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Research Report

Neural correlates associated with intermanual transfer of sensorimotor adaptation

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ABSTRACT

Investigations of intermanual transfer of learning have demonstrated that individuals can transfer acquired motor skills from one hand to the other. The purpose of the current study was to use fMRI to investigate the potential overlap of neural regions engaged during learning and at transfer of learning from the dominant arm to the non-dominant arm during sensorimotor adaptation. Participants performed a visuomotor adaptation joystick task where they adapted manual aiming movements to a 30° rotation of the visual feedback display. They performed eleven blocks (24 trials/block) of right-hand adaptation before performing the task with their left hand (transfer). Participants showed a selective transfer of learning effect: prior right-hand practice led to reduced endpoint errors but not trajectory errors for the left hand. This is consistent with work showing that the right arm is specialized for trajectory control while the left is specialized for endpoint control [Sainburg, R.L., 2005. Handedness, Differential specializations for control of trajectory and position. *Exerc Sport Sci Rev* 33, 206–213.]. Early adaptation processes were associated with activation in frontal and parietal regions, including bilateral dorsal premotor cortex. At transfer, activation was seen in the temporal cortex as well as the right medial frontal gyrus and the middle occipital gyrus. These regions have been observed in other studies during the late phases of sensorimotor adaptation. Integrating these data with the existing literature, we suggest that the left dorsal premotor cortex contributes to trajectory control, while the left visual and temporal cortices contribute to endpoint control.

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1. Introduction

The sensorimotor system must have the ability to adapt in order to deal with the changing demands of everyday life. One common way of studying this adaptive capacity is with

visuomotor adaptation tasks, in which the mapping between visual and motor space is distorted (cf. Welch et al., 1974; Bock, 1992; Pine et al., 1996; Ghilardi et al., 2000). Neuroimaging studies of visuomotor adaptation in human participants have revealed that a variety of cortical and subcortical brain regions

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contribute to this adaptive process, including initial contributions by the primary motor cortex (M1), prefrontal cortex (PFC), parietal cortex, supplementary motor area (SMA), cerebellum, and striatum (Ghilardi et al., 2000; Imamizu et al., 2000; Inoue et al., 2000; Miall et al., 2001; Krakauer et al., 2004; Graydon et al., 2005; Seidler et al., 2006). Later in learning, activation has been observed in the cerebellum, as well as the visual, parietal and temporal cortices (Imamizu et al., 2000; Inoue et al., 2000; Miall et al., 2001; Krakauer et al., 2004; Graydon et al., 2005). These studies have contributed greatly to our understanding of the neural and behavioral mechanisms underlying visuo-motor adaptation. However, the aforementioned studies tested adaptation only with the right (dominant) hand. Investigation of transfer of adaptation from one hand to the other would allow for identification of brain regions associated with the creation of the abstract representation of what is learned during adaptation, regardless of the hand being used, as well as an examination of whether the regions involved with learning are also engaged at transfer.

Studies on the lateralization of brain activity during sequence learning have found evidence for left-hemisphere dominance (Grafton et al., 1998, 2002). Specifically, the left dorsal premotor cortex and the left SMA contributed to sequence learning regardless of which hand was used during practice. These findings support Taylor and Heilman's (1980) (callosal)

access model, which proposes that there is a single controller (defined here as the neural system mediating behavior) for both hands which is lateralized exclusively to the dominant (left) hemisphere. According to this model, when participants first practice with the right hand and then transfer to the left, the right hemisphere gains access to the acquired sequence representation, stored in the left hemisphere, via the corpus callosum (see Fig. 1). This model is based on the work of Liepmann (1905), who first proposed left-hemisphere dominance for motor planning in right-handers (for a recent review on lateralization of motor control, see Serrien et al., 2006).

There is an extensive behavioral literature demonstrating transfer of skill learning between the two hands (Laszlo et al., 1970; Taylor and Heilman, 1980; Parlow and Kinsbourne, 1989; Parlow and Dewey, 1991; Halsband, 1992; Shadmehr and Mussa-Ivaldi, 1994; Teixeira, 2000; Nezafat et al., 2001; Sainburg and Wang, 2002; Schulze et al., 2002; Criscimagna-Hemminger et al., 2003; Wang and Sainburg, 2003, 2004). Work by Sainburg and colleagues on intermanual transfer of learning has led to a refinement of the idea of left hemisphere dominance for motor control. This refinement is based on their dynamic dominance hypothesis, which proposes that the dominant arm is better at trajectory control while the non-dominant arm is better at position control (Sainburg and Kalakanis, 2000; Sainburg, 2002). Although Sainburg and

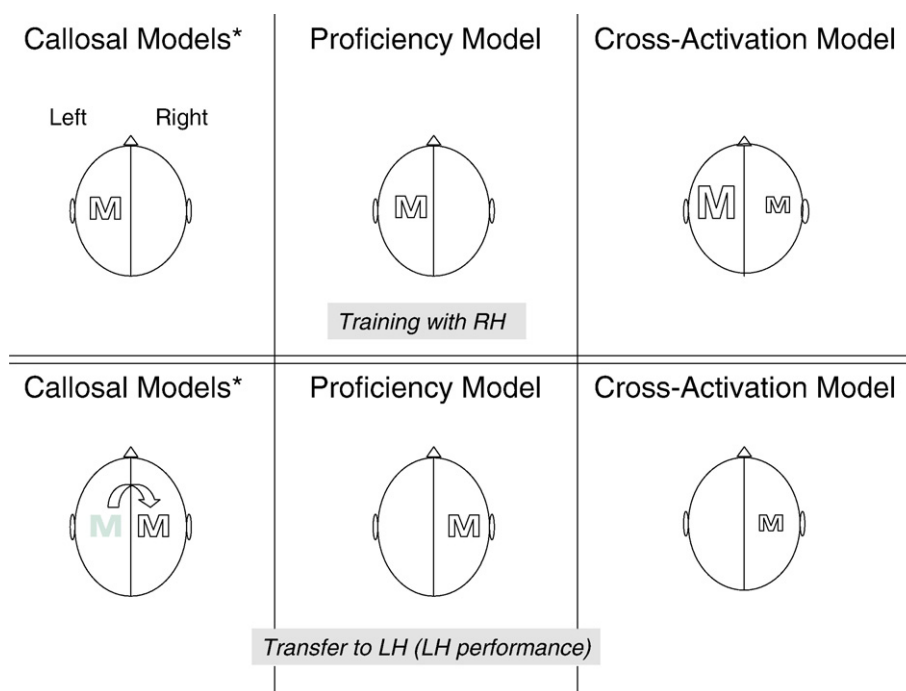


Fig. 1 – Diagram of each model of interlimb transfer. The top row represents activation during right-hand (RH) adaptation for each model, while the bottom row represents activation at transfer with the left hand (LH). ‘M’ illustrates the location of the motor programs used/developed during RH adaptation or at transfer with the LH following RH adaptation. ‘Left’ designates the left hemisphere, ‘Right’ the right hemisphere. * indicates that the predictions for both the original callosal (access) model and the ‘modified’ callosal (access) model are equivalent for right hand adaptation and transfer to the left hand. The callosal (access) model and ‘modified’ version both state that at transfer, the right hemisphere gains access to the acquired representation (note the faded ‘M’), which was stored in the left hemisphere, via the corpus callosum. For the proficiency model, activation at transfer could only occur following LH adaptation, thus there should be no activation at transfer following RH adaptation. The cross-activation model states that during RH adaptation, an ‘inferior’ version of the motor program is created in the right hemisphere (note the smaller ‘m’), and it is this program that would be used at transfer.

colleagues (Sainburg and Wang, 2002; Wang and Sainburg, 2003; Sainburg, 2005) often refer to the two controllers as being for the “left arm” and “right arm”, it is not necessarily the case that each arm’s controller is found in the contralateral hemisphere. In fact, the bulk of the literature suggests a left hemisphere dominance for motor planning and control, regardless of the arm being used (cf. Serrien et al., 2006). Sainburg and colleagues have shown that sensorimotor adaptation differentially transfers from the right to the left hand and likewise from the left to the right hand (Sainburg and Wang, 2002; Wang and Sainburg, 2003). Sainburg and Wang (2002) found that non-dominant (left) arm adaptation to a visuomotor rotation improved trajectory control of the dominant (right) arm adapting to the same transformation. In contrast, dominant (right) arm adaptation improved endpoint position but not trajectory control of the non-dominant (left) arm adapting to the same transformation. Sainburg and colleagues proposed that learned information about trajectory and endpoint position is stored in two distinct memory resources located in each hemisphere (Wang and Sainburg, 2003), with the arm used during adaptation determining the nature of the information transferred across limbs. These behavioral results can be used as a model to make predictions regarding the neural activity associated with sensorimotor adaptation. The theory put forth by the Sainburg group would predict that sensorimotor adaptation is associated with bilateral activation, regardless of the hand used during practice. This is in contrast to what has been shown with sequence learning: namely, a preponderance of left hemisphere activation regardless of the performing hand (Grafton et al., 1998, 2002).

