Separating brain regions involved in internally guided and visual feedback control of moving effectors: An event-related fMRI study

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Online visual information of moving effectors plays important roles in visually guided movements. The present study used event-related functional resonance imaging to temporally separate neural activity associated with internally guided and visual feedback control of moving effectors. Using a cursor controlled by a computer mouse, participants traced curved lines on a screen. During this movement, vision of the moving cursor was occluded after tracing had begun and then was restored after variable intervals. The results showed that when visual feedback was unavailable, bilateral activation was significantly greater in the basal ganglia, thalamus, premotor cortex and mesial motor areas, peaking at the presupplementary motor area (pre-SMA). In contrast, when visual feedback was available, significantly greater activation was observed bilaterally in the posterior parietal cortex (PPC) and cerebellum and in the middle and inferior frontal gyrus and occipito-temporal cortex in the right hemisphere. Pre-SMA activity was significantly negatively correlated with tracing error when visual feedback was unavailable. In contrast, right PPC activation showed a significant positive correlation with tracing error after visual feedback became available. These findings suggest that the pre-SMA is involved in internally guided movements in the absence of visual feedback, and that the PPC is related to visual feedback control by evaluating online visuomotor error. The current study clarifies the different functional roles of fronto-parietal and cerebellum circuits subserving visually guided movements regarding visual feedback control of effectors.

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Introduction

Although online vision plays a prominent role in visually guided movements, the role of visual feedback of moving effectors has been hotly debated in the past. Behavioral studies have indicated that online vision of moving limbs is not important for successful movements (Goodale et al., 1986; Prablanc and Martin, 1992). These studies showed that reaching movements could be properly corrected online to compensate for target position changes, even in the absence of visual feedback of limbs. However, the importance of online visual feedback from moving effectors has been indicated by several recent studies (Sheth and Shimojo, 2003; Saunders and Knill, 2003, 2004). Saunders and Knill (2003) have indicated the importance of online visual feedback of effectors in motor control. By introducing online perturbation into vision of moving effectors ( cursors), the study revealed that humans use continuous visual feedback from effectors to correct ongoing movements. As motor commands cannot be generated by pure feedback control due to feedback delays, the proposal has been made that human movement is not mediated solely by either feedforward or feedback control, but that online integration of these two processes is essential for visuomotor control (Desmurget and Grafton, 2000; Wolpert and Ghahramani, 2000; Desmurget and Grafton, 2003).

Previous studies have suggested that the posterior parietal cortex (PPC) is involved in feedback control based on internal estimates of effectors (Desmurget and Grafton, 2000; Blakemore and Sirigu, 2003). Studies from neuropsychological patients, functional neuroimaging and virtual lesion studies using transcranial magnetic stimulation (TMS) have indicated that the PPC is involved online correction of visually guided movements in the absence of vision of moving effectors (Desmurget et al., 1999, 2001; Grea et al., 2002). Desmurget and Grafton (2003) proposed that the PPC constitutes a ‘non-visual feedback loop’ by building internal representations of instantaneous hand location and contentiously compared this internal representation and target position online. However, whether the PPC is also involved in feedback control based on online visual information of moving limbs is unclear. Considering that the PPC integrates not only efferent motor copy and proprioceptive information, but also visual feedback in the dorsal visual stream (Andersen et al., 1997), the PPC seems likely to be involved in feedback control based on visual feedback of moving limbs.

Few functional neuroimaging studies have studied online processing of visual feedback for effectors in motion. Inoue et al. (1998) investigated neural correlates in the processing of visual
feedback using positron emission tomography (PET). They compared brain activity accompanied by visual feedback from the hand during a pointing movement to that without such feedback and found several brain regions related to the integration of visual feedback from hand movements to achieve accurate pointing; including the supramarginal cortex, premotor cortex and posterior cingulate cortex of the left hemisphere, the caudate nucleus and thalamus of the right hemisphere and the right cerebellum. However, that study evaluated gross differences in brain activity between two experimental conditions; therefore, distinct processes are blurred together and differential contributions across regions are difficult to discern. In addition, a blocked design allowed subjects to anticipate the presence or absence of visual feedback and might have resulted in different strategies between conditions. The visual feedback components of the observed activity were thus possibly accompanied by feedforward planning. Seidler et al. (2004) also separated brain regions involved in feedforward and feedback control. A speed–accuracy tradeoff (Fitt's Law) was used to manipulate the relative contribution of feedforward and feedback processes, showing that regions including the sensorimotor cortex, cerebellum and thalamus were predominantly involved in feedback control. However, that study also used a blocked paradigm and manipulated overall task difficulty by changing the target size, and the results were thus not specific to visual feedback control of effectors.

