1996). Although these studies show some evidence that neglect is fixed in retinal coordinates, these opposition methods are extremely incompatible tasks even for neurologically intact subjects, and the participants may give up after just a few initial attempts, therefore

biasing the results.

The present study sought to address this question: Do spatial errors in left hemispatial neglect as a result of the PPC damage arise in visual- or action-based coordinates? One way to test this question is to train left neglect patients with right posterior parietal damage due to stroke to point at left and right visual targets (dots) while looking through left-right optical reversing prisms (Fernandez-Ruiz et al., 2007, Marotta et al., 2005; Kohler, 1962; Sugita, 1996). We have recently shown that young healthy adults can rapidly learn to reverse their visual-motor transformation for pointing to remembered targets (Fernandez-Ruiz et al., 2007; Marotta et al., 2005).

The use of such prisms reverses the normal spatial relationship between the retinal stimulus and the direction of movement (Kohler, 1962; Sugita, 1996), placing the retinal stimulus in one visual hemifield and the direction of movement towards the other visual hemifield. This condition is called visual-motor dissociation task. Since the left-right reversing prisms reverse the horizontal position of an object across a vertical midline, a target whose actual position is on the left is seen on the right with prisms.

The correct pointing movement with reversing prisms to a particular left target seen on the right will be to the left, and in a closed loop condition subjects will see their hands going to the right (where the target was seen). At the beginning of the adaptation training, subjects will do the opposite. They will point to the apparent (seen) right position of the target and, having visual feedback, will see their pointing hands going to the left (away from the viewed target position) (Fernandez-Ruiz et al., 2007; Marotta et al., 2005). After the training period, the majority of the subjects were found to have learned to adapt their pointing so that they could successfully point to actual target location while looking through left-right reversing prisms. This visuomotor adaptation consisted of pointing in a direction that was opposite to the direction where the target was seen.

The reversing prism technique used in the present study differs from the opposition tasks by allowing a direct visual feedback of both the remembered target location and the pointing hand, promoting a more natural reaching behavior and adding only one new visuomotor transformation to be learned (left-right reversal), thus eliminating other possible confounding visuomotor transformations.

In the current study, if left neglect (quantified here as failure to respond/point to left targets) due to right PPC damage remains fixed in visual coordinates, the neglected targets should reverse from left (without prisms) to right (with prisms) in real space. On the other hand, if neglect remains fixed in motor coordinates, the prisms will not reverse the motor behavior. Prism-reversal training might reveal new adapted visuomotor pathways, or even help to alleviate the symptoms due to damage to these pathways, as observed in neglect patients after rightward displacing prism adaptation (Farne et al., 2002; Newport and Jackson, 2006; Rossetti et al., 1998).

In summary, using a reversing prism pointing paradigm, we investigated whether unilateral right parietal patients (with or without left neglect) could be trained to point with reversing prisms (parietal cortex would normally be required to control pointing in contra-lesional space) and, if so, what effect the reversing prism training had on the pointing pattern of neglect patients.

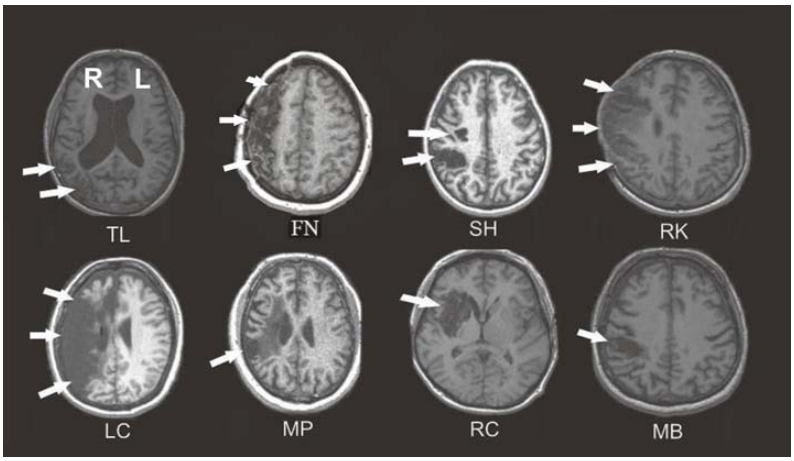

Figure 7.1. MRI imaging scans for eight of the nine patients tested. All scans confirmed that only the right hemisphere was affected by stroke, with no involvement of the left hemisphere (R = right hemisphere, L = left hemisphere, white arrows - location of the lesion(s)).