Three distinct models have been proposed to explain the contribution of each hemisphere to the control of hand movements in light of the data on transfer of learning: (i) the aforementioned (callosal) access model, (ii) the proficiency model (Laszlo et al., 1970), which proposes that motor programs are formed and stored contra-laterally to the hand being trained, (iii) and the cross-activation model (Parlow and Kinsbourne, 1989), which proposes that dual motor programs are formed in each hemisphere following dominant hand training. Each model would have unique predictions regarding whether brain activation is unilateral or bilateral at transfer of learning and how this activation overlaps with areas engaged during the adaptation period (for a schematic interpretation of these predictions, see Fig. 1).

The callosal (access) model (and the Sainburg modified callosal (access) model) predicts unilateral activation at transfer which would not normally overlap with activation that occurred during the adaptation period.¹ However, this model, unlike the cross-activation model, leaves open the possibility of brain activation that is independent of the hand being used, as left-hand usage could engage similar regions within the dominant (left) hemisphere that would be activated

with right-hand usage. Thus, it is possible that some activation at transfer may overlap for regions whose function is independent of the hand being used. The proficiency model would predict that brain activity would switch to contralateral, homologous regions from learning to transfer, as it proposes that separate engrams are formed in the hemisphere contralateral to the hand being used. Therefore, this model would be unable to explain any type of overlap in brain activation during learning and at transfer. Finally, the cross-activation model predicts bilateral activation during adaptation, and non-overlapping unilateral activation at transfer. We base this on the proposal by Parlow and Kinsbourne (1989), which states that the non-dominant motor cortex uses an ‘inferior’ motor program independent of the ‘superior’ motor program found in the dominant motor cortex during performance. These authors also suggest that the use of the non-dominant hand would lead to unilateral activation at the non-dominant hemisphere, which would be congruent with activation observed at transfer.

The purpose of the current study was to determine the activation pattern of brain regions associated with learning and transfer of a visuomotor adaptation task. In doing so, we hoped to evaluate the models of hand controllers described above with regards to their specific predictions of brain activation patterns during adaptation and transfer. Specifically, we wished to determine to what extent the brain regions contributing to learning overlap with areas engaged at transfer of learning, if at all. Participants performed a sensorimotor adaptation task with their dominant (right) hand and then subsequently transferred performance to their non-dominant (left) hand. Given the findings of Grafton and colleagues (1998, 2002), we hypothesized overlapping activation in the left hemisphere for both adaptation and transfer, which would argue against the predictions made by the proficiency and cross-activation models of hand controllers. Trajectory control during prism adaptation has been associated with the left dorsal premotor cortex (Lee and van Donkelaar, 2006), and we expected to see similar activation for our visuomotor adaptation task during the learning stage. Furthermore, in line with the dynamic dominance hypothesis (Sainburg, 2002), we predicted that differential activation would be observed for right-hand performance (indicative of trajectory control processes) and left-hand performance (indicative of endpoint control processes) during sensorimotor adaptation.

2. Results

2.1. Behavioral – adaptation

Twenty-five right-handed participants (13 men) between 18 and 30 years of age (mean age 21.4 years, S.D.=2.2 years) participated in this study. In order to verify that transfer of learning occurred, 9 participants (5 men) served as a control group which performed an abbreviated version of the task in a mock fMRI scanner environment, with the remaining 16 participants making up the fMRI group. Data from four participants in the fMRI group were excluded due to excessive head movement in the scanner, and another participant’s data were lost due to technical difficulties. Thus, the

¹ The predictions of activation between the callosal (access) and Sainburg-modified callosal (access) models would be different if transfer of learning went from the left to right hand. With transfer progressing from the right to left hand, the two models are equivalent in their predicted activation patterns.

Table 1 – Condition block order			
Block number	Rotated feedback	Right or left hand	Control group
P1	No	Right (DOM)	Right (DOM)
P2	No	Left (NON)	Left (NON)
B1	No	Right (DOM)	Right (DOM)
B2	No	Left (NON)	Left (NON)
B3	30°	Right (DOM)	Left (NON; 30°)
B4	30°	Right (DOM)	Left (NON)
B5	30°	Right (DOM)	
B6	30°	Right (DOM)	
B7	30°	Right (DOM)	
B8	30°	Right (DOM)	
B9	30°	Right (DOM)	
B10	30°	Right (DOM)	
B11	30°	Right (DOM)	
B12	30°	Right (DOM)	
B13	30°	Right (DOM)	
B14	30°	Left (NON)	
B15	No	Left (NON)	
B16	No	Left (NON)	

P=practice block (no scanning), B=scanning block. 30°=adaptation blocks with rotated feedback.
DOM=dominant hand, NON=non-dominant hand.

adaptation and transfer data below are from eleven participants (6 males).

The participants were instructed to use the joystick to position a cursor in a target circle which appeared in one of four locations on the screen. For each block, the feedback display was either normal or rotated clockwise about the center start position by 30°. Participants were instructed prior to the initiation of each block which hand (dominant (DOM) or non-dominant (NON)) would be used for the duration of that block. Blocks were performed as presented in Table 1. Sample

spatial trajectories for a single participant are depicted in Fig. 2 at the early stages of adaptation (panel A), late in adaptation (panel B), and at transfer (panel C). In this figure, the open circles represent the location of the targets as viewed by the participant in real time, while the closed circles represent the shifted location of the targets. Adaptation to the rotated feedback is shown through the less distorted trajectories employed in reaching the targets in panel B versus panel A. Representative speed profiles for a single participant from the fMRI group for each trial at the first adaptation block (panel a), last adaptation block (panel b), and at transfer (panel c) are shown in Fig. 3, as well as a representative speed profile from the control group at the transfer block (panel d). For the fMRI group, speed profiles at the transfer block better resembled late adaptation with respect to the number of secondary peaks observed. However, the speed profile of the control group at transfer appeared more like the early adaptation block for the fMRI group versus late learning or transfer.

Two separate measures were used to assess learning (see Fig. 2 for illustration of these two variables): direction error (DE) and initial endpoint error (IEE). Fig. 4 illustrates performance for the fMRI group (diamond symbols) by block for DE and IEE, with the control group's performance at the corresponding blocks (circular symbols). There was no difference between the fMRI and control groups across the baseline blocks [DE: $F_{(1,18)} = .127, p = .726$; IEE: $F_{(1,18)} = .208, p = .654$]. Within the fMRI group, repeated contrasts revealed that performance differed for the fMRI group between P1 and P2 [DE: $F_{(1,10)} = 6.53, p = .029$; IEE: $F_{(1,10)} = 12.70, p = .005$], but not between any subsequent baseline blocks ($p > .05$). A repeated-measures ANOVA (RM ANOVA) with block (16) and trial (24) for DE [$F_{(10,100)} = 17.18, p < .001$] and IEE [$F_{(10,100)} = 27.26, p < .001$] resulted in significant main effects for block, so follow up tests were conducted. Performance differed between the baseline and early adaptation period for the fMRI group (see

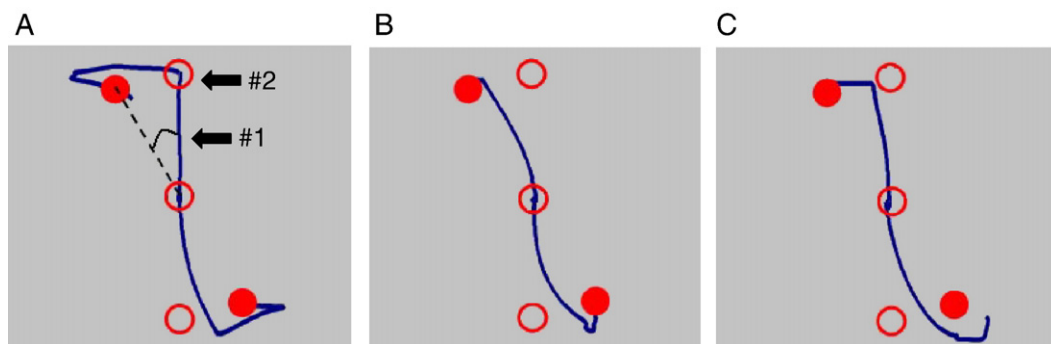


Fig. 2 – Data from a representative participant during adaptation. Panel A depicts single trial spatial trajectories for two trials under the 30° feedback rotation condition early in adaptation. The open circles represent target location in visual space, while the filled circles represent the target locations in joystick space. The spatial trajectory is presented in joystick coordinates as well (participants would view the cursor moving along this path in real time, rotated clockwise by 30°). Panel B depicts single trial spatial trajectories from the same participant performing under the 30° rotation late in adaptation. Learning is evidenced by the straighter trajectories compared to panel A. Panel C depicts single trial spatial trajectories from the same participant at the transfer block. Transfer is reflected through the straighter trajectories than in panel A. The arrow labeled #1 in panel A indicates where direction error (DE) is calculated, and refers to the point along the spatial trajectory at which peak velocity was achieved. DE is the angle between the dashed line from the start to the target position, and a straight line from the start to the position at peak velocity. The arrow labeled #2 indicates where initial endpoint error (IEE) is calculated, which is at the endpoint of the initial ballistic movement towards the target. IEE is the distance from this spatial location to the target.

