Critical neural substrates for correcting unexpected trajectory errors and learning from them

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Our proficiency at any skill is critically dependent on the ability to monitor our performance, correct errors and adapt subsequent movements so that errors are avoided in the future. In this study, we aimed to dissociate the neural substrates critical for correcting unexpected trajectory errors and learning to adapt future movements based on those errors. Twenty stroke patients with focal damage to frontal or parietal regions in the left or right brain hemispheres and 20 healthy controls performed a task in which a novel mapping between actual hand motion and its visual feedback was introduced. Only patients with frontal damage in the right hemisphere failed to correct for this discrepancy during the ongoing movement. However, these patients were able to adapt to the distortion such that their movement direction on subsequent trials improved. In contrast, only patients with parietal damage in the left hemisphere showed a clear deficit in movement adaptation, but not in online correction. Left frontal or right parietal damage did not adversely impact upon either process. Our findings thus identify, for the first time, distinct and lateralized neural substrates critical for correcting unexpected errors during ongoing movements and error-based movement adaptation.

Keywords: visuomotor adaptation; online correction; cognitive control; motor planning; voluntary movement

Introduction

Most everyday actions are thought to involve a process where movement commands are derived based on a desired goal state and information of the current state of the limb. This process presumably incorporates internal representations, or ‘models’ of our limbs properties and features of the environment in which movements are performed (Gandolfo et al., 1996; Sainburg et al., 1999; Wolpert and Ghahramani, 2000). Such representations are also believed to be used to predict the sensory consequences of movement commands (Miall and Wolpert, 1996; Wolpert and Flanagan, 2001). The difference, or ‘error’ between the predicted and actual sensory outcomes is thought to be used to adjust motor commands to update, or correct, the ongoing movement (Miall et al., 2007), as well as to modify our internal representations so that performance on subsequent movements...
can be improved (Mazzoni and Krakauer, 2006; Krakauer, 2009; Galea et al., 2011). Some previous studies (Tseng et al., 2007; Schaefer et al., 2009; Shabbott and Sainburg, 2010) have shown that learning to adapt future movements in response to errors is not dependent on the occurrence of online correction of those errors, leading to the suggestion that the mechanisms mediating these two processes may be distinct. However, the characterization of neural substrates critical for these processes remains incomplete.

Recent research has suggested that movement adaptation relies extensively on cerebellar and parietal brain regions. These studies have argued that as actions become highly learned and more ‘automatic’, they could be represented in these areas (Shadmehr and Holcomb, 1997). Damage to the cerebellum has been shown to impair learning of novel, but predictable task contingencies such as force perturbations and arbitrary visuomotor relationships, presumably due to a failure in modifying our previously stored internal representations (Martin et al., 1996; Smith and Shadmehr, 2005; Tseng et al., 2007). Several previous studies have also demonstrated parietal involvement during adaptation, but have been inconsistent with regard to whether parietal regions in one or both hemispheres are critical for this process (Clower et al., 1996; Ghilardi et al., 2000; Krakauer et al., 2004; Diedrichsen et al., 2005; Danckert et al., 2008). We recently provided evidence that adaptation critically depends on parietal regions in the left hemisphere (Mutha et al., 2011). We found that stroke patients with damage to left, but not right, parietal regions were profusely impaired in learning a novel visuomotor relationship and as a result, failed to appropriately plan movements of the contralesional arm. Furthermore, our previous results in patients with damage to widespread regions of the left hemisphere showed a similar deficit in learning when using their ipsilesional arm to perform the task (Schaefer et al., 2009). Together, these findings suggested that an intact left hemisphere is critical for learning-based improvement in motor planning regardless of the arm used to perform the task, and indicated an important role for parietal regions in these functions.

In contrast to the planning of learned movements that might be dependent on left parietal regions, our results on lateralization of movement control mechanisms in healthy individuals have suggested a right hemisphere specialization for achievement of a spatial task goal through feedback-mediated mechanisms (Sainburg and Kalakanis, 2000; Sainburg, 2002). This advantage appears to be particularly pronounced when ongoing movements are required to be corrected following novel and unpredictable perturbations (Bagesteiro and Sainburg, 2003; Duff and Sainburg, 2007). For example, in right-handed subjects, Bagesteiro and Sainburg (2003) showed that when unexpectedly perturbed by an inertial load, the left arm showed better load compensation and better movement accuracy than the right arm. This performance was associated with specific changes in muscle activity during the later phases of the movement, suggesting a specialized role for the right hemisphere system in formulating more appropriate corrective responses under unpredictable conditions through the use of sensory feedback. Importantly, we also found that right hemisphere lesions resulted in deficits in achieving a stable final position, but not in planning initial movement parameters, even when movements were made with the ipsilesional right arm (Haaland et al., 2004; Schaefer et al., 2007, 2009a, b). These results suggest that the right hemisphere has become specialized for achieving greater spatial accuracy, especially when task conditions are unpredictable and the association between a stimulus (error) and response (correction) is not well known or not well learned.

