Impairment of Gaze-centered Updating of Reach Targets in Bilateral Parietal–Occipital Damaged Patients

Recent studies have suggested that internal updating of visuospatial targets in humans occurs in gaze-centered coordinates and takes place in the parietal and extrastriate cortices. We explored how information for reaching is updated in two patients with bilateral lesions in these areas. Subjects performed two visuomotor tasks: (i) a fixation reaching task, which began with the appearance of one of five fixation positions (varying eye positions) followed by a central reaching target. Subjects reached to the target while fixating on the presented fixation position (relative to gaze the target was always presented in the periphery); and (ii) a saccade reaching task, in which subjects fixated on the central reaching target, then made a saccade to the presented fixation position before reaching to the central target. In both tasks, subjects reached to targets after a 500 or 5000 ms delay. Gaze-centered updating predicts similarities in reaching errors between fixation and saccade trials. Control subjects showed evidence for gaze-centered updating during both 500 and 5000 ms delay conditions. In contrast, patient AT, who had extensive occipital–parietal damage, only showed signs of gaze-centered representation after 5 s. Patient IG, with a more focal lesion in the parietal cortices, showed partial updating in gaze-centered coordinates when reaching with the small memory delay but recovered a complete gaze-centered representation after the longer delay. This suggests that patients with bilateral occipital–parietal lesions may rely on non-gaze-centered frames to store immediate target locations in reaching space but, given enough time, this information may be rerouted to access other gaze-centered motor cortical mechanisms.

Keywords: eye-centered coordinates, eye–hand coordination, optic ataxia, posterior parietal cortex, reference frames, visual updating

Introduction

We are constantly interacting with the visual environment; for example, we point, reach for and handle objects. To do this successfully, our brains need to coordinate our hands/arms with what we see through our eyes. In particular, the brain needs to transform visual information about object location from gaze-centered (retinal) coordinates into coordinates for the arm (Soechting et al., 1991, 1995; Flanders et al., 1992). However, this gaze-centered information entering our brain does not remain constant, but rather changes often. This is mostly due to eye movements known as saccades, which constantly change the position of objects on the retina. Therefore, to keep a stable representation of an object’s spatial location, the brain must update such a representation after each saccade (reviewed in Pisella and Mattingley, 2004).

In a head-centered frame, the location of an object is represented relative to the head by calculating the location of the object relative to the eye and the position of the eye relative to the head (Zee et al., 1976; Henriques et al., 1998). Once calculated thus, an eye movement would not change the location of the targets represented in this frame. Similar mechanisms could be used to calculate target directions in body or space coordinates (Soechting et al., 1991, 1995; Flanders et al., 1992).

However, behavioural studies in normal subjects suggest that information about the spatial location of objects for reaching and pointing in both near and far space are updated or remapped in retinal coordinates (Henriques et al., 1998; Medendorp and Crawford, 2002; Pouget et al., 2002). In a retinal coordinate system, objects in space are represented in a frame that is centered on current gaze direction. Thus, the location of objects represented in this frame changes with every eye movement and so their representations must be internally updated by rotating them in opposition to the saccade (Henriques et al., 1998).

Some studies have suggested that such gaze-centered updating may occur in the posterior parietal cortex (PPC); specifically, fMRI investigations have suggested that a similar gaze-centered updating mechanism exists for both saccades and pointing movements in the human PPC (Medendorp et al., 2003; Merriam et al., 2003). This area is extensively involved in eye–hand coordination tasks and contains gaze-centered maps of object locations for saccades and reaching in the monkey (Snyder et al., 1997; Batista et al., 1999; Colby and Goldberg, 1999). Moreover, single-unit recordings have shown that when an eye movement brings the spatial location of a recently flashed stimulus into the receptive field of a neuron in the parietal cortex, it responds to the memory trace of that stimulus, i.e. the neuron updates the position of the stimulus relative to the eye movement (Colby et al., 1995). Recent findings have also suggested that extrastriate visual areas such as area V3 are involved in updating visual information in gaze-centered coordinates (Nakamura and Colby, 2002).

The purpose of this study was to determine whether gaze-centered updating for reaching movements is impaired in patients with bilateral parietal and parietal/occipital damage. Previous studies have shown that patients with lesions in the parietal cortex (patients with neglect) are unable to update the location of targets for saccades [Duhamel et al., 1992 (lesions included parietal cortex); Heide and Komps, 1997]. We tested if damage to the PPC (superior parietal damage) also reduces the reliance on gaze-centered updating for reaching and if a delay...
imposed before the motor action — shown previously to assist visuomotor processing in parietal-damaged patients with optic ataxia (Milner et al., 1999, 2001, 2003; Revol et al., 2003; Rossetti et al., 2004; review: Rossetti et al., 2003) — could aid in updating visual information in gaze-centered coordinates.