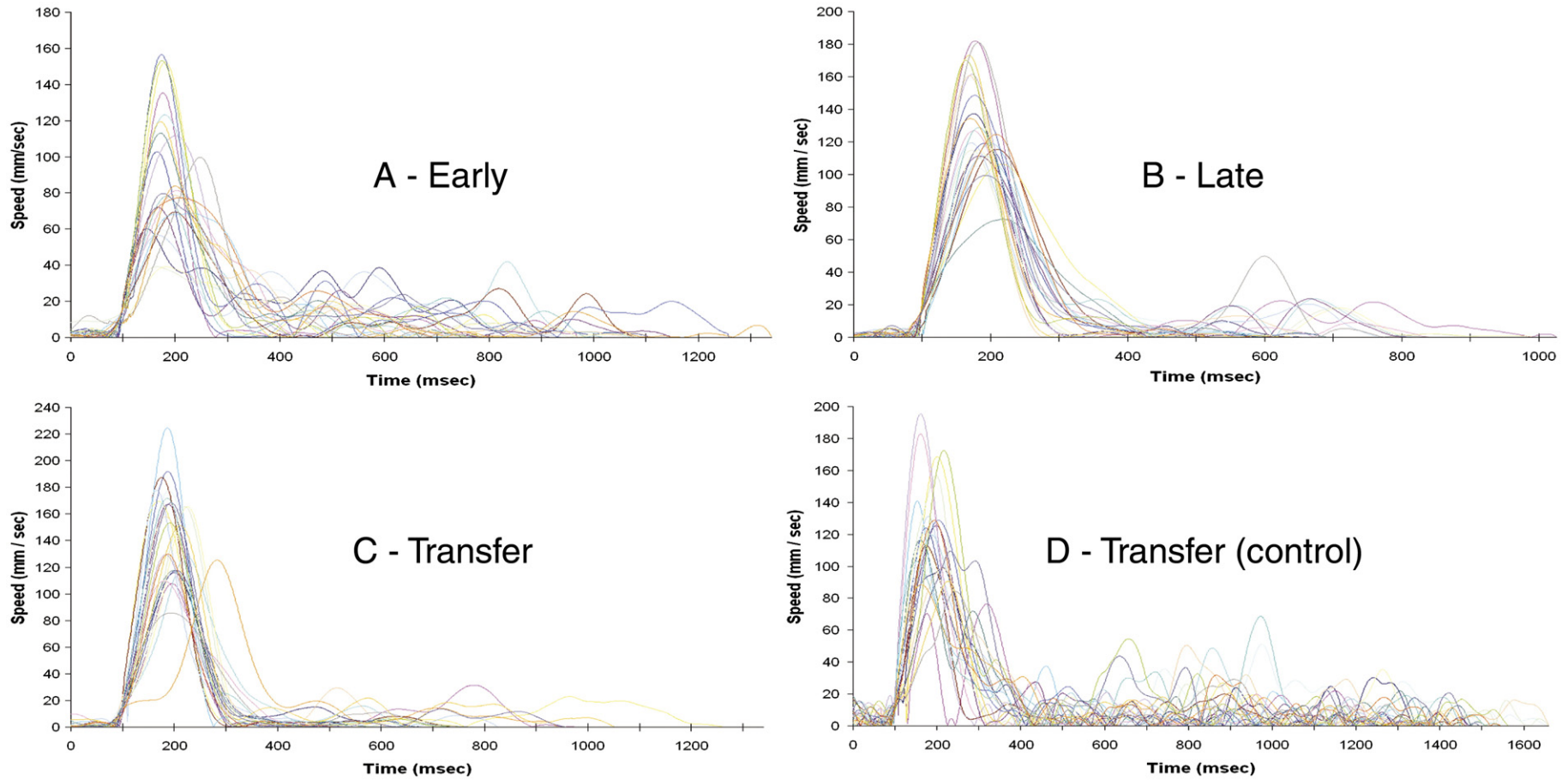


Fig. 3 – Speed profiles from a representative fMRI participant. Panel A depicts each trial’s speed profile at B3 (early adaptation), panel B is for B13 (late adaptation), and panel C is for B14 (transfer). A speed profile from a representative control group participant at the transfer block is also shown (panel D). Time 0 reflects 100 ms before the initiation of movement for each series. Trajectory variability is more evident in panel A through the presence of larger secondary peaks; this variability is reduced at late learning and transfer, suggesting transfer better resembles late versus early adaptation. The control group’s speed profile (panel D) better resembles the fMRI group’s early adaptation versus transfer profile, supporting a transfer of learning effect in the fMRI group.

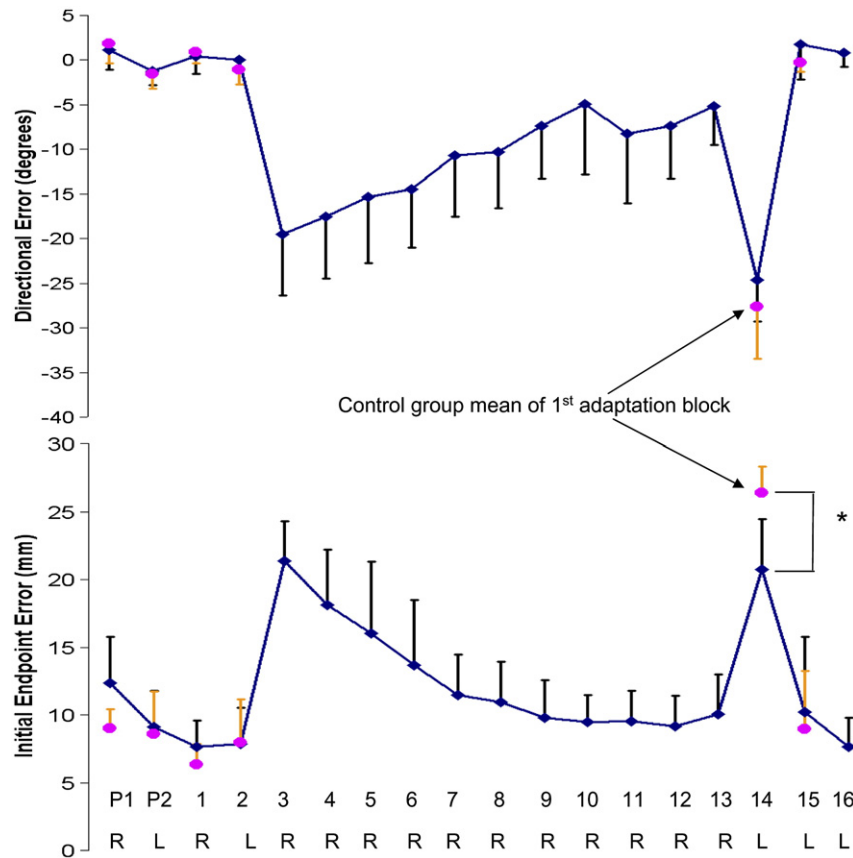


Fig. 4 – Group means and standard deviations for DE and IEE are presented for each block of the experiment. Block number corresponds with scanning block; P1 and P2 indicate pre-scanning blocks where fMRI data were not acquired. The use of right (R) and left (L) hand for each block is noted as well. The performance of the control group is indicated by a circular point at the corresponding blocks. B1 and B2 were baseline blocks, blocks B3–B13 were adaptation blocks in which visual feedback of the cursor movement was rotated 30°, B14 was the transfer block which had rotated feedback, and B15–B16 were the after-effect blocks with normal feedback display. Learning is evidenced across the adaptation period as performance improved (e.g. mean block scores were closer to zero) with practice. The asterisk indicates a significant difference between the fMRI and control groups for IEE at the transfer block ($p < .001$).