Studies employing cognitive tasks have demonstrated that responses to novel, unlearned stimuli require ‘top–down’ processing that engages frontostriatal circuits (Cools et al., 2006; Buschman and Miller, 2007; Joti et al., 2007; Tsuchida and Fellows, 2009). Recent studies have argued that such circuits in the right hemisphere might be particularly important for updating ongoing actions under unpredictable task conditions by inhibiting predominant, habitual movements and potentiating corrective responses (Mars et al., 2007; Swann et al., 2009; Neubert et al., 2010). For example, Mars et al. (2007) showed activation of the right insular and inferior frontal regions as well as the right pre-motor cortex when required to alter an existing plan for an action and initiate a new response. Critically, these authors demonstrated that the activation of these regions was not exclusive to inhibition of preponderant responses, but was also related to selection of the new online response. These results, combined with our findings of a right hemisphere specialization for feedback mediated movement corrections, suggest that frontal regions in the right hemisphere might play a key role in facilitating appropriate corrective motor responses under novel and unfamiliar task conditions.

The goal of this study was therefore to determine whether distinct and lateralized neural substrates mediate correction of errors introduced using a new and unfamiliar mapping between hand movement and its visual feedback, and adaptation of future movements based on those errors. We expected that left parietal regions would be critical for adapting to the novel conditions, while right frontal regions would be important for correcting movement errors until the new conditions had been learned. In order to establish a causal role between these neuroanatomical regions and function, we examined patients with focal damage to frontal or parietal regions of the left or right cerebral hemispheres (Fig. 1), and assessed the nature of their deficits relative to healthy control subjects performing the same task.

Materials and methods

The institutional review board of the New Mexico Veterans Affairs Healthcare System approved the study and all subjects gave informed consent prior to participation according to the Declaration of Helsinki.

Participants

We tested 20 stroke patients (10 left hemisphere damaged, 10 right hemisphere damaged) and 20 healthy normal control participants (10 left normal controls, 10 right normal controls depending on the arm used to perform the task, see below). Within both the left hemisphere damaged and right hemisphere damaged group, five patients had primarily frontal damage, while five others had primarily parietal damage. All patients were in the chronic phase of injury (>6 months post stroke). Subjects were screened and excluded for a significant history of substance abuse, severe psychiatric diagnoses, peripheral
movement restrictions from neuropathy or orthopaedic injuries, non-stroke-related neurological problems for stroke patients, or any neurological diagnoses for the controls. All subjects were right-handed; handedness was determined using a 10-item version of the Edinburgh inventory (Oldfield, 1971). Auditory comprehension was assessed using the sequencing subtest of the Western Aphasia Battery (Kertesz, 1982). Stroke patients were also given the Fugl-Meyer test of arm function (Fugl-Meyer et al., 1975) to provide an indication of the degree of contralesional hemiparesis.

We defined deficits in performance of stroke patients relative to controls using the same arm to perform the task. We used a similar approach to investigate any differences in demographics and auditory comprehension between our patients and controls. As shown in Table 1, age, education and handedness score were comparable in the left normal controls, groups with left frontal damage and left parietal damage as well as the right normal controls, and groups with right frontal damage and right parietal damage (P > 0.05 in all cases). Auditory comprehension could not be statistically analysed because all subjects in three groups had perfect scores (zero standard deviation), but mean scores across the groups were fairly close. Importantly, the performance of all subjects indicated that they were able to follow task instructions fairly well. Time post stroke was marginally smaller in the patients with left frontal damage relative to the subjects with left parietal damage (P = 0.0506), but these patients were still, on average, close to 4 years post stroke. Lesion volume and upper extremity Fugl-Meyer motor score was matched between the left frontal damage and left parietal damage stroke groups, as well as the right frontal damage and right parietal damage stroke groups (P > 0.05 in all cases).

MRIs were obtained in 15 stroke patients, while CT scans were done for 5 patients due to medical contraindications for MRI. The area of damage for each patient was traced on standardized horizontal sections derived from the DeArmond atlas (DeArmond et al., 1989) by a board certified neurologist who was blinded to the behavioural characteristics of the patients. Lesion overlap images were created and lesion volume was calculated from the digitized tracings using a

![Figure 1](https://example.com/figure1.png)

**Figure 1** Lesion overlay. Overlap of lesion location in at least 60 (blue), 80 (red) and 100 (yellow) per cent of patients in the groups with left frontal damage, right frontal damage, left parietal damage and right parietal damage.

**Table 1 Participant information**

<table>
<thead>
<tr>
<th>Variable (mean ± SD)</th>
<th>Healthy controls</th>
<th>Stroke patients</th>
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<tbody>
<tr>
<td></td>
<td>LNC</td>
<td>RNC</td>
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<tr>
<td>n</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Age (years)</td>
<td>63.7 ± 5.57</td>
<td>61.8 ± 8.44</td>
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<tr>
<td>Education (years)</td>
<td>15.4 ± 2.63</td>
<td>15.3 ± 1.56</td>
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<tr>
<td>Handedness(^a)</td>
<td>94.5 ± 7.43</td>
<td>86.2 ± 16.1</td>
</tr>
<tr>
<td>Auditory comprehension(^b)</td>
<td>80 ± 0</td>
<td>80 ± 0</td>
</tr>
<tr>
<td>Years post stroke(^c)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Lesion volume (cm(^3))</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Fugl-Meyer score(^d)</td>
<td>–</td>
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\(^{a}\) Handedness score was calculated using the Edinburgh Laterality Quotient and could range from −100 (strongly left handed) to +100 (strongly right handed). In stroke patients, handedness is from the time prior to their stroke.

\(^{b}\) Auditory comprehension was assessed using the sequencing subtest of the Western Aphasia Battery. The maximum possible score on this subtest is 80.