7.2 Materials and methods

Subjects Informed consent was obtained from all subjects prior to the beginning of the experiment. All procedures were approved by the York University Human Participants Review Sub-Committee and the Sunnybrook Health Sciences Centre Human Participation Ethical Review Board. We tested nine right hemisphere stroke-affected patients (all right-handed, mean age $= 55.7 \pm 13.7$ years, see Table 7.1). The lesion locations were obtained from patients' clinical charts, neurological assessments, and MRI imaging scans where available (scans for eight patients are shown in Fig. 7.1).

Patients had no right (pointing) hand sensorimotor deficits and had normal or corrected-to-normal visual acuity. Visual fields were assessed by clinical confrontation testing. The presence of hemispatial neglect was assessed using the Sunnybrook Neglect Assessment Procedure (SNAP), consisting of four sub-tests: a shape cancellation task, spontaneous drawing and copying of a clock and daisy, line bisection, and a line cancellation task (Black et al., 1990; Leibovitch et al., 1998). Depending on the total score, performance is classified either as within normal limits, or as mild or severe neglect. All stroke patients were tested in the chronic stage with a mean of seven years post-stroke.

Three of the nine patients tested were diagnosed with mild hemispatial neglect prior to the testing using the SNAP. They were classified as the "neglect group" and are described in some detail in subsequent sections.

Patient TL is a right-handed 71-year-old male who had right hemisphere ischemic strokes in July 1999 and April 2000. He was admitted to the hospital for marked confu-

Patient	Age	Gender	Location of Stroke	Time post-stroke at testing (months)	Performed Task Without Disclosure?	Performed Task After Disclosure?	Sensorimotor Deficits	Visual Field Deficits	Other Observations
T.L.	71	M	Right frontal, parietal and occipital areas.	62	Yes	-	Normal motor and sensory findings.	Left inferior quadrantanopia by clinical confrontation testing.	Mild left hemispatial neglect and optic ataxia in the baseline testing.
M.L.	67	F	Right frontal, temporal and parietal areas.	134	Yes	-	Moderate left hemiparesis and normal sensory findings.	Normal visual fields to clinical confrontation testing.	Showed mild left hemispatial neglect in the baseline testing.
F.N.	27	F	Right temporal and parietal areas.	75	Yes	-	Moderate left hemiparesis and normal sensory findings.	Normal visual fields to clinical confrontation testing.	Showed mild left hemispatial neglect in the baseline testing.
S.H.	59	M	Right frontal, temporal, parietal and supplementary motor areas.	84	No	No	Normal motor and sensory findings.	Normal visual fields confirmed by formal testing.	Very confused when pointing with prism.
R.K.	53	M	Right frontal, temporal and parietal areas.	6	Yes	-	Mild left hemiparesis and normal sensory findings.	Normal visual fields to clinical confrontation testing.	-
L.C.	56	F	Right frontal, temporal and parietal areas.	135	Yes	-	Moderate left hemiparesis and left tactile extinction.	Normal visual fields to clinical confrontation testing.	-
M.P.	63	M	Right frontal, temporal and parietal areas and right basal ganglia.	178	No	Yes	Left arm paralysis, moderate leg paresis and normal sensory findings.	Normal visual fields to clinical confrontation testing.	-
R.C.	42	M	Right frontal, temporal and parietal areas and right basal ganglia.	28	Yes	-	Left arm paralysis, moderate leg paresis and normal sensory findings.	Normal visual fields to clinical confrontation testing.	-
M.B.	64	M	Right frontal and parietal areas and thalamus.	59	Yes	-	Normal motor function and mild sensory deficits.	Normal visual fields confirmed by formal testing.	-

Table 7.1. Characteristics of the patients tested.

sion and peripheral vision problems. On admission, TL showed severe left hemispatial neglect and left hemifield deficits. CT scans taken in February 2005 showed stroke lesions involving the right parietal, right frontal and occipital areas (Fig. 7.1), with no involvement of the left cerebral hemisphere. At the time of experimental testing (October 2004), he had fully recovered (no sensorimotor deficits) except for mild residual left neglect and left inferior quadrantanopia.

Patient ML is a right-handed 67-year-old female that had a right carotid dissection in September 1993 with right middle cerebral artery infarction involving right frontal, parietal and temporal cortices and sparing deep structures. On admission, she showed significant left hemispatial neglect and anosognosia (impaired awareness of illness). The left cerebral hemisphere was not affected by stroke. She was ambulatory with a residual left hemiparesis, but at the time of the present study, showed only mild left neglect.