Fig. 4), as shown by paired contrasts on block which revealed a significant difference between B2 and B3 ($p < .001$). Within-participants polynomial contrasts² across block for the adaptation period (11 blocks) for each measure showed a significant quadratic fit [DE: $F_{(1,10)} = 13.61$, $p = .004$; IEE: $F_{(1,10)} = 41.95$, $p < .001$], indicating improvements in both performance measures with practice. Furthermore, there was a significant linear trend for trial within each of the first three adaptation blocks, which reflects the improvement in IEE performance as a function of task experience [B3: $F_{(1,10)} = 11.41$, $p = .007$; B4: $F_{(1,10)} = 23.43$, $p = .001$; B5: $F_{(1,10)} = 5.87$, $p = .036$]. Removal of the rotation resulted in after-effects of learning for the fMRI group, quantified by a comparison of the left-hand non-rotated block following adaptation (B15) with the second left-hand baseline

² A polynomial fit was used here as this function had a higher r -value across the adaptation data compared to an exponential function for both DE and IEE (DE: polynomial – $r = .637$, exponential – $r = .447$; IEE: polynomial – $r = .668$, exponential – $r = .417$). However, there was no significant difference for both DE and IEE between the r -values for each function (DE: $p = .293$; IEE: $p = .239$).

block (B2) [block \times trial RM ANOVA; block \times trial interaction for DE [$F_{(11.1, 221.8)} = 1.83$, $p = .050$] and IEE [$F_{(18.6, 372.6)} = 1.73$, $p = .031$]. Fig. 5 shows a representative trial series for a single subject across B15 and B2 for both DE and IEE. There were no differences between the fMRI and control participants at B15 for either behavioral measure, suggesting that the after-effect observed for the fMRI group was not particularly strong [see Fig. 4; trial \times group RM ANOVA; IEE: $F_{(1,18)} = .862$, $p = .336$; DE: $F_{(1,18)} = 1.18$, $p = .291$].

2.2. Behavioral – transfer

To assess the benefit of right-hand practice on left-hand performance, we compared the control group's left-hand adaptation block (B5) to the fMRI group's transfer block (B14). A group \times trial ANOVA revealed no group main effect for DE [$F_{(1,18)} = .253$, $p = .633$]. However, there was a group difference for the IEE measure, with the fMRI participants showing superior performance to the control group after prior exposure to the rotation perturbation [$F_{(1,18)} = 19.2$, $p < .001$] (see Fig. 4).

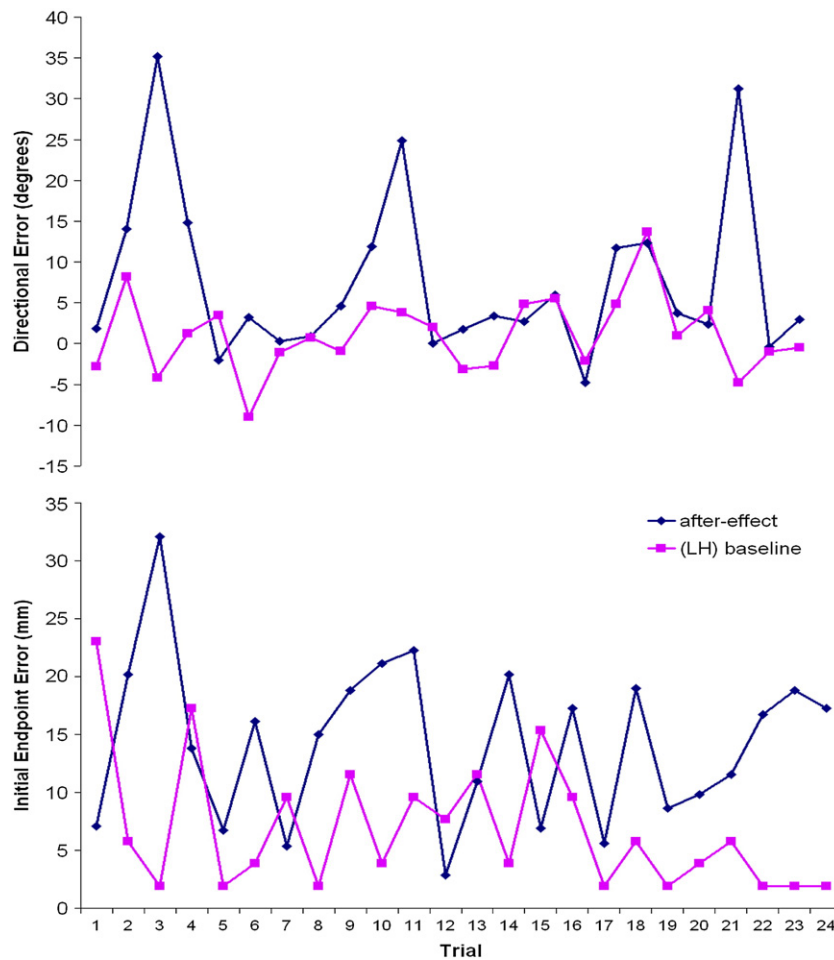


Fig. 5 – Trial by trial performance of a representative fMRI participant for B2 and B15. For the fMRI group, there was a significant block \times trial interaction for DE ($p=.050$) and IEE ($p=.031$) with this interaction being driven by performance across the block, reflecting an adaptive component rather than a strategic compensation.

We also examined the within-group transfer effect by comparing performance at B14 minus that at the left-hand baseline block (B14–B2) to the 1st adaptation block (minus the right-hand baseline block (B3–B1)) for each behavioral measure. For DE, there was a significant difference between the two scores reflecting a slightly greater effect at transfer [$t_{(1,10)} = -2.26$, $p=.050$]. However, for IEE there was no difference between the two scores [$t_{(1,10)} = -.752$, $p=.469$].

2.3. fMRI – early adaptation activation

Early adaptation (see Table 2: novelty contrast and early exponential contrast) was associated with bilateral activation at different regions within frontal and parietal cortices, among other areas. Frontal regions activated included middle frontal gyrus (bilateral), right inferior frontal gyrus, and right pre-supplementary motor area; parietal regions included right inferior parietal lobule and precuneus (bilaterally). The middle frontal gyrus (bilateral) and right pre-supplementary motor area activations are overlaid onto an anatomical slice in Fig. 6 with the percent signal change averaged across each block shown in the lower portion of the figure. The coordinates of local maxima are presented in Table 3.

2.4. fMRI – late adaptation activation

Late adaptation was not associated with any significant brain activation when compared to the early adaptation phase (see Table 2: late exponential and adapted contrasts). However, the conjunction early–late analysis (see Table 2) showed activation in the right cerebellum, the parahippocampal gyrus, and the left insular cortex (see Table 4), indicating that these areas were equally engaged during both the early and late stages of adaptation.

2.5. fMRI – activation at transfer

Brain activation during transfer of learning (determined with the transfer 2 contrast; no regions reached significance using the transfer 1 contrast; see Table 2 for contrast descriptions) was localized to the temporal cortex bilaterally as well as the right medial frontal gyrus. These areas are overlaid onto anatomical slices in Fig. 7, and the coordinates of local maxima presented in Table 5. DE was not correlated with activation at transfer (DE regression analysis, see Table 2). This was as expected, since participants did not exhibit significant intermanual transfer of learning on this measure. However,

Table 2 – Contrast design for each comparison

Contrast name	Blocks/contrasts compared	Location of results
<i>Early adaptation</i>		
Novelty	B3>B1	Table 3, Fig. 6
Early exponential	B3–B13: Decaying exponential function	Table 3, Fig. 6
<i>Late adaptation</i>		
Adapted	B13>B3	No suprathreshold voxels
Late exponential	B3–B13: Increasing exponential function	No suprathreshold voxels
<i>Transfer</i>		
Transfer 1	B14>B16	No suprathreshold voxels
Transfer 2	B14>B2	Table 5, Fig. 6
<i>After-effects</i>		
After-effect 1	B15>B14	Table 7
After-effect 2	B15>B2	No suprathreshold voxels
<i>Conjunction</i>		
Early–Late	B3 and B13	Table 4
Early–Transfer 1	‘Novelty’ and B14	No suprathreshold voxels
Early–Transfer 2	‘Early exponential’ and B14	No suprathreshold voxels
Late–Transfer 1	‘Adapted’ and B14	No suprathreshold voxels
Late–Transfer 2	‘Late exponential’ and B14	No suprathreshold voxels
<i>Performance regression with transfer activation</i>		
DE	B14	No suprathreshold voxels
IEE	B14	Table 6, Fig. 7
<i>Early vs. Transfer</i>		
Early>Transfer	‘Novelty>Transfer 2’	No suprathreshold voxels
Transfer>Early	‘Transfer 2>Novelty’	Table 8

activation in the left middle temporal gyrus and the right middle occipital gyrus was significantly correlated across individual participants with IEE (*IEE regression analysis*, see Table 2) at transfer (see Table 6). A conjunction analysis between early adaptation (both *early exponential* and *novelty contrasts*) and transfer showed no activation. Similarly, conjunction analyses between each late adaptation contrast and activation at the transfer block showed no overlap. No regions reached significance for the *Transfer 2>novelty* contrast. However, an examination between early adaptation and transfer (*novelty contrast>Transfer 2*) showed activation at the left inferior parietal lobule (Table 5).

2.6. fMRI – after-effects

After-effects of learning (observed only with the *after-effect 1* contrast, see Table 2) were associated with brain activity in the left superior temporal gyrus and right cuneus (see Table 7 for coordinates of local maxima).