\(^{c}\) Years post stroke were calculated as the time elapsed between incidence of stroke and day of data collection.

\(^{d}\) Maximum possible score on the upper-extremity motor portion of the Fugl-Meyer assessment is 66. This assessment was for the contralesional limb only. LFD = left frontal damage; LNC = left normal controls; LPD = left parietal damage; RFD = right frontal damage; RNC = right normal controls; RPD = right parietal damage.
The reliability of which has been previously verified (Knight et al., 1988). These overlap images are shown in Fig. 1. In patients with frontal damage (left and right), lesions were primarily in inferior [pars opercularis Brodmann area (BA) 44, pars triangularis BA 45] and middle frontal (dorsolateral prefrontal BA 9, BA 46) cortical regions of the left or right hemisphere. These patients also had lesions to premotor cortex (BA 6), but damage to primary motor cortex was not separately distinguishable from premotor damage on inferior slices. On more superior levels, where a clear distinction could be made between premotor and primary motor cortices (e.g. slice 9), we did not find evidence of motor cortical involvement in most (>60%) subjects in either the left or right frontal damage groups. In patients with damage to the parietal lobe (left and right parietal damage), maximum overlap occurred in superior parietal (BA 7) as well as inferior parietal (angular gyrus BA 39, supramarginal gyrus BA 40) regions. Lesions in these parietal patients also tended to extend somewhat into the caudal portion of BA 22.

**Experimental setup and task**

Subjects sat facing a table with their forearm supported over the table using an air sled system. A cursor representing the position of the index finger tip, a start circle and targets were projected using a horizontally mounted high definition television onto a mirror placed beneath it. The mirror blocked direct vision of the subjects arm, but reflected the visual display to give the illusion that the display was in the same horizontal plane as the fingertip. Subjects performed reaching movements below the mirror. Position and orientation of the forearm and upper-arm segments were sampled using a Flock of Birds system (Ascension Technology). The positions of the index finger tip, the lateral epicondyloyle of the humerus and the acromion were computed and recorded using custom software, with the X-Y plane parallel to the tabletop. We used the computed X-Y coordinates of the fingertip to define the projected cursor position.

Stroke subjects performed the task with their ipsilesional arm (i.e. left arm for left frontal damage and left parietal damage, and right arm for right frontal damage and right parietal damage) so that the influence of contralesional arm hemiparesis on motor performance was minimized. Control subjects were randomly assigned to perform the task with either their left (left normal controls) or right (right normal controls) arm. The task consisted of reaching movements from a single start position to eight targets at a radial distance of 12 cm, arranged along the circumference of a circle, 45° apart. On any given trial only one of the targets was pseudorandomly selected to be displayed on the screen, such that no target appeared consecutively. To initiate a trial, subjects brought the cursor (which represented their index finger) into the start circle. After a brief delay, the target for that trial appeared along with an audio-visual ‘go’ signal, which served as the cue for subjects to reach to the target. Velocity feedback was provided and subjects were encouraged to attain a peak speed of at least 0.5 m/s. Points based on final position accuracy were given if this speed requirement was satisfied.

Each subject performed three sessions of movements. Feedback regarding hand position by means of the screen cursor was given during all trials of every session. The first session of ‘baseline’ movements had 120 trials, during which cursor and hand motion were veridical. This session was used to establish baseline measures of performance. During the second ‘exposure’ session, subjects were exposed to a novel visuomotor mapping (visuomotor rotation) where the position of the cursor was rotated counterclockwise by 30° relative to the start circle. Thus, during these trials, motion of the cursor was dissociated from the actual direction of hand motion. This session included 208 trials and was used to examine how subjects corrected their movements online in response to the unfamiliar cursor deviation and adapted their movements over time. The third session consisted of 120 trials during which the cursor and hand motion were again veridical. This session was used to examine the effects of removing the visuomotor rotation and the presence of after-effects.

**Data analysis**

Finger, elbow and shoulder positions were calculated from Flock of Birds sensor position and orientation data. These were then used to calculate shoulder and elbow joint angles. All kinematic data were low-pass filtered at 8 Hz (third order dual pass Butterworth), and angular data were differentiated to yield velocity and acceleration values. We identified movement onset by noting the time of peak velocity and searching backwards in time for the first minimum in velocity <3% of peak tangential velocity. Movement end was determined by searching forward from peak velocity to find the first minimum <3% of the peak. In order to ensure that our results were not dependent on our choice of the criterion used to determine these time points, we also identified movement start and end using a second method that was not dependent on peak velocity (White and Diedrichsen, 2010). The start of the movement was noted when the hand velocity first crossed a fixed threshold of 2.5 cm/s and the end of the movement was recorded when velocity fell <1.5 cm/s. Using this criterion, the values obtained for movement start and end corresponded very closely to those using the first criterion (mean r = 0.91 for both movement start and movement end). We also verified that our other measures (described below) and our overall pattern of results were not affected by our choice of method. Therefore, for the sake of brevity, we present results obtained only using the first criterion based on peak tangential velocity.