Patient FN, a right-handed 27-year-old female, suffered a severe right middle cerebral artery territory stroke (temporal, parietal and frontal) with hemorrhagic transformation and malignant edema in December 1998, for which she underwent a partial right temporal lobectomy and skull removal for decompression. At the time of the present testing she was ambulatory with residual hemiparesis and showed mild left hemispatial neglect.

The other 6 stroke-affected patients (RK, LC, MP, RC, SH and MB) had cortical damage that included the right parietal lobe and other non-parietal areas, such as right frontal, temporal, occipital, basal ganglia and thalamus, but in every case only the right cerebral hemisphere was affected (unilateral stroke) (see Table 7.1 and Fig. 7.1). They were not diagnosed with neglect prior to testing, and were classified as "brain-damaged controls".

We also tested 10 neurologically intact age-matched controls (all right handed, mean age = 58.2 $\pm$ 9.7 years) (Table 7.2), in order to identify whether this healthy population could perform the reversing prism task. All subjects were naïve as to the aims of the experiment.

7.3 Apparatus and procedure

We have recently showed that pointing with reversing prisms in young healthy subjects produces a rapid task-specific visuomotor adaptation (Marotta et al., 2005). Similar methods were used here. In brief, subjects' heads were stabilized and vision was obstructed by opaque goggles, except through a rectangular tube placed in front of the right eye (Fig. 7.2A). Visual stimuli were presented through the tube, in dim light, on a computer screen located 40 cm in front of the subject. Subjects were instructed to maintain visual fixation throughout the experiment on a central cross that remained on the screen at all times.

A target (5 mm dot) was presented for 500 ms at 3.2 cm (4.7° visual angle) to the left or right of the cross (Fig. 7.2B) (this was considered one trial). Subjects were instructed to point-to-touch the screen where they saw the target (therefore at the actual position of the target in space) as soon as the target was off and do this as fast and as accurately as possible. If they did it correctly, they would see their pointing index finger

Control	Age	Gender	Performed task without disclosure?	Performed task after disclosure?	Other observations
F.F.	55	M	No	No	Very confused when pointing with prism.
G.K.	46	M	Yes	-	-
T.M.	54	F	No	No	Very confused when pointing with prism.
T.F.	50	F	Yes	-	-
H.W.	57	F	No	No	Pointed to the wrong direction with prism.
I.N.	52	M	Yes	-	-
G.N.	54	F	No	Yes	-
E.L.	68	F	Yes	-	-
D.G.	71	M	No	No	Pointed to the wrong direction with prism.
S.M.	75	F	Yes	-	-

Table 7.2. Characteristics of the neurologically intact controls tested

landing where they saw the target. Six seconds were allowed for the subject to touch the remembered target location with the index finger of their right hand, and return to resting position.

Fifteen experimental blocks were run in total, each block consisting of 20 trials, 10 to the left and 10 to the right presented in random order. Two blocks were run in the baseline condition (no reversing prism). A dove reversing prism was then inserted into the viewing tube, and subjects were then required to point for an additional eleven blocks (subjects received the same initial pointing instructions). If subjects were not able to perform the reversing prism task after two of these blocks, we disclosed the nature of the task to them and then continued recording (see Tables 7.1 and 7.2 for details). Two more blocks were run at the end without prisms (recovery condition).

Pointing performance was recorded using an Optotrak recording system (Northern Digital, Inc., Waterloo, Canada; sampling rate = 200 Hz) and analyzed off-line. We used three IRED markers placed on the distal phalanx of the pointing index finger of the right hand, arranged so that we could record the position of the finger even if subjects performed pronation/supination movements during pointing.

The initial position of the hand was not visible at all, with the hand being visible starting about half way into the pointing movement. We did not select a particular starting position for the pointing hand (which was at each patient's discretion, but as close to their bodies as possible) because we did not want patients to focus on placing hand on a particular location on the table instead of focusing on performing the task properly (given the challenge of the task).