3. Discussion

In an effort to determine the brain regions contributing to sensorimotor adaptation, we measured fMRI BOLD activation while participants learned a visuomotor adaptation task with the right hand and subsequently transferred performance to the left hand. We found bilateral engagement of prefrontal, premotor, and parietal cortex and right-lateralized cerebellum and temporal cortex associated with sensorimotor adaptation, as has been found previously (Clower et al., 1996; Inoue et al., 1997, 2000; Ghilardi et al., 2000; Imamizu et al., 2000; Krakauer et al., 2004; Seidler et al., 2006). The right temporal cortex showed significant activation during transfer of learning to the left hand, accompanied by the right medial frontal gyrus, right middle occipital gyrus, and the left perirhinal cortex; these areas did not overlap with those engaged during the adaptation period in the current study. In the ensuing discussion, we place these findings into the context of the current literature on sensorimotor adaptation and the models of hand controllers outlined in the Introduction.

3.1. Early and late adaptation

fMRI participants’ behavioral performance measures (DE and IEE) across the adaptation period (B3–B13) demonstrated that they learned to adapt to the visuomotor perturbation. The two contrasts which identified the brain areas associated with early adaptation examined (a) the *novelty* of the task (B3>B1), and (b) the sustained learning effect across the adaptation period (the *exponential* contrast). The *novelty* contrast identified activation in the inferior frontal gyrus (IFG), localized to the right hemisphere. The sustained early adaptation contrast resulted in bilateral, highly symmetrical activation of the dorsal premotor cortex (middle frontal gyrus, PMC), among other regions. Recent work has demonstrated that the left dorsal premotor cortex plays a role in on-line movement corrections during prism adaptation (Lee and van Donkelaar, 2006). Transcranial magnetic stimulation (TMS) applied to the left dorsal premotor cortex at the onset of movement resulted in straight trajectories (i.e. the typical “hooking” corrections evident in Fig. 2 were not observed) and a reduced rate of adaptation. In contrast, TMS applied to the dorsal premotor cortex at the end of each movement did not disrupt the adaptive process, suggesting that this region plays a role in on-line trajectory adjustments but not trial-to-trial learning (Lee and van Donkelaar, 2006). TMS work by Praeg and colleagues (2005) has recently demonstrated that the right PMC is not involved in associative sensorimotor learning, but rather plays a more general role in movement preparation. Combined, these data suggest that the left dorsal PMC makes a specific contribution to trajectory adjustments during adaptation, while the right may play a more general role in execution.

The anterior cingulate cortex may also contribute to movement corrections in this task, since it has been suggested to be part of an active monitoring system that reacts to the presence of conflict and/or errors. This interpretation of anterior cingulate cortex function has been developed using reaction time tasks (Gehring et al., 1993; Carter et al., 1998; Botvinick et al., 1999; Gehring and Knight, 2000; Yeung et al., 2004), but work

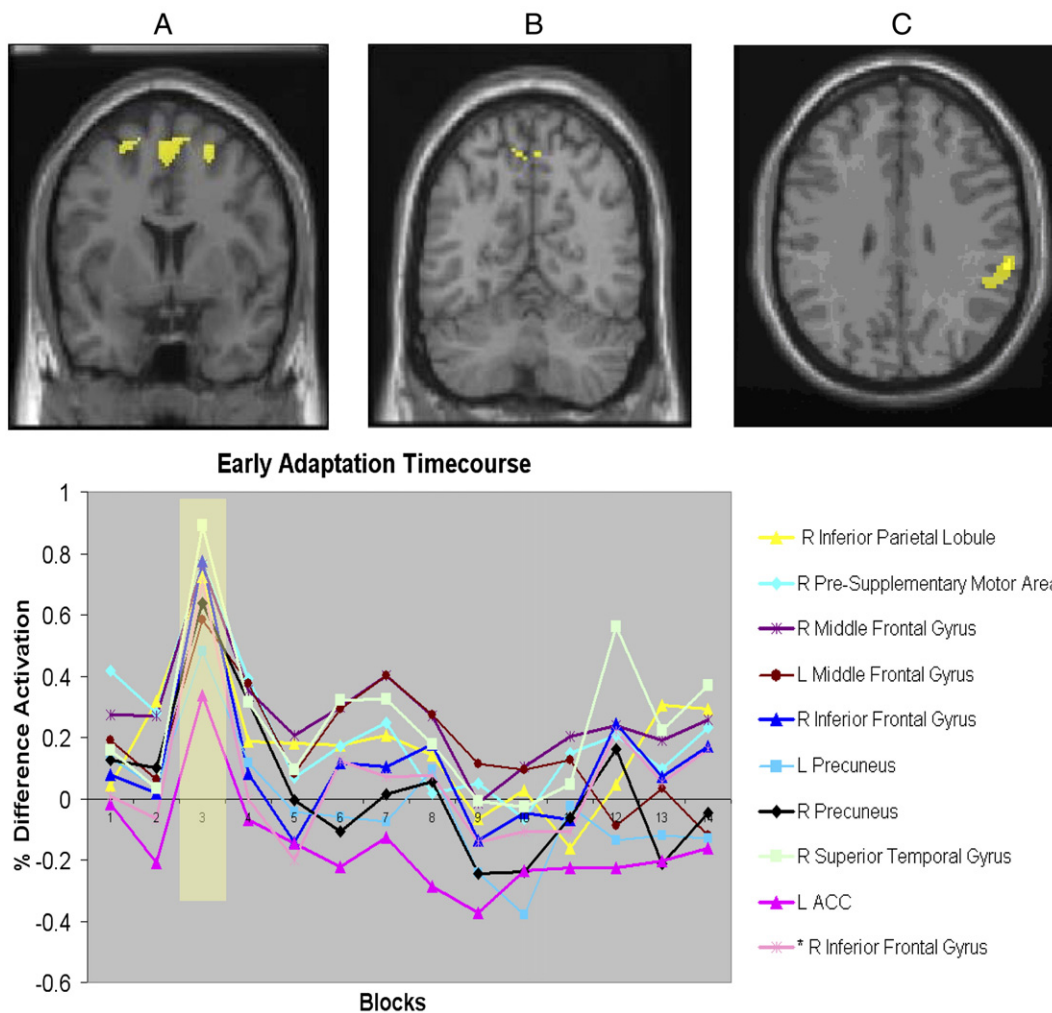


Fig. 6 – These images present activation at (A) the left middle frontal gyrus, right pre-supplementary motor area, and right middle frontal gyrus ($y=5$), (B) bilateral precuneus ($y=-62$), and (C) right inferior parietal gyrus ($z=31$) during early adaptation. Left in this image corresponds to participant's left. The percent signal change for all regions participating in early adaptation processes are presented in the panel below, with activation at the first adaptation block highlighted in yellow.

showing its activation in motor learning paradigms supports this idea as well (Grafton et al., 1998; van Mier et al., 1998; Contreras-Vidal and Kerick, 2004; Graydon et al., 2005; Seidler et al., 2006).

Similar to our previous neuroimaging work with this task, we found right lateralized activation in the inferior frontal gyrus, middle frontal gyrus, premotor and inferior parietal cortex early in learning. We have previously proposed that this network contributes to the spatial cognitive processes contributing to adaptation, particularly in terms of spatial working memory and spatial attention (Seidler et al., 2006).

We did not find any brain regions that consistently increased their activation across the course of the adaptation period. This might be because both behavioral performance measures showed that adaptation had reached a plateau by late practice, with minimal improvements observed across the final blocks of adaptation. These minimal improvements suggest the possibility that participants may have reached an overlearned state, and the lack of activation here may reflect more efficient hand control. Conversely, it may be that our

paradigm was not long enough to reach a late learning stage. It is important to note that the definition of late learning used here is relative to the parameters of our study. Late learning occurring over hours or days may lead to very distinct patterns of activation. For example, other imaging studies in which late adaptation was measured across hours or days showed significant activation of the cerebellum, as well as visual, parietal, and temporal cortices (Inoue et al., 1997; Imamizu et al., 2000; Krakauer et al., 2004; Della-Maggiore and McIntosh, 2005; Graydon et al., 2005). It is thought that this later activation reflects visuo-spatial processing in the aforementioned cortical regions and storage of the new internal model in the cerebellum (Imamizu et al., 2000; Graydon et al., 2005). Our results do not suggest that no areas were engaged during the late adaptation period of our study, only that there were no areas which displayed increasing activation. By definition, the conjunction analysis between activation at the first and final adaptation blocks shows areas which were equivalently engaged at each stage of the adaptation period. We did find that the right cerebellum (H IV/V), the right parahippocampal

Table 3 – Regions engaged in early adaptation

Anatomic location	BA	Coordinates of peak	Pseudo t score
<i>Frontal</i>			
R IFG ^a	45	50, 25, 1	6.0
R IFG	44	48, 13, 23	6.4
R PreSMA	6	6, 5, 61	6.5
R MFG	6	26, 3, 55	6.1
L MFG	6	-26, 5, 55	5.8
<i>Parietal</i>			
R IPL	40	61, -32, 29	5.9
L PREc	7	-4, -57, 54	5.4
R PREc	7	4, -55, 56	5.4
<i>Others</i>			
R STG	22	54, 11, -4	5.3
L ACG	24	-2, 17, 25	5.1

BA=Brodman area; IFG=inferior frontal gyrus; PreSMA=pre-supplementary motor area; MFG=middle frontal gyrus; IPL=inferior parietal lobule; PREc=precuneus; STG=superior temporal gyrus; ACG=anterior cingulate gyrus.