We tested for gaze-centered updating by comparing reaching errors during two visuomotor tasks (Fig. 1). The first — fixation task (Fig. 1A) — tested reaching errors to a peripherally viewed target. Previous studies have shown that during this task, neurologically intact subjects typically overshoot the target when reaching for it (Fig. 1C). This is known as the retinal exaggeration effect (Bock, 1986; Henriques et al., 1998; Medendorp and Crawford, 2002; Pouget et al., 2002; Poljac and van den Berg, 2003). Reaching errors during this fixation task were then compared with reaching errors to the second — saccade — task. In this saccade task (Fig. 1B), subjects viewed a target foveally before making a saccade away from the target and then reaching to it. The gaze-centered updating model predicts that reaching errors in both tasks should co-vary because the target representation would be updated toward the retinal periphery in the saccade task (Fig. 1D). Thus, when subjects reach for the target using this updated representation, they should reach just like they do when they view the target peripherally, i.e. with the same retinal exaggeration effect seen in the fixation task. On the other hand, if the target representation is stored in a frame that does not move with the eye (e.g. head, body or space coordinates), one predicts that the reaching errors during the saccade task would be independent of subsequent eye movements, i.e. they would not co-vary with the reaching errors shown during the fixation task.

Materials and Methods

Subjects

Two patients with parietal lobe lesions were tested. These patients often show difficulties in making correct reaching and grasping movements to targets viewed in peripheral vision (Balint, 1909; Jeannerod, 1986; Perenin and Vighetto, 1988; Jakobson et al., 1991; Revol et al., 2003; Rossetti et al., 2003). In the present study only (rare) patients with bilateral lesions were tested.

The first patient, IG, is a right-handed, 34-year-old female who shows specific problems with visually guided movements (bilateral optic ataxia) without neglect, nor any somatosensory or visual deficits. An ischemic stroke resulted in the blockage of the posterior cerebral arteries causing lesions involving mainly Brodmann’s area 7 and 39 almost symmetrically in both hemispheres (Fig. 2A). She has some damage to superior occipital areas (Brodmann’s areas 18 and 19, leaving the human equivalent of V3a intact), but most of the damage is limited to the parietal cortex. IG shows no somatosensory or visual deficits except for a small scotoma in the lower right visual field (Pinella et al., 2000). Simultanagnosia was also initially present in IG (Pinella et al., 2000). She has visually guided reaching movements that are comparable to normal subjects for targets presented foveally, but exhibits impairments for on-line modification of goal-directed movements in response to a change of the goal occurring during or before movement execution (Pinella et al., 2000; Milner et al., 2001, 2003; Grèga et al., 2002; Rossetti et al., 2004); however, her reaching and grasping are inaccurate in her peripheral vision, with a slightly greater inaccuracy for her right hand in her right peripheral field (Pinella et al., 2000).

The second patient, AT, is a right-handed, 47-year-old female with extensive lesions in both parietal lobes as well as the superior occipital lobes (V3A) which resulted from an eclamptic attack with consequential hemorrhagic softening near both posterior cerebral arteries (Jeannerod et al., 1994). MRI images showed damage involving Brodmann’s areas 18, 19, 39 and 7 (Fig. 2B), but sparing V1, V2, V3 ventrally and V5 bilaterally (Michel and Henaff, 2004). These lesions, in addition to lesions in the parietal cortex, resulted in severe visuomotor deficits (bilateral optic ataxia). Perimetric examinations reveal a normal visual field (and vision) except for a small scotoma in the right lower visual field (Michel and Henaff, 2004). Extensive tests with AT suggest that she may have some degree of simultanagnosia involving covert attention; however, her passive attention, required in this task, is normal (for details see Michel and Henaff, 2004). Figure 2C shows traces of the damaged areas from both patients on one brain. The highlighted areas in grey show the damaged areas in patient IG, whereas the highlighted areas in black show the damaged areas in patient AT.

A group of five right-handed neurologically intact subjects whose ages ranged from 26 to 33 years (mean ± SD = 29.2 ± 2.77) were also tested. Four of the subjects were naive to the goal of the study. All subjects (including patients) gave informed consent to participate in the experiment according to French law (4 March 2002) on subjects’ rights.

Apparatus and Procedure

Figure 3 shows the set-up of the experimental device. Subjects were seated in front of a horizontal table on which they performed their reaching movements (Fig. 3A) using their right hand. The subject’s head was fixed using a chin rest vertically aligned with the 0° fixation and reaching targets. A light-emitting diode (LED) target array was located above the table and was projected onto it using a half-reflecting mirror. The mirror allowed subjects sight of their hand at the beginning of each trial [known to improve reaching accuracy (Prablanc et al., 1979; Rossetti et al., 1994; Vindras et al., 1998)] but not during the trial itself. The target array consisted of five fixation lights (open circles) located at 24° left, 12° left, 0°, 12° right and 24° right from the subject’s eyes at a distance of 39 cm from the subject’s torso (Fig. 3B). Additionally three reaching targets (filled circles) were located at 12° left, 0° and 12° right, slightly below the fixation lights. The starting hand position was aligned
with these targets and was located 17 cm away from the subject’s torso (see Fig. 3B).