Because it was not possible to monitor eye movements with our goggle set-up, the subjects were instructed and tested "off-line" before the beginning of experimental tri-

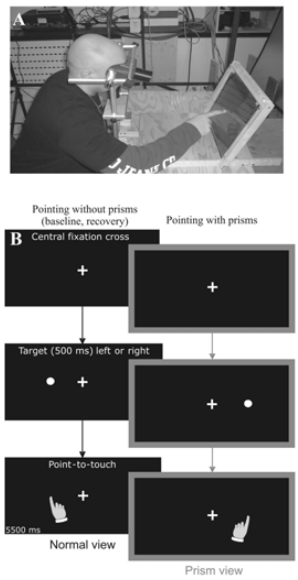

Figure 7.2. Apparatus (A) and conditions of the experiment (B). A. The goggles-chin rest setup was affixed on a custom-built, modular aluminum pipe apparatus that was firmly attached vertically to a table. The subjects were seated in an adjustable chair in front of a tabletop with their heads at the level of the goggles-chin rest setup. They looked through the tube and pointed-to-touch a computer screen that was situated within comfortable pointing distance from their body. B. Baseline and recovery conditions (left). Prism condition (prisms are worn) (right): the left target is viewed on the right, and, when pointing to the left, subjects will see the image of their hand reversed and moving in the opposite direction to where they pointed (right), and vice-versa.

als in order to ensure that they understood how to perform the task (the subjects were not, however, aware that their eyes were not monitored during the experiment). The experimenter and the subject were seated facing each other, with no other piece of equipment/setup in between. The "off-line" testing began by instructing the subjects to fixate a point located in between experimenter's eyes. The experimenter then positioned his left and right index fingers at about 20 cm to either side of the subject's fixation point. The fingers were moved briefly up and down, one at a time and in random order, without moving the hands, while the experimenter kept looking at the subjects' gaze, and the subjects were instructed to point-to-touch the experimenter's moving index finger while maintaining the fixation. The experimenter observed the subject's gaze direction during these pointing tasks, and the "off-line" testing was considered successful if the subject made five consecutive pointings without shifting their gaze. All of our subjects met this condition.

7.4 Data analyses

Pointing errors in the x (left-right) and y (up-down) directions were computed for each trial, relative to the coordinates of the two target positions. We counted the number of trials that subjects failed to point to the presented target ("neglected" trials) in each of the three conditions of the experiment.

7.5 Results

Target neglect related to our task was considered present when patients consistently failed to point (move their pointing hand) to targets presented in their contralesional visual field in the baseline condition (Heilman et al., 2000).

7.5.1 Neurologically intact controls

Half (five) of our age-matched, neurologically intact control subjects (Table 7.2) were able to rapidly learn the prism reversal task. The other half of intact controls failed to perform the prism-reversal task after two blocks of visually guided trials. The latter subjects were then informed of the nature of the prism reversal task, but still, only one additional subject was then able to perform the task. During experiments with the 4 remaining "non-learning" intact controls, we often observed that they began pointing in the wrong direction and, after the pointing hand became visible, they continued to make movements further and further in the same (wrong) direction.

7.5.2 Stroke-affected subjects

Seven of the nine stroke patients learned the prism reversal task quickly. Of the remaining two patients, one learned the task after we disclosed its nature, so only one patient (SH) was not able to learn the task (he kept pointing to the perceived location of the targets, and not to their reversed spatial location).

The "brain-damaged control group" (six subjects) did not fail to point to any target presented in their contralesional visual field in the baseline testing. Regardless of whether they learned or not how to perform the prism task, they did not fail to point to any target presented on the screen during prism training as well.

All (three) subjects in the "neglect group" failed to respond (point) to some of the trials presented in their left (contralesional) visual hemifield during baseline testing (we defined this deficit within the parameters of our task as left target neglect, see Fig. 7.3). For example, TL neglected 5% of the trials presented on the left, ML neglected 10% of trials and FN neglected 25% of them. All three subjects pointed to all targets presented in their right (ipsilesional) visual field.

The question posed was what would happen to the left inattention (specific to our task) when these three patients pointed while looking through the left-right reversing prisms, where the left targets would then be seen on the right, and the right targets would be seen on the left (subjects still had to point toward their actual location). If target neglect remained fixed in visual coordinates, reversing vision should reverse