^a 1st adaptation block>baseline block contrast; all other areas from exponential contrast.

gyrus, and the left insular cortex exhibited steady activation throughout the practice session. As this conjunction was made without reference to the baseline blocks, the results may instead reflect basic motor execution processes, rather than adaptation, as the *novelty* contrast did not reveal activation in these areas. However, the areas identified in this *conjunction analysis* have been attributed to adaptation in other studies (e.g. Graydon et al., 2005; Seidler et al., 2006).

It should also be noted that any study of learning is confounded by time, a factor that is independent of the effects of learning. In the present study, it could be argued that the results may be due to any one of multiple non-specific effects (e.g. subject fatigue, scanner drift, etc.). However, we do not believe this to be the case in the present study, as the presentation of a 30-s visual fixation period within each run both before and after each block of trials would have allowed the participants to rest and would account for scanner drift issues. Additionally, participants' motor performance did not reveal signs of fatigue, such as increasing error with practice. Moreover, we tested and analyzed baseline performance blocks both at the beginning and at the end of the experiment, allowing us to account for the effects of time.

3.2. Intermanual transfer of learning

Participants developed a new mapping between visual and motor space to compensate for the rotated feedback, which could be used by either hand controller following DOM hand training. This agrees with the literature suggesting left hemisphere dominance for motor planning and control regardless of the arm being used (cf. Serrien et al., 2006). Sainburg and Wang (2002) have demonstrated that, following DOM adaptation, transfer of learning to the NON arm was apparent only in final position accuracies, not in the movement trajectory. Our data replicate these results, since DE

(measure associated with the movement trajectory) did not show transfer from the DOM to the NON hand, but IEE (measure of endpoint control) did. Furthermore, the within-subject comparison of the transfer and adaptation scores (B14–B2 score versus B3–B1 score, respectively) shows slightly greater impairment of performance for DE, unlike the IEE scores (Table 8). The difference between these scores for each measure reflects a greater impairment for trajectory accuracy versus endpoint proficiency when using the left hand at transfer versus right-hand use when initially exposed to the rotated feedback. This suggests that the controller for each hand uses transferred information differently, depending on its proficiency for specifying particular features of movement. For the within-subject comparison, the non-dominant hemisphere showed difficulty in properly interpreting the transferred trajectory information, which is also an effect that would be predicted by the cross-activation model. This is in accord with Sainburg and Wang's (2002) modified callosal (access) model, which proposes that information stored during learning with either arm can subsequently be accessed by its contralateral homologue.

There were no areas of overlap observed in our study when comparing activation at transfer and at early/late learning. However, there is partial support for the regions engaged at transfer being more related to late learning based on the findings of other visuomotor adaptation studies (Graydon et al., 2005; Seidler et al., 2006). Thus, the question of whether some form of abstract representation was observable through the activation present at transfer can only be partially answered with the present data. Brain activation at transfer was localized primarily to areas within the temporal cortex, along with activation at the middle occipital and medial frontal gyri. These areas are in common with what has been observed previously for the latter stages of sensorimotor adaptation (Graydon et al., 2005), presumably reflecting visuo-spatial refinement of learning. In particular, right medial frontal gyrus activation has been previously associated with the initiation of an inhibitory response to an erroneous decision (Matthews et al., 2005). In the context of our findings, we suggest that this region's engagement at transfer was due to the uniqueness of using the left hand when performing the task in trying to limit erroneous trajectories. We hypothesize that the lack of significant areas engaged for the *transfer 1* contrast may reflect execution-related areas for the left hand which overlap with transfer associated areas. Transfer activation may selectively recruit areas that are involved in both the

Table 4 – Regions engaged via conjunction analysis (early and late adaptation)

Anatomic location	BA	Coordinates of peak	Pseudo t score
R CER H IV		20, -38, -20	4.8
R CER H V		24, -44, -12	4.8
L Insula	22	-36, -14, 14	4.8
R PHG		20, -46, 2	4.7

BA=Brodman area; CER=cerebellum; H IV, H V=hemispheres four and five of the cerebellum; PHG=parahippocampal gyrus.

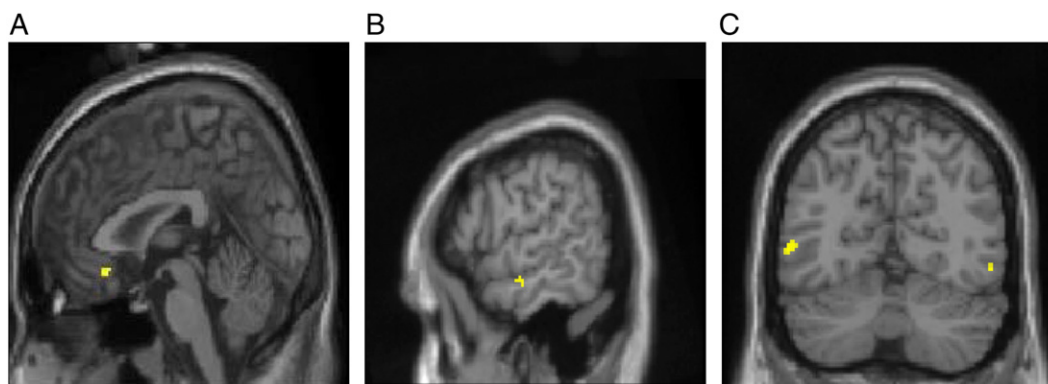


Fig. 7 – These images present activation from the transfer block. Image A ($x=2$) depicts activation in the right medial frontal gyrus, image B ($x=61$) shows activation at the right middle temporal gyrus. Image C ($y=-64$) depicts activity at the left middle temporal gyrus and right middle occipital gyrus for the contrast showing a correlation with IEE performance at transfer. Left in this image corresponds to participant's left.

execution of the left-hand movements, as well as with the contextual recall of an already acquired recalibration process.

Activation of the right middle temporal gyrus (MTG) and the left perirhinal cortex (within the medial temporal cortex) was observed at transfer of learning as well, with the left MTG showing a correlation across participants with IEE at transfer. Other studies have shown temporal cortex involvement during visuomotor learning (Maquet et al., 2003; Della-Maggiore and McIntosh, 2005), with the middle temporal gyrus specifically having been shown to contribute to visuo-spatial perception tasks (Malach et al., 1995; Owen et al., 1996; Wheeler et al., 2000). These tasks involved tracking a moving target, and temporal cortex activation has been attributed to visual motion processing in previous studies of sensorimotor adaptation (Maquet et al., 2003; Della-Maggiore and McIntosh, 2005). However, in our study, targets were stationary. Similar to the interpretations of Graydon et al. (2005), we propose that visual and temporal cortical activation contributes to the learning of visuo-spatial endpoint control during visuomotor adaptation, because these regions are engaged during performance with the NON hand, which is specialized for this type of control.

The two transfer contrasts (*transfer 1* and *transfer 2*) did not reveal re-activation of the right-lateralized prefrontal, premotor, and parietal cortex. We have previously proposed that this network is engaged in the spatial cognitive processes of adaptation, including spatial working memory and spatial attention processes (Seidler et al., 2006). The need for such

cognitive control decreases as a function of practice, and it may be that participants can rely on more automatic processes at transfer of learning as well. Moreover, the contribution of the left IPL decreased from early learning to transfer (*novelty*>*transfer 2*). This brain region has been previously implicated as playing a role in strategic corrections during prism adaptation (Pisella et al., 2004). Overall, the neural landscape at transfer of learning looks more like that of late learning, as opposed to what is observed earlier in adaptation, based on the engagement of similar areas at late learning in other studies (e.g. Graydon et al., 2005) and from our laboratory (Seidler et al., 2006). We also did not see re-engagement of the left dorsal premotor cortex at transfer of learning. As described previously, this area contributes to on-line trajectory adjustments during sensorimotor adaptation (Lee and van Donkelaar). It may be that this structure contributes to the trajectory control that the DOM hand is specialized for (Sainburg, 2005), and is therefore not recruited during NON performance under the rotated feedback because this hand is specialized for endpoint control.

Each of the three models of hand controllers were evaluated in terms of their predictions at transfer with regards to the behavioral and activation results in the present study. The (callosal) access model (Taylor and Heilman, 1980) proposes that there is a single controller for both hands located exclusively within the dominant (left) hemisphere. These authors argue that because of this, the right hand has 'direct' access to the motor program for this skill while the left hand would only have 'indirect' access facilitated via the corpus callosum. In their study, there was a transfer effect from the

Table 5 – Regions engaged in transfer

Anatomic location	BA	Coordinates of peak	Pseudo t score
L PERI	35	-24, -26, -12	5.6
R MeFG	11	2, 27, -11	5.5
R MTG	21	61, -8, -13	5.1
L IPL ^a	40	-38, -50, 52	5.6

BA = Brodmann area; PERI = perirhinal cortex; MeFG = medial frontal gyrus; MTG = middle temporal gyrus; IPL = inferior parietal lobule.