Reaching movements were recorded using an Ascension Flock of Bird’s (Vermont, USA) magnetic tracking system. The position of a receiver attached to the right index finger of the subject (sampling frequency = 144 Hz) was measured relative to a transmitter located off-center on the table (1.2 m range, 1.8 mm accuracy) in millimetres and converted to degrees using standard trigonometry.

Horizontal eye movements were recorded binocularly through an electro-oculogram (EOG) using a DC electro-oculograph system (sampling frequency: 50 Hz). To measure horizontal eye movements, electrodes are placed outside the left and right eye. A horizontal rotation of the eye results in a difference of potential between the two electrodes (Malmivuo and Plonsey, 1995). Eye movements were monitored for both patients and four of the five control subjects; the fifth control’s eye movements were monitored online but not recorded due to technical problems. At the beginning of each trial, subjects fixated on their hand at center and the EOG signal was set to 0 volts (meaning no difference in potential between the two eyes). Any horizontal movement thereafter would be recorded as a deviation from 0 either in negative or positive voltage depending on the direction of the movement. During the task, all subjects’ eye movements were monitored to confirm that they were performing the task correctly. Immediately following the completion of each trial, we confirmed that after the appropriate eye movement, fixation was held for the remainder of the trial (important for the delayed condition). If any eye movement occurred or if the trial was performed incorrectly for any reason, the trial was repeated.

Subjects were tested in complete darkness using two paradigms. Every trial in both paradigms began with the illumination (3000 ms) of an LED signalling the finger’s start position (see Fig. 3B). Subjects fixated and placed their finger at the viewed location of the LED. The first paradigm — the fixation task (Fig. 1A) — was as follows: one of the five fixation lights (open circles in Fig. 3B) was illuminated for 3000 ms and subjects were required to fixate on it. After 2000 ms, a reaching target (closed circles) was illuminated for 1000 ms. Subjects were asked to saccade from the finger’s start position to the fixation target as soon as they saw it and then to hold their fixation at that location. They were asked not to make a saccade to the reaching target but to continue maintaining gaze on the fixation light. After both LEDs were extinguished and they heard an auditory tone, they reached to the remembered location.
location of the reaching target while continuing to maintain their gaze on the remembered location of the fixation light. The second paradigm — the saccade task (Fig. 1B) — began with an illuminated reaching target (closed circle) for 2000 ms followed by a fixation light (open circle) for 1000 ms. Subjects were asked to first saccade to the reaching target as soon as it was illuminated and then saccade again to the subsequently illuminated fixation light. After the extinction of the fixation light and the auditory tone, they were to reach toward the remembered location of the reaching target while maintaining their gaze on the remembered location of the fixation light. Both paradigms were performed in two conditions, an immediate condition, where the auditory tone sounded right after both LEDs were extinguished (500 ms), and a delayed condition, where the auditory tone sounded after 5000 ms. Fixation lights were presented in a block design in a (left-right-left sequence or vice versa). Each session began with one set of fixation trials (immediate and delayed condition), followed by two sets of saccade trials (both conditions) and a final set of fixation trials (both conditions), with 12 trials per condition/paradigm. Control subjects took part in only one session, whereas the patients each took part in two sessions (IG’s sessions were 2 months apart and AT’s sessions were 1 month apart). For patient IG, mean test-retest reliability for errors across all trials, i.e. static and dynamic trials for immediate and dynamic conditions, was 88.7% (max = 97.58%, min = 81.72%). For patient AT, the test-retest reliability was 92.08% (max = 97.45%, min = 86.69%). For subsequent analysis, data were pooled across the two sessions. In 80% of the trials (in both paradigms), the center-reaching target was illuminated, whereas in the remaining 20%, either the 12° left or the 12° right reaching target was illuminated. These trials served as catch trials to ensure that subjects were reaching toward the visual targets they saw rather than making identical arm movements across the trials. All catch trials as well as the subsequent trials (to account for influence of the previous catch trial) were removed from the analysis to ensure that only reaching to the center target was analyzed. An additional session of only fixation trials with the three reaching targets was performed on the patients and controls to test whether errors were in retinal or non-retinal coordinates (see Reaching Errors in Retinal versus Non-retinal Coordinates).

Eye Movement Analysis

The EOG system measures eye movements by recording the difference in electrical signals (difference in potential between the cornea and the retina) between the two eyes and these signals are somewhat variable due to a number of factors, e.g. variable corneoretinal potential, muscle artefacts and the nonlinearity of the method (Malmivuo and Plonsey, 1995). These factors make it very difficult to accurately measure the actual size of the eye movement. However, EOG does provide the timing of saccades and fixations and rough (relative) measure of their actual size of the eye movement. However, EOG does provide the timing of saccades and fixations and rough (relative) measure of their amplitudes. Therefore, the EOG data were examined offline to ensure that all subjects were performing the tasks as directed, using the following criteria.