Adaptation was quantified in terms of changes in initial direction error during the exposure session. Initial direction error was measured as the angular difference between the line from the centre of the start circle to the target and the line joining the centre of the start circle to the finger position at peak acceleration. Negative values of this measure indicated that hand paths were directed medial (counterclockwise) to the target line. Changes in hand path curvature and final position accuracy of the movements were quantified as secondary measures of adaptive performance. Final position error was calculated as the distance between the finger position at movement end and the centre of the target. Hand path curvature was calculated as the minor axis divided by the major axis of the hand path. The major axis was defined as the largest distance between any two points in the hand path, while the minor axis was defined as the largest distance perpendicular to the major axis. We also quantified the amount of correction that each subject made during the exposure trials, normalized to baseline movements. Similar to the method proposed by White and Diedrichsen (2010), for each subject, the difference between hand direction at movement end and initial movement direction was calculated as the amount of correction for a trial. This measure was then normalized by subtracting the mean baseline correction amplitude for that subject.

For analysis purposes, we considered each session as cycles of movements. A cycle was defined as a complete series of movements to each of the eight targets. The baseline, exposure and after-effects blocks thus included 15, 26 and 15 cycles, respectively. Statistical analyses were conducted using two-way ANOVAs with group (left normal controls, left frontal damage, left parietal damage or right normal controls, right frontal damage, right parietal damage) as the between...
Subject factor and cycle (first or last) as the within subject factor. Tukey’s post hoc tests were conducted when warranted by significant main effects and interactions.

Results

Right frontal damage impairs the ability to correct movements online in response to unexpected trajectory errors

Baseline performance

Figure 2A shows the hand trajectories during the last cycle of the baseline session for representative subjects of the control (right normal controls) and right frontal and parietal damaged groups performing with their right arm. Overall, these movements were initiated in the appropriate direction, were fairly straight and ended accurately on the intended target. Across all groups, for the baseline session, we did not observe any significant differences in initial movement direction \([F(2,17) = 1.0842, P = 0.3604]\) or final position accuracy \([F(2,17) = 0.8303, P = 0.4528]\).

Initial exposure to visuomotor rotation

Figure 2B shows the hand paths for the same subjects when they were first exposed to the 30° counterclockwise cursor deviation. As expected, movement trajectories were in the same direction as the previously practiced baseline trials, but a large error occurred because of the dissociation between cursor and hand motion. Across all subjects, this direction error on the first cycle of the exposure session was close to −30°, similar to the magnitude of the imposed rotation (Fig. 3A, cycle 1). This was statistically confirmed using a Group × Cycle (last baseline, first exposure) ANOVA, in which we found only a significant effect of cycle \([F(1,17) = 356.03, P < 0.0001]\) and no significant group \([F(2,17) = 1.3894, P = 0.2761]\) or interaction effects \([F(2,17) = 0.2105, P = 0.8123]\). This indicated that all three groups showed a similar magnitude of direction error when initially perturbed by the rotation.

Due to the unexpected cursor deviation resulting in errors in the seen movement trajectory, subjects tended to initiate corrective movements during the trial to bring the cursor to the target. Such corrections are evident on a majority of the trials for the right normal controls and subjects with right parietal damage in Fig. 2B, and are discernible as large deflections in the movement trajectory, nearly perpendicular to the initial direction of motion. Notably however, the subject with right frontal damage in Fig. 2B failed to initiate such corrections and instead, simply terminated the ongoing movement on six out of eight trials shown. The lack of online corrections resulted in large final position errors for this patient. The consistency of this pattern of results in the three groups is evident in Fig. 3B and C. Statistically, we observed a significant Group × Cycle (last baseline, first exposure) interaction for both, hand path curvature \([F(2,17) = 5.7646, P = 0.0123]\) and final position error \([F(2,17) = 5.0883, P = 0.0185]\). Post hoc tests confirmed that while curvature was large but similar for the right normal controls and subjects with right parietal damage on the first exposure cycle \((P > 0.05)\) (Fig. 3B, right), it was considerably smaller in the group with right frontal damage \((P < 0.05)\) (Fig. 3B, left). This indicated that while right normal controls and patients with right parietal damage updated and corrected their ongoing movements resulting in curved hand paths, movements of the patients with right frontal damage were much straighter due to a deficit in trajectory correction when initially exposed to the novel rotation condition. Therefore, final position errors in the patients with right frontal damage were much larger on the first exposure cycle \((P < 0.05)\), as shown in Fig. 3C (left). This was not the case for the subjects with right parietal damage who demonstrated similar accuracy as controls \((P > 0.05)\) (Fig. 3C, right).

Adaptation of movement direction with continued exposure to rotation and presence of after-effects upon its removal

As subjects continued to experience the rotation, they began to appropriately adapt their movements so that the cursor could be brought directly to the target without having to rely on online corrections. Figure 2C shows the hand paths for our representative subjects on the last exposure cycle. In all subjects, these movements were significantly straighter and in the direction of the target. We quantified the change in initial direction error during the exposure session as a measure of adaptation to the novel visuomotor conditions. Figure 3A shows the decrease in initial direction error over the course of the exposure session, with similar errors across the three groups on the last cycle. Statistically, we found a significant effect of cycle (first exposure, last exposure) \([F(1,17) = 119.11, P < 0.0001]\), but no significant effect of group \([F(2,17) = 1.9089, P = 0.1787]\) or Group × Cycle interaction \([F(2,17) = 0.3605, P = 0.74]\) for initial direction error, indicating that all three groups adapted similarly over the course of the exposure session.