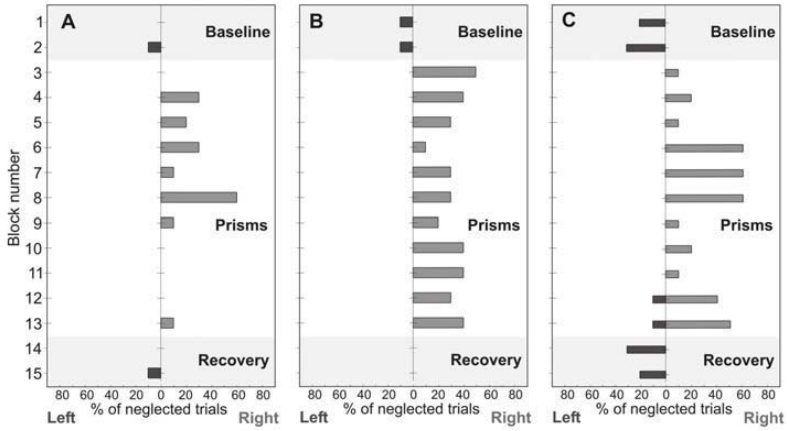

Figure 7.3. Target neglect patients' performances. These three patients (A - patient TL, B - patient ML, C - patient FN) neglected left targets in the baseline condition (darker bars), right targets in the prism condition (lighter bars) and left targets in the recovery condition (darker bars). Bars represent percentage of neglected trials in each block; horizontal axis - percentage of neglected trials; vertical axis - conditions of the experiment.

neglect to rightward-positioned targets. On the other hand, if target neglect stayed fixed in motor coordinates, then reversing the vision should not affect the subject's overt behavior.

During reversing prism training, target neglect reversed from left to right in the "neglect group": all three patients failed to respond to some targets that they viewed on the left, although they were presented on the right (ipsilateral to the lesion) (Fig. 7.3). TL neglected 15.45%, ML 32.72% and FN 31.81% of the right-positioned targets. TL and ML did not neglect any of the left targets with prisms, and FN neglected only two (out of 110). There was an increase in the percentage of overall neglected trials for each patient during prism training compared to trials neglected in the baseline condition; the increase was from 5% to 15.45% for TL, from 10% to 32.72% for ML and from 25% to 31.81% for FN.

In the recovery condition, the left/right neglect pattern reversed again in the "neglect group": TL and FN failed to point to some targets presented only on the left (5% and 25% of the trials, respectively). ML did not neglect any targets in the recovery condition.

7.6 Discussion

Our three right parietal patients diagnosed pre-testing with mild left neglect showed signs of some type of left neglect in the baseline condition, defined in relation to our task as target neglect (i.e., they consistently failed to point toward some of the leftward targets). This type of left neglect reversed to the right with prisms and then it reversed back to the left when the prisms were taken off. These results support the hypothesis that target neglect (related to our task) obeys visual coordinates rather than motor coordinates.

A remarkable observation is the high capacity of our "recovered" unilateral parietal patients – in particular our brain-damaged controls with extensive lesions including much of the right cerebral hemisphere – to accurately perform this particular memory-guided pointing task. How could patients with so much brain damage be similar to age-matched controls at performing/learning the prism task? The answer may be in the nature of the mechanisms required to point with reversing prisms. To do this task, the subjects must learn to reverse the feed-forward motor command, based on the visual information and memory of performance in previous trials (Marotta et al., 2005). They must also ignore direct visual feedback from the hand during pointing, because it (being reversed) provides inappropriate information to guide the hand. We did not consistently observe problems with this in our previous study, which employed young adult subjects (Marotta et al., 2005), but it is thought that older adults (like those used here) may differ in their use of visual feedback (Collins et al., 1995; Baugh and Marotta, 2007). If some of our neurologically intact subjects were unable to disengage the use of (inappropriate) visual feedback during the prism task, this would account for the anti-corrective movements that we observed in subjects who failed to learn the task. On the other hand, parietal cortex is thought to be an important target for these visual feedback signals (Pisella et al., 2000; Prablanc et al., 2003). Thus, it is possible that in parietal-damaged patients the visual control may be compromised, which in this special case - pointing with reversing prisms – could be an advantage.

Anti-pointing paradigms may also seem to produce a left-right reversal in visuomotor coordinates. However, reversing prism tasks and anti-pointing tasks are different. In anti-pointing task, subjects are instructed to point in a direction opposite to the perceived location of the target (Connolly et al., 2000; DeSouza et al., 2003; Hallett, 1978). The motor command produces a congruent corollary discharge, because subjects see the pointing hands (vision) going to the same direction where the motor commands were (motor). Moreover, anti-pointing does not alter subjects' perception of the target (Fischer and Weber, 1992). In contrast, in reversing prism pointing task, the subjects are not given any specialized instructions, but to point where the target was. The motor command with prisms produces an incongruent corollary discharge, because the subjects see the pointing hands (vision) going to the opposite direction where the motor commands were (motor) (dissociation between vision and proprioception). Reversing prism pointing task provides direct visual feedback of pointing errors and affects perception.