First, the time at which the eye movement toward the fixation light began was compared between a typical control and the two patients during the fixation task. Figure 4 shows sample eye movement data recorded from the EOG system for a typical control, IG and AT, showing five typical movements made by each subject during the immediate fixation trials. The figure shows that the timing of eye movements was similar between the control and the patients. We found that the patients began their eye movements on average −75 ms after the control subject [e.g. mean start time for eye movement for immediate static condition: controls (mean = 205.2 ms, min = 108, max = 398), IG (mean = 291.1 ms, min = 147, max = 452), AT (mean = 295.2 ms, min = 155, max = 454)]. The reason for the relatively quick eye movements for all subjects is likely because of the blocked nature of the trials which allowed subjects to anticipate the next trial.

Second, we confirmed that all eye movements occurred in the correct direction for the fixation light. Additionally, to ensure that the subjects did not take longer to make eye movements during the delayed trials, the beginning and end eye movement times for the immediate and delayed conditions were compared within each patient and one representative control for the fixation task. There were no significant differences between the two conditions for any of the three subjects (t-test, P > 0.05).

Results

Fixation Task — Control Subjects

Figure 5A depicts reaching trajectories and 95% confidence ellipse fits to end points for one representative control subject for each of the five fixation targets during the immediate fixation condition. The reaching target was always straight-ahead in space coordinates, but eye position/fixation position (top row) varied from 24° right (leftmost panel) to 24° left (rightmost panel). The subject slightly but systematically undershot the target in depth for all eye positions, as did all controls but one. The subject was more consistent in estimating the horizontal position of the target than its depth, as is evident by the long, narrow, 95% confidence ellipses. More importantly, the subject varied her reaching systematically with the fixation target. She overestimated the horizontal location of the reaching target in gaze-centered coordinates (she reached too far to the left in panel 1 and too far to the right in panel 5). This was true for all five control subjects (each subject’s confidence ellipses are shown in Fig. 5B). All controls showed a similar overshoot in the horizontal axis in delayed reaching (Fig. 5C). Across both the immediate and delayed condition, the 95% confidence ellipses showed that controls tended to be more consistent in horizontal reaching (be it with a systematic overshoot) than in depth. Data from the controls were analyzed by comparing the range (max−min) of left-right errors to those in depth. In the immediate condition (Fig. 5B), the analysis revealed a significantly smaller range (P < 0.05) in the horizontal axis for all controls except one who showed a smaller range of
errors in horizontal axis for all fixation positions except for one (12° right fixation). In the delayed condition (Fig. 5C), the analysis revealed a significantly smaller range ($P < 0.05$) in the horizontal axis for four of the five controls.

These results support those of previous studies that similarly found this retinal exaggeration effect (Bock, 1986; Henriques et al., 1998; Medendorp and Crawford, 2002; Pouget et al., 2002; Poljac and van den Berg, 2003).

### Fixation Task — Patient IG (Bilateral Parietal Lobe Lesions)

The same task was performed on the two patients to evaluate their ability to reach toward a remembered visual target and its dependence on eye position. Figure 6 shows reaching trajectories (Fig. 6A) and endpoints (Fig. 6B) for patient IG during the immediate fixation condition. In contrast to the controls, IG made greater variable errors in reaching (control = $-0.523 \pm 2.888^\circ$; IG = $-0.847 \pm 4.69^\circ$). IG did not show any undershoot in depth and demonstrated a greater scatter of reaching endpoints both horizontally and in depth. However, the center of her endpoint ellipses also showed a shift from left to right as the reaching target moved from left (panel 1) to right (panel 5) in gaze coordinates. This overshoot pattern is also seen during delayed fixation trials (Fig. 6C). Taken as a whole, IG showed the slight increase in errors but more importantly, also showed signs of the retinal exaggeration effect seen in the controls.

### Fixation Task — Patient AT (Extensive Bilateral Parietal and Superior Occipital Lobe Lesions)

AT’s errors were comparable to those made by IG for rightward fixations but she made larger reaching errors both stochastically and systematically for leftward fixations. Figure 7A shows her reaching trajectories to the center target during the immediate fixation condition. Although she also horizontally overestimated target location, the overshoot was large especially for leftward fixations (all errors = $2.639 \pm 7.06^\circ$). She also showed a large...
Fixation Task — Effect of Delay

In the fixation task, increasing the delay from 0.5 to 2 s seemed to have little effect on the reaching performance in either the control or patient population. To test this more rigorously, reaching errors for immediate and delayed fixation conditions were compared directly. Figure 8 shows reaching errors for the central reaching target in degrees in the horizontal axis for immediate (solid lines—filled circles) and delayed (dotted lines—open circles) trials for control subjects (Fig. 8A), IG (Fig. 8C) and AT (Fig. 8E). In all three panels, the curves for the immediate and delayed trials appeared to be similar. The errors for the immediate and delayed trials were compared directly performing a linear regression on the horizontal errors during the delayed trials as a function of the same horizontal errors during immediate trials as seen in Figure 8B (controls), 8D (IG) and 8F (AT). The slopes of the three regression lines were close to 1 (dashed line) at 1.09 ± 0.38 (controls), 1.18 ± 0.63 (IG) and 1.04 ± 0.38 (AT). Thus, when the immediate and delayed fixation trials were compared, both patients and control subjects showed nearly equal errors.