Another way to assess whether the novel conditions have been learned is to examine after-effects once the rotation is removed. Under these circumstances, subjects initially typically show trajectories directed opposite to the direction of the previously imposed rotation. Figure 2D shows that this was indeed the case for our representative subjects in all three groups. Their movements were directed similar to those on the last exposure cycle, indicating continued implementation of the learned strategy. However, because the cursor followed the same path as the hand, these movements were associated with direction errors opposite to those on the early exposure trials. The magnitude of these errors on the first after-effect cycle across all subjects in the three groups is shown in the insets of Fig. 3A. Statistical comparison revealed no significant effect of group \([F(2,17) = 0.8155, P = 0.4590]\) on the magnitude of the after-effect. Thus, the similar improvement in initial direction during the exposure session and presence of large but comparable after-effects in the groups with right frontal and parietal damage relative to the right normal controls indicated that these stroke patients were able to appropriately adapt to the novel visuomotor conditions. Importantly also, when the rotation was first removed during the after-effect session, the patients with right frontal damage showed no corrections (Fig. 2D), further confirming their deficit in updating ongoing movements when task conditions were unexpectedly changed.
Movement correction in response to the novel visuomotor rotation

The parallel improvement in initial direction error in the right normal controls, right frontal damage and right parietal damage groups during the learning of the rotation was not evident in the hand path curvature and final position error measures. As shown in Fig. 3B and C (left), hand path curvature was smaller, while final position error was larger during the early phases of the exposure session (~10 cycles) for the patients with right frontal damage compared with the right normal controls. This was not the case for the patients with right parietal damage who showed a similar improvement in curvature and accuracy as the right normal controls (Fig. 3B and C, right). During this early learning phase, we observed a significant Group × Cycle (first exposure, 10th exposure) interaction for both hand path curvature \([F(2,17) = 4.1783, P = 0.0334]\) and final position error \([F(2,17) = 4.1651, P = 0.0337]\). Post hoc tests indicated that the slope of the change in these measures was different for the group with right frontal damage relative to the right normal controls and group with right parietal damage. Thus, during the early learning phase, the subjects with right frontal damage learned to adapt their initial movement direction, but continued to show straighter hand paths and larger position errors, reflecting limited movement correction. As learning progressed, curvature and position errors
became more similar across the groups, eventually reaching the same level towards the end of the exposure session. Thus, the improvement in accuracy in the patients with right frontal damage during the exposure session was associated with a refinement in initial movement direction such that the cursor headed straight to the target and within-trial corrections were not necessary.

We quantified the amount of correction that each subject made in response to the cursor deviation. These values are plotted in Fig. 4A across all subjects of the right normal controls, right frontal damage and right parietal damage groups for the first and last exposure cycles. Correction magnitude was considerably smaller in the group with right frontal damage even on the first exposure cycle compared with the other two groups. While we did not observe a significant Group × Cycle (first exposure, last exposure) interaction for this measure ($F(2,17) = 1.2056, P = 0.3239$), our a priori comparisons to test for group differences on the first and last exposure cycles revealed significantly smaller corrections in the group with right frontal damage relative to the right normal controls and the group with right parietal damage at the beginning ($P < 0.05$ in both cases), but not at the end of the exposure session ($P > 0.05$ in both cases). We then examined whether the correction magnitude was associated with the subjects initial direction error. The slope of this relationship provides an indication of the efficacy of their corrections, or correction gain (White and Diedrichsen, 2010). These regressions are shown in Fig. 4B for

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Figure 3  Performance across all subjects in the right normal controls (RNC, black) and groups with right frontal damage (RFD) and right parietal damage (RPD, grey) during all cycles of the exposure session. (A) Mean ± SE initial direction error. Inset shows the initial direction error on the first cycle of the after-effect session across all subjects in each group. (B) Mean ± SE hand path curvature; (C) mean ± SE final position error.
our representative subjects. As can be seen from these plots, correction gain was much smaller for the patient with right frontal damage relative to the right normal controls and participants with right parietal damage. Across all subjects, we observed a significant group effect \( F(2,17) = 4.0389, P=0.0367 \) for correction gain (Fig. 4C), with pairwise comparisons showing smaller values for the group with right frontal damage relative to both other groups \( P<0.05 \) in both cases).

In summary, the patients with right frontal damage showed a deficit in updating their ongoing movements when initially exposed to the novel visuomotor rotation and when the rotation was first removed in the after-effect block. However, they were able to adapt their movement direction over time. In contrast, right parietal damage did not adversely impact upon adaptation or movement correction processes.

**Left parietal damage impairs the ability to adapt initial movement direction**

**Baseline performance**

Figure 5 shows the hand trajectories for representative subjects from the left normal controls, left frontal damage and left parietal damage groups, all of whom performed the task with their left hand. The last cycle of baseline movements of these subjects is shown in Fig. 5A. As can be seen, these movements were fairly straight and directed accurately towards the target. We found no significant differences in initial movement direction \( F(2,17) = 1.7746, P=0.2 \) or final position error \( F(2,17) = 1.4047, P=0.2725 \) among the three groups for the baseline movements.

**Initial exposure to visuomotor rotation**

Figure 5B shows the hand paths of the representative subjects on the first cycle of movements of the exposure session. As expected, hand path directions were initially similar to baseline movements, but the cursor deviation resulted in large direction errors. We found no significant Group × Cycle (last baseline, first exposure) interaction \( F(2,17) = 0.3136, P=0.7349 \) for the magnitude of the initial direction error, which was close to \(-30^\circ\) for all three groups. Thus, all subjects were similarly affected when they first experienced the rotation.