^a Novelty>transfer 2 contrast; all other areas from B14>B2 contrast.

Table 6 – Regions engaged via IEE regression with transfer activation

Anatomic location	BA	Coordinates of peak	Pseudo t score
L MTG	21/37	-54, -61, 5	9.4
R MOG	19	53, -62, -4	8.9

BA = Brodmann area; MTG = middle temporal gyrus; MOG = middle occipital gyrus.

DOM to NON arm. Support for this model would involve unilateral activation at transfer which does not overlap with activation observed during the adaptation period. This model would also allow for nonlateralized control of movement, so that left-hand use could engage similar regions within the left hemisphere that would also be activated with right-hand usage. We hypothesize that access of a stored representation via the corpus callosum would produce brain activation in the storage site that is equal to or less than the activation of the storage site for direct hand control, supporting the unilateral activation prediction at transfer. Our data provide mixed support for this model, as we observed activation at transfer that did not overlap with areas that were engaged during the adaptation period, as well as activation within the non-dominant hemisphere during the adaptation period. Based on our findings, we propose that NON arm endpoint control is localized to the temporal cortex, and DOM arm trajectory control is achieved by the left dorsal premotor cortex.

An issue regarding the modified (callosal) access model involves how different types of information stored in separate hemispheres could be effectively used for the DOM condition but not at transfer. Sainburg’s dynamic dominance hypothesis (Sainburg, 2002) states that the essential difference between DOM and NON arm coordination is the facility in governing control over limb dynamics. Each controller uses learned information differently, depending on its unique proficiency for controlling specific features of movement. For example, endpoint errors for DOM arm movements were either equally accurate to, or slightly less accurate than those of the NON arm (Sainburg and Kalakanis, 2000; Sainburg, 2002; Bagesteiro and Sainburg, 2002), even with the NON hand controller being more adept at specifying endpoint position. Thus while the information may be available to each limb, the ability to use this information is dependent upon each limb’s ability to control specific features of movement.

The proficiency model (Laszlo et al., 1970) predicts the formation of engrams which are stored contralaterally to the trained hand. In their study, there was no transfer of performance improvements from the DOM to the NON hand; however, transfer was observed from the NON to DOM hand (Laszlo et al., 1970). These authors describe the transfer of learning that they observed as being ‘unidirectional’, as it was only observed from NON to DOM. Findings from several studies (Grafton et al., 1998; van Mier et al., 1998), including the present study, do not support this model as we observed a transfer of learning effect for the left hand (i.e. overlapping activation for learning and transfer) as well as bilateral activation that did not overlap areas engaged during the adaptation period.

Table 7 – Regions associated with after-effects of adaptation

Anatomic location	BA	Coordinates of peak	Pseudo t score
L STG	22	-57, -36, 9	5.4
R Cuneus	19	10, -74, 35	5.3

BA=Brodmann area; STG=superior temporal gyrus.

Table 8 – Regions associated with [B5>B3]>[B14>B2]

Anatomic location	BA	Coordinates of peak	Pseudo t score
L IPL	40	-38, -50, 52	5.6

BA=Brodmann area; IPL=inferior parietal lobule.

The cross-activation model (Parlow and Kinsbourne, 1989) predicts the formation of dual engrams in each hemisphere following DOM hand training. At transfer, the NON hand would have access to a separate, yet inferior, motor program found in the non-dominant hemisphere which would be reflected through unilateral activation that does not overlap with activation observed during the adaptation period. According to these authors, this motor program would reflect the non-dominant hemisphere’s ‘inferior’ interpretation of the information obtained from the dominant hemisphere, as each hemisphere’s proficiency for specifying particular features of movement are not congruent. In their study, there was a behavioral transfer effect from the DOM to NON hand. Our behavioral findings support this model, as we observed a between group transfer of learning effect from the right to left hand. With regards to the predicted activation at transfer for this model, Parlow and Kinsbourne suggest that the non-dominant motor cortex uses this ‘inferior’ motor program independently from the dominant motor cortex when the non-dominant hand is required to perform the practiced task. At transfer, we observed brain activation within both hemispheres, which did not overlap with activation from the adaptation period. It may be that the lack of overlapping activation at transfer may reflect no observable fMRI activation for the formation of the inferior motor program. However, we do not believe this to be the case, as the left temporal cortex showed an activation pattern that was independent of the hand being used. While such activation is not predicted by this particular model, our finding of additional areas engaged at transfer (right medial frontal gyrus and right middle temporal gyrus) does fit with this theory.

A potential concern regarding the results in this study involves the changes in kinematics that occurred during the adaptation period and at transfer, as the reported neural activations may be associated with adaptive processes or they may simply reflect the change in kinematics (e.g. reduced error rates and movement times) at these periods (cf. Seidler et al., 2002). We addressed this issue by having participants perform a control experiment in the context of the task used in the present study (Seidler et al., 2004). This control experiment involved inducing performance changes in the absence of learning by having subjects move a joystick to hit targets of differing sizes in a counter balanced fashion using a block design. The variations in target size induced changes in the magnitude of corrective movements and the overall movement durations as typically occur during adaptation.

In this control study (Seidler et al., 2004), we found that better performance (movements to larger targets) was associated with greater activation at the left premotor cortex (BA 6), left sensorimotor cortex, left inferior frontal gyrus, left insular cortex, left putamen, and right caudate. In the present study,

we found activity in the left premotor cortex as well. The findings from Seidler et al. (2004) would predict more activation at this area later in learning for performance effects. In contrast, we found more activation in the premotor cortex early in learning, suggesting a true learning effect. Seidler et al. (2004) also found that poorer performance was associated with greater activation in a number of regions, including the insular cortex and the cerebellum. In the present study, these regions were also engaged through a conjunction analysis of the early and late phases of adaptation. Based on the findings from Seidler et al. (2004), we would suggest that the medial cerebellar activation in the present study may be related to performance effects, such as error correction. The remaining regions identified in the present study did not exhibit significant changes in activation during the control study (Seidler et al., 2004), suggesting that these regions are more likely contributing to the adaptation (and transfer) process rather than reflecting changes in performance.

Another concern is that participants in the current study may have exclusively used strategic control (e.g. on-line or strategic movement corrections; Redding and Wallace, 1996) as opposed to adaptive realignment of control, with the latter often quantified through the presence of after-effects and transfer of learning. The fact that we observed significant intermanual transfer of learning at a between-groups level indicates that adaptive calibration did indeed take place, however. In addition, we have previously shown after-effects using this joystick task following only 72 trials (Seidler et al., 2006), and here participants showed after-effects with the opposite hand from training following 264 trials under perturbed conditions. The slight after-effect observed here is likely due to the use of the left, rather than right, hand during the after-effect period. This idea is supported by a prism adaptation study by Pisella et al. (2004), where left-hand after-effects were measured following right-hand adaptation. At transfer there were small, yet significant after-effects, similar to our data.

It should be noted that this study only addresses a portion of the question regarding which brain regions are engaged at transfer of learning, as adaptation of the left hand followed by transfer to the right hand may have unique brain activation patterns that differ from what we observed in the present study. This seems likely based on the nonuniform transfer effects that have been reported in the behavioral literature (cf. Sainburg and Wang, 2002; Wang and Sainburg, 2003; Sainburg, 2005).

3.3. Conclusions

We found transfer of sensorimotor adaptation from the DOM to the NON arm when performance was assessed in terms of endpoint accuracy, but not in terms of trajectory control. These results are consistent with the dynamic dominance hypothesis (cf. Sainburg, 2005). We found that early adaptation activation was localized to the right prefrontal, premotor, temporal and parietal cortex, along with the bilateral dorsal premotor cortex and anterior cingulate cortex. Areas showing sustained activation over the course of adaptation included the right cerebellum, the left insular cortex and the right

parahippocampal gyrus. The right temporal cortex was re-activated at transfer of learning to the left hand, accompanied by the right medial frontal gyrus, the right middle occipital gyrus, and the left temporal cortex. We propose that the left dorsal premotor cortex contributes to trajectory control for the DOM hand, while the left temporal cortex contributes to endpoint control for the NON hand.

4. Experimental procedure

4.1. Participants

All participants were recruited from the University of Michigan student population and were paid for their participation. Each participant signed an IRB-approved informed consent document and filled out a health history questionnaire prior to their participation. All participants were right-handed as assessed using the 20-item version of the Edinburgh Inventory (Oldfield, 1971; mean handedness score = $.88 \pm .08$).