Reaching Errors in Non-retinal versus Retinal Coordinates

Previous pointing studies suggested that this horizontal overshoot is an exaggeration in gaze-centered coordinates rather than an eye position effect per se, i.e. head-centered coordinates (Bock, 1986; Henriques et al., 1998). We checked to see if the same were true for our reaching task. Subjects performed additional fixation trials where the reaching target was either 12° left, 0° center or 12° right. These trials were used to test whether this overshoot effect obtained during this study was a function of retinal error or of eye position.

Unlike the previous pointing task (Henriques et al., 1998), the position of the reaching target in this study influenced the error function — shifting it up or down for all fixation targets. These errors were presumably due to factors unrelated to fixation direction (like arm motor control), but were difficult to disambiguate from the fixation-related errors. Therefore, to treat both on an even footing, we assumed that both of them were correct, shifting each error function of each model so that it aligned at the origin. Figure 9 depicts these normalized errors for each of the three targets, plotted first in head-centered coordinates, i.e. as a function of eye position (left column), and then in gaze-centered coordinates where the reaching target is at center, i.e. reaching target relative to gaze (right column). The three curves should show the best superposition for one of the two models (retinal or eye position).

Figure 9A,B shows the average control data pooled across immediate and delayed fixation trials for the 0° center (solid lines), the 12° left (dotted lines) and the 12° right (dashed lines) reaching targets. The average correlations comparing the three slopes to one another showed that the curves’ shapes were more similar in gaze-centered coordinates (average 0° center versus 12° right: r = 0.994; 0° center versus 12° left: r = 0.966; 12° right versus 12° left: r = 0.993) than in head-centered coordinates (average 0° center versus 12° right: r = 0.996; 0° center versus 12° left: r = 0.996; 12° right versus 12° left: r = 0.993) then in head-centered coordinates (average 0° center versus 12° right: r = 0.994; 0° center versus 12° left: r = 0.966; 12° right versus 12° left: r = 0.993) then in head-centered coordinates (average 0° center versus 12° right: r = 0.996; 0° center versus 12° left: r = 0.996; 12° right versus 12° left: r = 0.993). Thus, the conclusion that for the neurologically intact subjects, targets were encoded in a gaze-centered frame. The sum of the distribution of differences in error (differences between errors at each overlapping point of the three curves) was calculated as a measure of goodness of fit of the two models.

For the curves in plotted as a function of eye position, the sum of difference errors was 8.85, whereas in gaze-centered coordinates the sum was less, at 4.19, showing that the curves fit better in gaze-centered coordinates.

The patient data are shown in Figure 9C,D (IG) and Figure 9E,F (AT) plotted in the same manner as for the controls. For undershoot in depth that was constant across all fixations. This undershoot in depth was also seen for four of our five controls. Undershoot in the vertical dimension and in depth has also been reported previously (Rossetti et al., 1994; Henriques et al., 1998; Coello and Magne, 2000; Coello et al., 2000).

The elongation of her confidence ellipses for the data from Figure 7A (shown in Fig. 7B) were similar to the controls when the reaching target was in the left visual field but were horizontally wider when the reaching target was in the right visual field. This may be due to asymmetries in her lesions. Increasing the memory delay to 2 s seemed to have little effect on this patient’s performance in the fixation paradigm (Fig. 7C). To summarize, although the accuracy of reaching declined in IG and AT, both showed the trend to exaggerate the retinal eccentricity of remembered reach targets as observed in neurologically intact subjects.
IG, the average correlation between the three curves in gaze coordinates was 0.926 (individually: $r = 0.903, r = 0.9$ and $r = 0.975$), whereas the correlation in head-centered coordinates was only 0.619 (individually: $r = 0.655, r = 0.968$ and $r = 0.234$) showing that the curves match better in gaze-centered than in head-centered coordinates. This was confirmed in the sum of error difference calculation resulting in a sum of 13.06 for the gaze-centered curves and 16.95 for the non-gaze centered curves. For AT, although visually the three curves matched better in gaze-centered than in head-centered coordinates. This was confirmed in the sum of error difference calculation resulting in a sum of 13.06 for the gaze centered curves and 16.95 for the non-gaze centered curves. For AT, although visually the three curves matched better in gaze-centered coordinates, the average correlations in both types of plots did not differ greatly (gaze-centered, $r = 0.993$; individually: $r = 0.999, r = 0.981, r = 0.999$; eye position, $r = 0.979$; individually: $r = 0.991, r = 0.956, r = 0.991$). This may be because, unlike the control subjects and IG, AT reaching errors did not saturate at larger eccentricities relative to the target, which are key in revealing the differences between the two models. However, using the goodness-of-fit criteria, we found that for the gaze-centered coordinate curves, the sum of error differences was only 6.53, compared with head-centered coordinate curve sum of 20.70.