The apparent increase in the number of neglected trials in the prism condition compared to trials neglected in the baseline condition may be due to a phenomenon similar to extinction, or it could be due to the increased difficulty of the prism task and subse-

quent shift of attentional resources. In contrast to neglect, extinction is defined as the inability to process or attend to the more contralesionally located stimulus when two stimuli are simultaneously presented (Rapcsak et al., 1987). Mattingley et al. (1997) showed that extinction can occur with two simultaneous stimuli from different sensory modalities (one visual and the other one tactile). In our study, in the prism condition, for pointing to right targets, the visual goal was on the left (contralesional) hemifield, and the required motor command was towards right (ipsilesional) space. The two "stimuli" (left-viewed target and right motor command) were not presented simultaneously per se. But, because of the nature of the prism task, some phenomenon similar to extinction may have occurred: the two stimuli may have competed with each other, resulting in the "extinction" of the stimulus located in the left (contralesional) visual hemifield (visual goal). Without a visual goal, there was no subsequent pointing movement (to the right).

Although we could not monitor subjects' eye movements during experiment (which would have been ideal), it is less likely that eye movements would change the results significantly due to the nature of the neglect itself. Subjects with left neglect will ignore stimuli presented on their left visual field even when they are allowed full head and eye movements. Therefore, we consider that lack of fixation would not influence the results.

Visual field deficit may be a confounding factor in this experiment, as patient TL was diagnosed with left inferior quadrantanopia prior to testing. Patients with this condition will not see/perceive all targets presented on a fixed area within their left visual hemifield, area that has the same spatial location relative to patient's gaze. In our experiment, had it been an overlap between TL's left quadrantanopic field and the location of left targets, TL should not have been able to perceive all left targets. However, all baseline leftward targets were presented on the same left location with respect to his gaze and he did not perceive only some (not all) of them. Therefore, it seems that the omitted baseline targets on the left in patient TL were due to some form of neglect rather than due to left visual field loss.

In short, our results from the prism task suggest quite clearly that this form of neglect remained fixed in visual coordinates. Of course, this is a very special type of neglect: we cannot directly conclude that all types of neglect that have been tested experimentally and clinically (Behrmann and Tipper, 1999) would show the same reversal. Further studies are warranted regarding this issue.

Acknowledgments

The authors would like to thank subjects for their kind participation in the experiments, as well as the Heart and Stroke Foundation Centre for Stroke Recovery for infrastructure support, Valerie Closson for help with recruiting subjects, Farrell Leibovitch and Fuqiang Gao for help with preparing the brain images, Gerald Keith, Farshad Farshadmanesh and Alina Constantin for their help with experiments and data analyses, Aarlenne Khan for help and comments on the manuscript, and Saihong Sun for help with technical programming. This work was supported by grants from the Canadian Institute of Health Research (CIHR) and Ontario Graduate Scholarship in Science and

Technology (OGSST). JDC holds a Canada Research Chair.

References

Andersen, R. A., Snyder, L. H., Bradley, D. C. and Xing, J. (1997). Multimodal representation of space in the posterior parietal cortex and its use in planning movements. *Ann. Rev. Neurosci.*, 20: 303–330.

Baylis, G. C., Driver, J. and Rafal, R. D. (1993). Visual extinction and stimulus repetition. *J. Cogn. Neurosci.*, 5: 453–466.

Baugh, L. A. and Marotta, J. J. (2007). Differential effects of aging on a visuomotor paradigm. Society for Neuroscience 397.16. Washington, DC: Society for Neuroscience.

Behrmann, M. and Tipper, S. P. (1999). Attention accesses multiple reference frames: Evidence from visual neglect. *J. Exp. Psychol.. Hum, Percept. Perf.*, 25: 83–101.

Bisiach, E. and Vallar, G. (1988). Hemineglect in humans. In F. Boller and J. Grafman (Eds.) *Handbook of neuropsychology, Vol. 1.*, Amsterdam: Elsevier, pp. 195–222.

Bisiach, E., Tegner, R., Ladavas, E., Rusconi, M. L., Mijovic, D. and Hjaltason, H. (1995). Dissociation of ophthalmokinetic and melokinetic attention in unilateral neglect. *Cerebral Cortex*, 5: 439–447.

Black, S. E., Vu, B., Martin, D. K. and Szalai, J. P. (1990). Evaluation of a bedside battery for hemispatial neglect in acute stroke. *J. Clinical and Exp. Neuropsychol.*, 12: 109.