As shown in Fig. 5B, all subjects made trajectory corrections to bring the cursor towards the target on a majority of the initial exposure trials. Remarkably, these corrections were largest in the patient with left parietal damage, who corrected all
movements towards the target location, resulting in final position errors that were smaller than the left normal controls and patients with left frontal damage. This trend was consistent across all subjects in the group with left parietal damage. We observed significant Group × Cycle (last baseline, first exposure) interactions for both, hand path curvature \[F(2,17) = 5.0495, P = 0.0190\] and final position error \[F(2,17) = 10.1782, P = 0.0012\]. As shown in Fig. 6B and C (right), and as confirmed by our post hoc tests, on the first exposure cycle, curvature was much larger, and position errors were much smaller in the left parietal damage \((P < 0.05 \text{ in all cases})\), but not the patients with left frontal damage \((P > 0.05 \text{ in all cases})\) relative to the left normal control subjects.

**Figure 5** Comparison of movement profiles for representative subjects in the left normal controls (LNC, black), and groups with left frontal damage (LFD) and left parietal damage (LPD, grey). (A) Last eight trials (last cycle) of the baseline session. (B) First cycle of movements following exposure to the visuomotor rotation (exposure session). (C) Last cycle of movements of the exposure session and (D) first cycle of the after-effect session when the visuomotor rotation was removed.

Adaptation of movement direction with continued exposure to rotation and presence of after-effects upon its removal

Upon continued experience of the rotation, the left normal controls and subjects with left frontal damage improved their initial movement direction. This was however not the case for the patients with left parietal damage, who showed only a modest change in initial direction error. Figure 5C shows that the hand paths for the left normal controls and subjects with left frontal damage on the last exposure cycle were considerably straighter compared with those on the first cycle, but the patient with left parietal damage continued to show incorrectly directed movements. Figure 6A (right) confirms this trend across all subjects.
While movement direction improved somewhat during the very early phases of the exposure session in the patients with left parietal damage, their performance quickly reached an asymptote, while the left normal controls and patients with left frontal damage continued to improve. We observed a significant Group × Cycle (first exposure, last exposure) interaction for initial direction error $F(2, 17) = 7.8808$, $P = 0.0038$. Post hoc tests showed that direction error on the last cycle was significantly larger for the patients with left parietal damage relative to the other two groups ($P < 0.05$ in both cases). However, there were no significant differences in the final performance of the left normal controls and participants with left frontal damage ($P > 0.05$). Thus, even while moving the ipsilesional arm, left parietal damage disrupted the ability to improve initial movement direction.

We also examined after-effects in the patients with left parietal damage relative to the other two groups. Figure 5D shows the hand trajectories on the first after-effect cycle for our representative subjects. While the left normal controls and patients with left frontal damage showed large after-effects, the magnitude of the after-effect in the patient with left parietal damage was smaller. This patient did show some deviation in the direction opposite to the previously imposed rotation, but across all subjects, this deviation was not as large as the left normal controls or subjects with left frontal damage (inset of Fig. 6A, right). We observed a significant effect of group $F(2, 17) = 4.8672$, $P = 0.0213$, and
Movement correction and adaptation

subsequent pair-wise comparisons confirmed a significantly smaller after-effect in the group with left parietal damage compared with the left normal control and left frontal damage groups ($P < 0.05$ in both cases). It is unclear what this small, but obvious after-effect in the group with left parietal damage is related to, but it could be associated with the small improvement in movement direction in this group during the first few exposure cycles. This possibility has been previously discussed (Della-Maggiore et al., 2004).

Movement correction in response to the novel visuomotor rotation

The poor adaptation of initial movement direction, but smaller position errors during the exposure session for the patients with left parietal damage suggests that they relied on correcting their movements during the trial to bring the cursor to the target. This was indeed the case, as can be seen from the movements of our representative subject with left parietal damage on the last exposure cycle (Fig. 5C) and the larger curvature across all subjects in the group with left parietal damage for the entire exposure session (Fig. 6B, right). While curvature did decrease over time, even on the last cycle, it did not reach the same level as the left normal controls or patients with left frontal damage. Furthermore, final position errors in the patients with left parietal damage remained small for the entire exposure session as a result of the online corrections made by these subjects. Our $\text{Group} \times \text{Cycle}$ (first exposure, last exposure) interaction did not reach significance $F(2,17) = 2.8534, P = 0.0854$ for curvature. However, we observed a strong group effect $F(2,17) = 5.3588, P = 0.0157$, with follow-up tests showing larger curvature in the left parietal damage group compared with the left normal control and left frontal damage groups ($P < 0.05$ in both cases). Tests on final position error also showed a strong effect of group $F(2,17) = 7.6613, P = 0.0042$, with significantly smaller errors for the group with left parietal damage compared with the other two groups ($P < 0.05$ in both cases).

The magnitude of the correction for our subjects on the first and last exposure cycles is shown in Fig. 7A. Patients with left parietal damage made larger corrections when they were first exposed to the rotation, and continued to do so even on the last cycle. In contrast, the left normal controls and subjects with left frontal damage showed a marked decrease in correction magnitude due to their improvement in movement direction as a consequence of adaptation to the visuomotor rotation. We did not observe a significant $\text{Group} \times \text{Cycle}$ (first exposure, last exposure) interaction $F(2,17) = 1.0179, P = 0.3823$ but a strong group effect $F(2,17) = 11.9984, P = 0.0006$ was revealed. A priori comparisons to test for group differences during the first and last exposure cycles revealed a significantly larger correction magnitude in the group with left parietal damage relative to the other two groups at both these time points ($P < 0.05$ in all cases). Figure 7B shows that correction gain was high and fairly similar for the subjects of all three groups. We confirmed this observation statistically with a non-significant group effect for correction gain $F(2,17) = 0.4552, P = 0.64$ (Fig. 7C). Importantly however, Fig. 7B also highlights the larger direction errors and bigger corrections for the patient with left parietal damage during the entire exposure session.