To summarize, our data agree with previous studies that the source of these fixation-related errors was primarily related to the retinal position of the target, which are key in revealing the differences between the two models. However, using the goodness-of-fit criteria, we found that for the gaze-centered coordinate curves, the sum of error differences was only 6.53, compared with head-centered coordinate curve sum of 20.70.

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Figure 8. Horizontal reaching errors and regression slopes comparing immediate and delayed fixation conditions. The first column depicts average horizontal reaching errors for the controls (A), IG (C) and AT (E) as a function of the fixation target. Solid lines with solid circles represent the immediate condition trials whereas open circles with dashed lines represent delayed trials. Data have been converted from millimeters (raw data from Figs 5-7) to angular degrees relative to the reaching target. Note the differences in range in the axes for both patients when compared with the controls. The second column shows the average reaching errors during delayed trials (y-axis) plotted as a function of immediate condition trials (x-axis) again for the controls (B), IG (D) and AT (F). The dashed line represents a perfect correlation in reaching errors between the immediate and delayed conditions, meaning that there is no difference between the errors in both conditions. The thin solid lines in (B) depict individual control slopes whereas the thick line represents the average control slope. The error bars shown for IG and AT depict standard errors for the mean reaching endpoints at each target. Error bars are not shown for the controls as the mean values shown are average values across subjects rather than within each subject as for IG and AT.
larger and more scattered than those of the controls, presumably suggesting that the neural mechanisms for this stage of their visuomotor transformation are damaged.

**Saccade Task: 500 ms Delay**

In order to quantify whether patients and controls remapped the position of targets in retinal coordinates, horizontal reaching errors during the saccade and fixation tasks at the 500 ms delay were compared. Gaze-centered remapping predicts similarities in reaching errors during fixation and saccade trials (Henriques et al., 1998; Medendorp and Crawford, 2002). Figure 10A illustrates horizontal reaching errors for the controls during immediate trials as a function of the fixation target. Solid lines with filled circles depict fixation trials whereas dashed lines with open circles represent saccade trials.

How well do these reaching errors match? When comparing the two types of paradigms, a gaze-centered hypothesis predicts a high correlation between the two, i.e. a slope of 1. This is because if remapping occurs in gaze-centered coordinates, the location of a target would be remapped after each saccade relative to the new gaze direction. Therefore, subsequent reaching to a target that has been remapped to a peripheral location in this gaze-centered map should have the same errors as reaching to a physical peripheral target. On the other hand, a non-gaze-centered (remapping in other reference frames, e.g. head-centered) hypothesis predicts no relationship between the two types of trials (a slope of 0). Non-gaze-centered remapping predicts that the errors during the saccade trials do not co-vary with the errors in the fixation trials but rather remain constant. In Figure 10B, horizontal reaching errors in the saccade paradigm were plotted as a function of reaching errors in the fixation paradigm during immediate trials for the controls (data replotted from Fig. 10A). The dashed line represents an ideal gaze-centered updating. The solid line represents the average best-fit regression line based on average reaching errors with individual best-fit thin lines in the background. The average slope ± 95% confidence interval ($R^2$ values in brackets show the goodness of fit of the average reach errors to the regression line) was $0.86 ± 0.18$ ($R^2 = 0.99$), ranging from 0.74 to 0.93 ($0.89 < R^2 < 0.97$). For all controls, slopes were significantly different from a slope of 0 ($t$-test, $P < 0.02$), but not from a slope of 1. This shows that controls did indeed update information in a gaze-centered frame. While there are differences between the slope predicting eye-centered updating (slope = 1) and the slopes shown by the controls (average slope = 0.86), they are not different from previous experiments on testing eye-centered updating using this method, e.g. Henriques et al. (1998), who found average slopes of ~0.91 for their subjects. Although a head- or body-centered model cannot account for any of these slopes, there are a number of reasons...
why the slopes might not reach the perfect 1.0 predicted by an ideal eye-centered model. The simplest explanation is that the brain slightly misestimates the amount of eye rotation (Henriques and Crawford, 2002).

The critical question is whether the patients also update information in a gaze-centered frame. Horizontal reaching errors for IG (the patient with parietal damage) and AT (the patient with greater parietal and superior occipital damage) are plotted in Figure 10. They show that the curves for the saccade reaching errors (dashed lines) seem to be flattened compared with the curves for the fixation reaching errors (solid lines), especially for AT. For IG the difference is only clear for leftward fixation positions. In contrast to the controls, the slopes of both patients differed from 1. IG's slope (Fig. 10D) was 0.61 ± 0.32 ($R^2 = 0.88$) and was significantly different from both a slope of 0 (t-test, $P < 0.01$) and a slope of 1 (t-test, $P < 0.05$), but not significantly different from the average control slope (0.86). AT's slope (Fig. 10F) was almost flat at 0.14 ± 0.15 ($R^2 = 0.64$) and was not significantly different from a slope of 0. Thus, for immediate trials, both patients' slopes suggest that they were not ideally updating the target locations in a gaze-centered frame. According to this test, AT seemed to be relying on a non-gaze-centered frame whereas IG was using a somewhat imperfect gaze-centered frame.