Colby, C. L. and Goldberg, M. E. (1999). Space and attention in parietal cortex. *Ann. Rev. Neurosci.* 22: 319–349.

Collins, J. J., De Luca, C. J., Burrows, A. and Lipsitz, L. A. (1995). Age-related changes in open-loop and closed-loop postural control mechanisms. *Exp. Brain Res.*, 104: 480–492.

Connolly, J. D., Goodale, M. A., DeSouza, J. F., Menon, R. S. and Vilis, T. (2000). A comparison of frontoparietal fMRI activation during anti-saccades and anti-pointing. *J. Neurophysiol.*, 84: 1645–1655.

Connolly, J. D, Andersen, R. A. and Goodale, M. A. (2003). FMRI evidence for a 'parietal reach region' in the human brain. *Exp. Brain Res.*, 153: 140–145.

Crawford, J. D., Medendorp, W. P. and Marotta, J. J. (2004). Spatial transformations for eye-hand coordination. *J. Neurophysiol.*, 92: 10–19,

DeSouza, J. F., Menon, R. S. and Everling, S. (2003). Preparatory set associated with pro-saccades and anti-saccades in humans investigated with event-related FMRI. *J. Neurophysiol.*, 89: 1016–1023.

Eskandar, E. N. and Assad, J. A. (1999). Dissociation of visual, motor and predictive signals in parietal cortex during visual guidance. *Nature Neurosci.*, 2: 88–93.

Farne, A., Rossetti, Y., Toniolo, S. and Ladavas, E. (2002). Ameliorating neglect with prism adaptation: Visuo-manual and visuo-verbal measures. *Neuropsychologia*, 40: 718–729.

Fernandez-Ruiz, J., Goltz, H. C., DeSouza, J. F., Vilis, T. and Crawford, J. D. (2007). Human parietal "reach region" primarily encodes intrinsic visual direction, not extrinsic movement direction, in a visual-motor dissociation task. *Cerebral Cortex*, 17: 2283–2292.

Fischer, B. and Weber, H. (1992). Characteristics of "anti" saccades in man. *Exp. Brain Res.*, 89: 415–424.

Goodale, M. A. and Milner, A. D. (1992). Separate visual pathways for perception and action. *Trends Neurosci.*, 15: 20–25.

Gottlieb, J. and Goldberg, M. E. (1999). Activity of neurons in the lateral intraparietal area of the monkey during an antisaccade task. *Nature Neurosci.*, 2: 906–912.

Hallett, P. E. (1978). Primary and secondary saccades to goals defined by instructions. *Vision Res.*, 18: 1279–1296.

Heilman, K. M., Valenstein, E. and Watson, R. T. (2000). Neglect and related disorders. *Seminars in Neurology*, 20: 463–470.

Husain, M. and Kennard, C. (1996). Visual neglect associated with frontal lobe infarction. *J. Neurol.*, 243: 652–657.

Jeannerod, M., Arbib, M. A., Rizzolatti, G. and Sakata, H. (1995). Grasping objects: The cortical mechanisms of visuomotor transformation. *Trends Neurosci.*, 18: 314–320.

Kalaska, J. F. (1996). Parietal cortex area 5 and visuomotor behavior. *Can. J. Physiol. Pharmacol.*, 74: 483–498.

Karnath, H. O., Ferber, S. and Himmelbach, M. (2001). Spatial awareness is a function of the temporal not the posterior parietal lobe. *Nature*, 411: 950–953.

Karnath, H. O., Fruhmann Berger, M., Kuker, W. and Rorden, C. (2004). The anatomy of spatial neglect based on voxelwise statistical analysis: A study of 140 patients. *Cerebral Cortex*, 14: 1164–1172.

Katz, N., Hartman-Maeir, A., Ring, H. and Soroker, N. (1999). Functional disability and rehabilitation outcome in right hemisphere damaged patients with and without unilateral spatial neglect. *Archives Physical Medicine and Rehabilitation*, 80: 379–384.

Kohler, I. (1962). Experiments with goggles. *Sci. Am.*, 206: 62–72.

Leibovitch, F. S., Black, S. E., Caldwell, C. B., Ebert, P. L., Ehrlich, L. E., Szalai, J. P. (1998) Brain-behavior correlations in hemispatial neglect using CT and SPECT: The sunnybrook stroke study. *Neurol.*, 50: 901–908.

Leibovitch, F. S., Black, S. E., Caldwell, C. B., McIntosh, A. R., Ehrlich, L. E. and Szalai, J. P. (1999). Brain SPECT imaging and left hemispatial neglect covaried using partial least squares: The sunnybrook stroke study. *Human Brain Mapping*, 7: 244–253.