4.2. Experimental setup and procedure

Participants in the fMRI group lay supine in a 3.0-T magnet (General Electric) at the University of Michigan fMRI center with their head comfortably restrained to prevent excess head movement. They viewed an LCD screen through fMRI-compatible goggles which projected the visuomotor adaptation task and provided real-time feedback of the participant's movements; a dual potentiometer joystick placed on the participant's stomach was used to control a cursor. Participants held the joystick with their thumb and index finger and made small wrist and finger movements to control the joystick; no arm movements were made.

Targets (0.8 cm in diameter) appeared for four seconds in one of four locations: 4.8 cm to the right, left, above, or below the centrally located home position (0.8 cm in diameter). Participants were asked to move the cursor into the target circle as quickly and accurately as possible and to maintain the cursor within the circle until the target disappeared. Upon target disappearance, they were told to release the spring-loaded joystick handle so that it would re-center for the subsequent trial. The next trial began one second later, resulting in an inter-trial interval (from one target presentation to the next) of five seconds. fMRI participants performed 18 blocks (B; see Table 1) of the task (24 trials per block), with 30-s control periods at the beginning and end of each block during which participants maintained their gaze on a central fixation point. Behavioral data were collected across all blocks; fMRI scans were not acquired for the first two baseline blocks because these blocks were used to familiarize participants with the task. Images were also acquired using arterial spin labeling (ASL) for scanning blocks 4 and 12 on seven of the participants. These data were for pilot purposes only and were not presented as part of this paper. In order to verify that transfer of learning occurred, a control group performed a portion of the experiment in a mock MRI scanner environment. The control group performed the adaptation task with their left hand without prior right-hand practice (see Table 1). It should be noted that for both

groups, there was only one ‘transfer’ block due to the fleeting nature of the transfer of learning effect (i.e., performance changes with practice at the task, obliterating the transfer effects).

4.3. fMRI acquisition parameters

Functional images were acquired using a single-shot gradient-echo reverse spiral pulse sequence (Bornert et al., 2000). The field of view was 220×220 mm, voxel size was 3.2×3.2×3.2 mm, TR (repeat time to accomplish a full volume) was 2 s, and TE (echo time) was 30 ms. Forty axial slices were acquired, encompassing the whole brain, including the cerebellum. Structural images were acquired using a T1-weighted gradient echo pulse sequence (TE/TR/FA=3.7 ms/250 ms/90°) with a field of view of 220×220 mm, voxel size=0.86 mm×0.86 mm×3.2 mm.

4.4. Behavioral data processing

The X and Y coordinates from the joystick were recorded at a rate of 100 Hz. We analyzed the joystick data offline using custom Labview 6.1 software (National Instruments) to track behavioral changes with learning. We first filtered the data with a dual low pass Butterworth digital filter (cf. Winter, 1990), using a cutoff frequency of 10 Hz. The resultant joystick path was calculated by computing the square root of the sum of the squared X and Y coordinate data at each time point. The tangential velocity profile was then calculated through differentiation. Movement onset and offset were computed through the application of the optimal algorithm of Teasdale et al. (1993) to the velocity profile for each movement. We used two measures to assess learning: direction error (DE; the angle between a straight line from the start to the target position and a line from the start to the position at peak velocity) and initial endpoint error (IEE; the distance from the end of the initial ballistic movement position to the target). See Fig. 2 for illustration of these two variables. IEE, rather than final endpoint error, was used for parsimony with the work from Sainburg’s group. IEE is equivalent to their ‘final position accuracy’ as their subjects were not allowed to make corrective movements after the first ballistic movement towards the target (personal communication).

A block×trial RM ANOVA was performed for each measure to evaluate performance differences across all blocks for the fMRI participants. We used a group×block×trial mixed model ANOVA to compare performance between the fMRI and control groups. Significant interactions were followed up with simple contrasts. The Huynh–Feldt epsilon (Huynh and Feldt, 1970) was evaluated to determine whether the repeated measures data met the assumption of sphericity ($\epsilon > 0.75$).

4.5. fMRI data processing

The first three volumes of each block were discarded to allow the MRI signal to reach its steady state. We performed movement correction for excessive head motion using the Automated Image Registration (AIR) package (Woods et al., 1998). The results were evaluated to ensure that participants

did not show head motion greater than 5 mm during the experiment. fMRI data were processed and analyzed using Statistical Parametric Mapping 99 (SPM99) (Wellcome Department of Cognitive Neurology, London, UK) and statistical nonparametric mapping (SnPM) (Nichols and Holmes, 2002). Following the computation of a mean functional image for each participant, a structural image was coregistered to this image and spatially normalized to the Montreal Neurological Institute (MNI) template (Evans et al., 1994). These images were then spatially smoothed with a Gaussian kernel with a full width at half maximum (FWHM) of 6 mm.

We created boxcar models time-locked to the effect of interest and convolved with an estimate of the canonical hemodynamic response function. Analyses were performed at the single participant level through SPM99 to determine regions activated in association with task performance. The single-participant contrast images were then taken to a second-level analysis using SnPM for group analysis to calculate pseudo t statistics, using the following parameters: maximum number of permutations (2048), variance smoothing at FWHM=6 mm, and threshold correction at $p < 0.05$ (pseudo $t = 4.56$). SnPM, rather than SPM99, was employed for the group analysis because the use of weighted locally pooled variance estimates (variance smoothing) makes the non-parametric approach considerably more powerful than conventional parametric approaches, as used in SPM99. Furthermore, the non-parametric approach is always valid, given only minimal assumptions. We applied a nonlinear transformation to convert the data from MNI coordinates to Talairach space (Talairach and Tournoux, 1988) (see <http://www.mrc-cbu.cam.ac.uk/Imaging/>). Significant areas of activation were then localized using this atlas, with medial motor areas identified as in Picard and Strick (1996) and cerebellar regions as in Schmahmann et al. (2000). We plotted the percent signal change from baseline and averaged across each block for all scanning blocks within areas identified by each contrast for each participant for illustrative purposes. This function was calculated using data from the single voxel exhibiting the peak activation for each cluster. This was done by computing the mean magnitude of activation for the control period using the average magnitude of activation during the control period prior to the task as well as the average magnitude of activation during the control period following the task. This mean control period activation was subtracted from the mean magnitude of activation during the task period, and this value was then divided by the mean control period activation and changed to a percentile.

4.6. fMRI contrasts – early and late adaptation

We designed two different contrasts to examine the early adaptation period (see Table 2). The first contrast (*novelty contrast*) searched for regions of statistically greater activation at the first adaptation block (B3) versus the baseline DOM block (B1). The second contrast (*early exponential*) evaluated the adaptation period (B3–B13) using an exponential function to search for regions which showed a steady decline in activation over this period, as this function provided the best fit of group learning compared with linear, power, and logarithmic functions. The exponential fit provided weights for said

blocks of 5.95, 2.51, 0.54, -0.57 , -1.21 , -1.57 , -1.78 , -1.90 , and -1.97 (with weighted values for B4 and B12 not included in the analysis for the seven participants in whom arterial spin labeling data were acquired at these blocks), respectively. We used the same exponential function, with the weights reversed (*late exponential*), as well as a second contrast (*adapted*) which examined greater activation at the final adaptation block (B13) versus the first adaptation block (B3), to determine regions contributing to late adaptation (see Table 2). In addition, we performed a conjunction analysis between the activation at the first adaptation block and the last adaptation block to establish which brain regions are in common for both early and late adaptation (*conjunction early-late*; see Table 2).

4.7. fMRI contrasts – transfer of learning and after-effects

We used multiple contrasts to define brain regions associated with transfer of adaptation (see Table 2). The first (*transfer 1*) searched for regions showing greater activation at the transfer block (B14) than the final non-rotated left-hand block (B16). The second contrast (*transfer 2*) searched for regions showing greater activation at B14 versus the baseline NON block (B2). We also performed a conjunction analysis between each early adaptation contrast (B3>B1 and early exponential) and activation at the transfer block (B14) to establish areas equally engaged at transfer and early adaptation (*conjunction early-transfer 1 and 2*). Another conjunction analysis was performed between each late adaptation contrast (B13>B3 and late exponential) and activation at the transfer block (B14) to establish areas equally engaged at transfer and late adaptation (*conjunction late-transfer 1 and 2*). We also tested the transfer effect by searching for regions showing greater activation at transfer versus early adaptation (*transfer 2>novelty*), and vice versa (*novelty>transfer 2*; see Table 2).

Magnitude of transfer achieved by each subject was quantified by calculating each participant's DE and IEE performance at B14 minus B3 for the average of the first three trials for each block. We then tested for brain regions sensitive to individual differences in the amount of transfer with a regression of activation at the transfer block against the aforementioned calculated difference in performance (*DE regression, IEE regression*).

We designed two contrasts to define brain regions specific to participants using their left hand following the adaptation period on non-rotated blocks (after-effects). The first searched for regions showing greater activation at B15 than B14 (*after-effect 1*). The second contrast searched for regions showing greater activation at B15 than the baseline NON block (B2) (*after-effect 2*).

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