**Saccade Trials: 5000 ms Delay**

During the fixation trials, no effect of the 5000 ms delay on reaching errors was found. We also investigated whether the same was true for the saccade trials by comparing the immediate (500 ms delay) and delayed (5000 ms delay) saccade trials. For the controls, the delay did not have an effect on reaching errors. Just like in the fixation trials, the shapes of the two curves were almost parallel (Fig. 11A) and directly plotting the delayed trials as a function of the fixation trials (Fig. 11B) resulted in a slope of 1.10 ± 0.21 ($R^2 = 0.99$).

In contrast, both IG and AT showed a difference in their reaching errors between the immediate and the delayed trials. IG's curve during immediate saccade trials appeared flattened when compared with the delayed curve (Fig. 11C), particularly...
for leftward fixations. This is confirmed in the direct comparison plot (Fig. 11D), which gave a best-fit regression line with a slope of 1.99 ± 0.40 ($R^2 = 0.98$). AT’s reaching errors showed a similar difference between the immediate and delayed saccade trials (Fig. 11E), and the slope of the best-fit regression line (Fig. 11F) was also much greater than 1 at $2.34 ± 2.33$ ($R^2 = 0.77$). Could this increase in reaching error be due to a slow updating of the gaze-centered representation leading to a recovery of the performance observed in the fixation task? To test this, best-fit regression analyses were repeated comparing the saccade and fixation task errors for the delayed trials.

This comparison is shown in Figure 12 for both patients and controls. Similar to their immediate results (Fig. 10A), no differences were found in the controls between their delayed fixation and saccade trials (Fig. 12A). When plotting the reaching errors during immediate and delayed saccade trials against one another, the average slope of the regression line across all controls was $0.81 ± 0.14$ ($R^2 = 0.99$). Individual slopes ranged from 0.74 to 0.88 ($0.81 < R^2 < 0.98$). Across all controls, the average slope was significantly different from 0 ($t$-test, $P < 0.01$), but not from a slope of 1. Thus, control subjects appear to immediately update nearby targets in gaze-centered coordinates and then maintain these representations across time. But what about the patients?

For both IG (Fig. 12C) and AT (Fig. 12E), the reaching errors during the delayed saccade paradigm (dashed lines) were more similar to the reaching errors during the delayed fixation paradigm (solid lines) than during immediate trials (Fig. 10). In fact, the reaching error curves for both paradigms matched extremely well for IG. This can be clearly seen in the slope plot for IG (Fig. 12D). After the delay, her slope rose from 0.61 (Fig. 9) to $1.06 ± 0.33$ ($R^2 = 0.97$) and was significantly different from 0 ($t$-test, $P < 0.01$) but not from 1, suggesting that after a delay, IG was able to update target locations in gaze-centered coordinates. AT (Fig. 12F) showed a similar trend to IG, showing a marked slope increase during the delay from 0.14 (Fig 10) to $0.43 ± 0.07$ ($R^2 = 0.99$). However, statistical analysis showed this slope to be significantly different from both 0 ($t$-test, $P < 0.01$) and 1.
and 1 (t-test, $P < 0.01$). Although AT’s slope did not match the ideal slope of 1, it nevertheless increased approximately threefold from her slope during immediate trials. Table 1 provides a summary of slope values corresponding to each comparison made. In summary, for both patients, although the errors increased during delayed saccade trials, this increase in errors resulted in a closer match to the pattern of errors during fixation trials. These results suggest that, with an extended delay, the patients relied on a more gaze-centered updating mechanism. This does not mean that the delay improved their performance. In fact, it got worse (Fig. 11C,E) just as their performance was degraded in the fixation task for peripherally viewed targets. This does suggest, though, that with the extended delay period subjects were making use of a more ‘normal’ visuospatial updating mechanism.

**Discussion**

To summarize: (i) according to this test, neurologically intact subjects update the location of targets in gaze-centered coordinates quickly and can retain this updated information across time; (ii) in contrast, the bilateral posterior parietal damaged patients tended to update this information in a non-gaze-centered frame; (iii) this tendency increased with the extent of parietal–occipital damage; and yet (iv) both patients showed signs of recovering an updated gaze-centered representation given a delay of 5000 ms.