In summary, the patients with left parietal damage showed a clear deficit in adapting their movement direction in response to the visuomotor rotation. Instead, to a large extent, they relied on updating their movements online to achieve the target position. In contrast, left frontal damage spared both, adaptation and online correction processes.

Discussion

We aimed to dissociate the neural substrates critical for updating ongoing movements in response to errors and adapting subsequent movements based on those errors by examining patients with focal damage to frontal or parietal regions in the left and right cerebral hemispheres. We used a single task that introduced a discrepancy between the direction of hand motion and its visual feedback, which enabled us to determine how people correct this trajectory error as their movement progresses, and how they learn from it to improve their performance over time. Only patients with right frontal damage showed a clear deficit in correcting errors during the movement, but their ability to learn from those errors remained intact. In contrast, only patients with left parietal lesions exhibited a deficit in movement adaptation, but online correction in these patients was spared. Our results thus identify distinct and lateralized neural substrates for error correction in response to novel task conditions and error-based motor adaptation.

Results from studies using cognitive tasks have suggested that frontal cortical regions are important in situations where the association between stimuli and responses are not definitely established, or more simply, when a task has not been learned (Miller and Cohen, 2001). Task success under such novel and unlearned conditions often requires the inhibition of a predominant response and the formulation of a new one in accord with the modified task conditions (response switching or action ‘reprogramming’). Recent research has suggested that right frontal regions, together with their connections to the basal ganglia, are particularly important for these functions (Aron and Poldrack, 2006; Aron et al., 2007; Mars et al., 2007; Swann et al., 2009; Neubert et al., 2010). Our current results may extend these ideas to conditions where an ongoing targeted-reaching movement has to be updated online in response to an unexpected trajectory error introduced through a novel visuomotor rotation. Our patients with right frontal damage showed a reduced ability to modify the predominant baseline response and initiate the response appropriate for the novel stimulus. We suggest that online responses to novel stimuli in cognitive or motor tasks might engage similar neural substrates in right frontal regions.

It is interesting to note that using positron emission tomography, Shadmehr and Holcomb (1997) observed increased regional cerebral blood flow signals in frontal regions, particularly dorsolateral prefrontal cortex (BA 46), in the right hemisphere when subjects were first exposed to an unfamiliar, but stable velocity dependent force field as they performed reaching movements with their right hand. They suggested that this activation was associated with the early learning of the novel dynamics. Their analysis was relative to a random, non-stationary force field that was unlearnable but had other task components such as error...
correction, which were also present in the stable force conditions. However, the neural correlates of error correction in random force fields are unclear and it is likely that subjects respond to such forces largely through co-contraction, without the formulation of a specific response that adequately corrects for the magnitude of the error (trajectory deviation). In contrast, while some co-contraction is expected during the early learning of unfamiliar, but stable forces, it is likely that subjects are also able to produce more accurate corrective responses under such conditions. Thus, it is unclear whether the right frontal activation seen by Shadmehr and Holcomb (1997) was related entirely to early learning or could also be associated with the formulation of an appropriate corrective response to the unexpected trajectory deviation when the stable force field was initially applied. Shadmehr and Holcomb (1997) also showed that as subjects adapted to the force field, the activation in the right frontal regions was gradually reduced. This decrease could be potentially explained by the fact that trajectory corrections were not required in the late learning phase because subjects compensated for the force fields and made straight movements to the target. Our patients with right frontal damage showed a poor ability to correct their movements during the trial, but were still able to learn the novel visuomotor conditions, suggesting, at least in our study, a more critical role for these regions in updating ongoing actions rather than motor learning.

It is important to emphasize that we do not suggest that right frontal regions are where the process of action updating occurs. Rather, this process is likely to rely on a network of regions, quite possibly including the basal ganglia and other cortical regions. Indeed, Smith et al. (2000) showed that patients with basal ganglia atrophy in Huntington’s disease failed to make online corrections when exposed to a novel dynamic environment in which arm movements were perturbed by a force pulse. Moreover, these patients also showed a deficit in correcting self-generated errors and stopping accurately on the target even when movements were not perturbed. Thus basal ganglia circuits also appear to be a key component of the error correction circuitry. It is highly likely then, that these processes are mediated by complex interactions within right frontal–basal ganglia regions.

In contrast, our findings suggest that the process of learning from visuomotor errors and adapting subsequent movements depends on mechanisms that appear to be distinct from the right hemisphere mechanisms involved in error correction. Only patients with left parietal damage showed a deficit in adapting movement
direction when exposed to the visuomotor rotation over a long period of time. Moreover, these patients showed larger magnitude corrections and better accuracy than the healthy control subjects throughout the entire exposure session. These findings are in line with our recent results in which we demonstrated a similar adaptation deficit, but intact accuracy, in patients with left parietal damage when making movements with their contralesional arm (Mutha et al., 2011). Our patients with left parietal damage used their ipsilesional, left arm to perform the task, and were still unable to completely adapt to the novel conditions, similar to the observations of Schaefer et al. (2009) in patients with damage to widespread regions of the left hemisphere. This strongly suggests that left parietal regions influence motor adaptation regardless of the effector used to perform the task.