Marotta, J. J., Keith, G. P. and Crawford, J. D. (2005). Task-specific sensorimotor adaptation to reversing prisms. *J, Neurophysiol*., 93: 1104–1110.

Marotta, J. J., McKeeff, T. J. and Behrmann, M. (2003). Hemispatial neglect: Its effects on visual perception and visually guided grasping. *Neuropsychologia*, 41: 1262–1271.

Mattingley, J. B., Driver, J., Beschin, N. and Robertson, I. H. (1997). Attentional competition between modalities: Extinction between touch and vision after right hemisphere damage. *Neuropsychologia*, 35: 867–880.

Medendorp, W. P., Goltz, H. C., Vilis, T. and Crawford, J. D. (2003). Gaze-centered updating of visual space in human parietal cortex. *J. Neurosci*., 23: 6209–6214.

Milner, A. D. and Goodale, M. A. (1993). Visual pathways to perception and action. *Progress in Brain Res*., 95: 317–337.

Mort, D. J., Malhotra, P., Mannan, S. K., Rorden, C., Pambakian, A., Kennard, C. and Husain, M. (2003). The anatomy of visual neglect. *Brain*, 126: 1986–1997.

Newport, R. and Jackson, S. R. (2006). Posterior parietal cortex and the dissociable components of prism adaptation. *Neuropsychologia*, 44: 2757–2765.

Nico, D. (1996). Detecting directional hypokinesia: The epidiascope technique. *Neuropsychologia*, 34: 471–474.

Pantano, P., Formisano, R., Ricci, M., Di Piero, V., Sabatini, U., Di Pofi, B., Rossi, R., Bozzao, L. and Lenzi, G. L. (1996) Motor recovery after stroke. morphological and functional brain alterations. *Brain*, 119: 1849–1857.

Parton, A., Malhotra, P. and Husain, M. (2004). Hemispatial neglect. *J. Neurol., Neurosurgery, and Psychiatry*, 75: 13–21.

Perenin, M. T. and Vighetto, A. (1988). Optic ataxia: A specific disruption in visuomotor mechanisms. I. Different aspects of the deficit in reaching for objects. *Brain*, 111: 643–674.

Pisella, L., Grea, H., Tilikete, C., Vighetto, A., Desmurget, M., Rode, G., Boisson, D. and Rossetti, Y. (2000). An 'automatic pilot' for the hand in human posterior parietal cortex: Toward reinterpreting optic ataxia. *Nature Neurosci*., 3: 729–736.

Prablanc, C., Desmurget, M. and Grea, H. (2003). Neural control of on-line guidance of hand reaching movements. *Progress Brain Res*., 142: 155–170.

Rapcsak, S. Z., Watson, R. T. and Heilman, K. M. (1987). Hemispace-visual field interactions in visual extinction. *J. Neurol., Neurosurgery, and Psychiatry*, 50: 1117–1124.

Robertson, I. H. and Marshall, J. C. (1993). *Unilateral Neglect: Clinical and Experimental Studies*. Hove, UK: Lawrence Erlbaum.

Rossetti, Y., Rode, G., Pisella, L., Farne, A., Li, L., Boisson, D. and Perenin, M.-T. (1998). Prism adaptation to a rightward optical deviation rehabilitates left hemispatial neglect. *Nature*, 395: 166–169.

Sereno, M. I., Pitzalis, S. and Martinez, A. (2001). Mapping of contralateral space in retinotopic coordinates by a parietal cortical area in humans. *Science*, 294: 1350–1354.

Sugita, Y. (1996). Global plasticity in adult visual cortex following reversal of visual input. *Nature*, 380: 523–526.

Tegner, R. and Levander, M. (1991). Through a looking glass. A new technique to demonstrate directional hypokinesia in unilateral neglect. *Brain*, 114: 1943–1951.

Vallar, G. and Perani, D. (1986). The anatomy of unilateral neglect after right-hemisphere stroke lesions. A clinical/CT-scan correlation study in man. *Neuropsychologia*, 24: 609–622.

Ward, R., Goodrich, S. and Driver, J. (1994). Grouping reduces visual extinction: neuropsychological evidence for weight-linkage in visual selection. *Vis. Cognit.*, 1: 101–129.

Zhang, M. and Barash, S. (2000). Neuronal switching of sensorimotor transformations for antisaccades. *Nature*, 408: 971–975.