**Remapping in Occipital–Parietal-damaged Patients**

During immediate saccade trials the patients did not show complete gaze-centered remapping: AT showed an almost flat
The slope of the regression line relating saccade to fixation errors and IG showed a somewhat steeper slope suggesting partial gaze-centered remapping. Moreover, IG showed clear evidence for gaze-centered updating after a delay whereas AT showed only a partial recovery of gaze-centered updating. In both senses, AT showed a more complete deficit whereas IG’s behaviour was closer to normal. The reason for the differences between AT and IG may be that AT’s lesions were more extensive compared with IG. AT’s lesions extend from the parietal lobe to the superior occipital lobes (see Materials and Methods), whereas IG’s lesions are largely limited to the parietal cortex. Recent physiological research on monkeys has shown that remapping also occurs in the extrastriate cortex (Nakamura and Colby, 2002). This may explain the greater disruption in gaze-centered remapping for AT. This suggests that damage in different areas results in somewhat distinct impairments: (i) a loss of gaze-centered updating in the case of extensive parietal-occipital damage; and (ii) a delayed or slowed gaze-centered updating in the case of more focal parietal damage.

Possible Physiological Correlates of Re-mapping in Occipital–Parietal Patients

Updating visual information in a gaze-centered map and using this map to reach requires the integration of at least three different kinds of information: (i) the original retinal information about the target; (ii) the eye rotation signal required to update the latter signal for the new eye position; and (iii) the eye position signal which provides the final eye orientation relative to the head. AT’s errors during the immediate saccade task are almost negligible; across all fixation targets, she seemed to be reaching to the center target as if she was looking directly at it. This would only occur if there were both no updating and no accounting for eye position. However, the data from the fixation task show that this is not the case. Clearly patients still had access to an eye position signal, or else they would have pointed in the direction of the original retinal stimulus resulting in left, center or right reaches to a central target.

A more feasible explanation is that the reaching movement was already planned in advance of the saccade in some body-centered coordinate frame appropriate for activation of the arm muscles (Soechting et al., 1991, 1995; Flanders et al., 1992; Henriques et al., 1998; Desmurget and Grafton, 2000). Cells in the frontal premotor and motor areas related to arm movements are modulated much less with gaze (Cisek and Kalaska, 2002) compared with the parietal reach areas lost in the patients (Batista et al., 1999). In intact subjects, non-visual motor plans appear to be immediately overridden by the visual updating process (Medendorp and Crawford, 2002), but this did not happen in the parietal patients, at least not without a memory delay. In the absence of the occipito-parietal cortex, the motor system does not seem to have immediate access to the visual updating signal. The information must reach the motor system by some other means — one that takes longer than the parieto-frontal network (Binkofski et al., 1999; Caminiti et al., 1999; Rossetti et al., 2000; Rossetti and Pisella 2002; Gregoriou and Savaki, 2003).

There are several alternative pathways by which visual information can reach motor centers. The use of such pathways would explain two things: (i) how information reaches the frontal and motor cortices; and (ii) the delay involved in updating the gaze-centered map. One possible alternative is the ventral visual pathway through the temporal cortex (Milner et al., 1999, 2001; Pisella et al., 2000; Rossetti and Pisella, 2002; Rossetti et al., 2003). This has been shown to be involved in pointing (Lee and van Donkelaar, 2002) and has connections to the prefrontal cortex, which in turn projects to the motor cortex (Rao et al., 1997; Rossetti et al., 2000). The stream appears to encode targets in object-centered coordinate frames (Dijkerman et al., 1998), perhaps consistent with the non-retinal storage mechanism observed during immediate trials.

Moreover, in delayed visuomotor tasks this ventral pathway may include activation of the hippocampus (O’Keefe and Nadel, 1978; Rolls, 1989; Felleman and Van Essen, 1991; McNaughton et al., 1991; Lacquaniti et al., 1997), a structure which stores information in allocentric coordinates (Feigenbaum and Rolls, 1991). Lacquaniti et al. (1997) suggested that allocentric information about targets from the inferotemporal cortex may be stored in the hippocampus then converted into an egocentric frame when transferred to the frontal cortex for movement planning.

An additional possibility is that our patients were re-routing information through both the ventral stream and some intact (ventral-most) parts of the dorsal stream itself. Rizzolatti and Mattelli (2003) suggest that there may be two divisions of the dorsal stream itself, the dorsal–dorsal stream, related to online action execution, and the dorsal–ventral stream, which involves mainly space and action perception but is also involved in controlling action. The ventral–dorsal stream includes the inferior parietal lobule (IPL). As this area is only partially damaged for both patients, the stream may still play a functioning role. However, it is as yet unclear whether this stream plays any role in spatial updating.

In summary, these findings suggest that while extrastriate visual areas may be necessary for updating, the PPC may not be necessary for updating itself but for rapid updating, i.e. quickly integrating various extra-retinal signals with retinal information to update the gaze-centered map rapidly enough for online adjustments of movement errors (Pisella et al., 2000; Gréa et al., 2002). This notion is compatible with the idea of at least two visuomotor processing streams that can be distinguished anatomically, functionally and on the basis of their speed of processing (Rossetti and Pisella, 2002; Rossetti et al., 2003, 2004). Further studies are needed to investigate the neurological substrates involved in the delay effect found for both updating (present data) and in the use of visual information for reaching (Rossetti et al., 2003, 2004). It also remains to be seen if other aspects of optic ataxia can be explained by the re-mapping deficits identified in this study.

Notes

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