Our findings are consistent with the idea that as actions are learned and become more ‘automatic’, they might be represented in left parietal regions. Shadmehr and Holcomb (1997) elegantly showed systematic changes in the regional cerebral blood flow signal as subjects adapted to, and consolidated, the dynamics of a force field. As described earlier, these authors showed increased activation in the right frontal regions upon early exposure to the perturbation. However, when subjects completely adapted to the force field and were tested with the same arm in the same field after a delay (~5.5 h), the neural activation profile was dramatically different. Parietal and premotor regions in the left hemisphere demonstrated strong activation during the retest. Shadmehr and Holcomb (1997) argued that while left premotor activation was perhaps associated with retrieval processes, left parietal activation most likely reflected where the learned dynamics were represented. This idea is also consistent with several reports of deficits in patients with ideomotor limb apraxia, a disorder that usually occurs following left hemisphere damage, most commonly, left parietal regions. These studies have suggested that these deficits result from damage to stored representations of highly learned, skilled actions (Haaland et al., 2000; Buxbaum et al., 2007; Goldenberg, 2009).

On a more general level, examining adaptation to a visuomotor rotation also informs us about the nature of the mechanisms underlying the planning of movement direction. The rotation introduces a directional bias around the hand and requires adjustments to our movement plan on subsequent trials in order to drive the cursor straight to the target. Our results indicate that this process is critically dependent on left parietal regions. The failure to adapt initial movement direction over time in our patients with left parietal damage suggests that their motor plan remained inaccurate throughout the exposure session. Importantly, our current and previous (Mutha et al., 2011) results together point to the possibility that left parietal regions might mediate the planning of movements for both arms. These results are consistent with the proposition that the left hemisphere, in general, is specialized for motor planning (Rushworth et al., 1998, 2003; Haaland et al., 2004; Sainburg, 2002, 2010). We have hypothesized that this occurs through a specialized ability to predict and account for dynamic interactions between limb segments during movement, based on an internal representation of the limbs dynamic properties (Sainburg and Kalakanis, 2000; Bagesteiro and Sainburg, 2002; Sainburg, 2002). Supporting this idea of a left hemisphere specialization for predictive control, our previous results have shown deficits in measures of motor performance and coordination during the early phases of movement in patients with left hemisphere damage (Schaefer et al., 2007, 2009a, b). Furthermore, we recently showed similar impairments during simple targeted reaching in patients with ideomotor apraxia following left hemisphere lesions, a majority of whom had lesions that included the parietal lobe (Mutha et al., 2010). These results collectively, strongly point towards the possibility of left parietal mediated planning of actions regardless of the effector being used, consistent with the recent proposal of Oliveira et al. (2010).

Finally, our results may appear to be inconsistent with studies that have used the ‘double step’ paradigm to demonstrate deficits in online correction with parietal disruption (Desmurget et al., 1999; Pisella et al., 2000; Reichenbach et al., 2011). In this task, the target that subjects are reaching toward is unpredictably displaced to a new location, and rapid corrections (120–150 ms after the target jump) are typically observed in healthy individuals. These corrections are relatively difficult to modify or inhibit (Day and Lyon, 2000; Pisella et al., 2000; Johnson et al., 2002; McIntosh et al., 2010), suggesting a strong, well-learned and well-established association between the stimulus (target jump) and the response (correction), perhaps developed through prior real-world experience. Parietal disruption either through transcranial magnetic stimulation (Desmurget et al., 1999; Reichenbach et al., 2011) or lesions (Pisella et al., 2000) impedes this corrective response and results in large position errors. However, our current and previous (Mutha et al., 2011) patients with left parietal damage, as well as patients with left hemisphere damage in general (Schaefer et al., 2009a), showed intact movement accuracy when correcting for errors introduced by unlearned visuomotor rotations. How can these differences be reconciled? As stated above, our contention here is that as an action becomes well learned, it is represented in parietal regions, particularly of the left hemisphere. We suggest that this may also include the set correction to a target jump stimulus. In fact, neural networks (which include left parietal areas) activated during the rapid correction of a target displacement (Desmurget et al., 2001) bear a striking resemblance to those thought to represent learned actions (Shadmehr and Holcomb, 1997). In the current and our previous study (Mutha et al., 2011), parietal damage prevented actions from becoming well-learned and largely reliant on within-trial corrections. In this sense, our current results may actually be consistent with studies demonstrating a disruption of corrections to target displacements with parietal lesions and suggest that these areas are critical for developing and using learned stimulus–response mappings. In contrast, our results show that accurately updating ongoing actions in response to the novel visuomotor stimulus requires intact right frontal regions. However, it remains to be seen whether these findings can be generalized to any novel task conditions. If this is the case, we expect that accurate responses to changing task contingencies such as, say, corrections to a few target jumps that are randomly interspersed within a large number of well-learned baseline trials, may also be dependent on intact right frontal regions. In such cases, we would predict...
a deficit in responding to target displacements with both right frontal and left parietal damage.

In conclusion, our current results show that online correction of unexpected trajectory errors and learning to adapt our movements in response to those errors can occur independent of each other. Our findings are unique in terms of identifying distinct and laterali-

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