Using event-related (ER) functional resonance imaging (fMRI), the current study directly investigated neural correlates of visual feedback control in addition to internal guidance of moving effectors in visually guided movements. Using a cursor controlled by a computer mouse, participants traced curved lines presented on a screen. Tracing tasks employed in the current study offer 2 advantages over the simple pointing movements often used in previous studies (e.g., Sheth and Shimojo, 2002; Saunders and Knill, 2003). First, a tracing task enables continuous quantitative measurement of motor error during trials. Second, it requires continuous estimation of effector’s position during movement. At the onset of the trial, the target curve and initial cursor position were displayed on a screen. As soon as the subject began tracing, the moving cursor image was occluded, then the cursor image was made visible again after variable intervals. Thus, in order to issue appropriate motor commands in the absence of visual feedback, subjects had to internally estimate current position of the invisible cursor and also correct movements when visual feedback became available. ER-fMRI was used to measure dynamic changes in brain activity within single trials and look at temporally separated neural activity of the two subcomponents of visually guided movements: internally guided and visual feedback control of moving effectors. In addition, parametric analysis of ER-fMRI results could reveal the functional roles of activated areas based on subject performance.

Methods

Participants

Subjects comprised 17 neurologically normal adults (10 men, 7 women; mean age, 24.0 years; range, 20–28 years). Of these, 1 male subject was excluded due to excessive head movement during scanning. All subjects were right-handed as assessed by the HN Handedness Inventory (Hatta and Nakatsuka, 1975), displayed normal or corrected-to-normal visual acuity and were familiar with manipulating a computer mouse (daily use; mean, 7.25 years; range, 2–15 years). Informed written consent was obtained from each participant, and the experimental protocol received approval from the ethics committee of the Advanced Telecommunication Research Institute.

Task

Experimental stimuli controlled by a personal computer external to the MRI scanner were presented on a liquid crystal display and projected onto a custom-made viewing screen. Subjects with the head immobilized lay supine in the scanner and viewed the screen via a mirror. At trial onset, a curved line and cursor were displayed on the screen. The cursor was automatically placed at a starting position that alternated between the left and right ends of the curve. Participants were instructed to accurately trace the curve using a computer mouse to move an on-screen cursor as soon as the images appeared. The cursor image was occluded once the subject began the tracing movement. Subjects were required to continue tracing smoothly, estimating the current position on the screen of the now-invisible cursor. At the end of the occlusion period, the cursor image was restored, and the tracing path after the delay was displayed on the screen. Occlusion periods of 2500 ms, 3250 ms and 4000 ms were pseudo-randomly selected. Form of the curved line was generated by pseudo-randomly combining 3 sinusoids of varying amplitude, frequency and phase. Mean size of the curve image was 8.8° wide and 2.1° high. A mouse pad was placed besides the hip of the subject, and the right hand and fingers were used to move the mouse while resting the arm on the bed of the scanner. Participants were unable to see their hand throughout this task. Fig. 1 shows the time-course of the experiment. Before scanning, subjects completed short practice sessions both inside and outside the scanner and were trained to complete tracing in a single movement within 5 s. Cursor image was not occluded during practice sections.

Experimental design

An ER-fMRI-based design was used in which 2 temporally separated events were set to isolate 2 distinct neural activations involved in visually guided movements (Zarahn et al., 1997; D’Esposito et al., 1999). Overlapping hemodynamic responses, evoked by events as little as 2 s apart, can be separated because the blood oxygenation level dependent (BOLD) signal behaves in a roughly linear fashion and can be modeled as linear time invariant (Friston et al., 1995; Rosen et al., 1998). To optimally sample evoked hemodynamic responses using rapid-presentation ER-fMRI, temporal jitter of stimulus onset asynchrony (SOA) was set to around the repetition time (TR), and null events were introduced (Friston et al., 1999). For the null event and inter-trial interval (ITI), a fixation point was displayed at the center of the screen and modeled as the baseline condition. Trial duration was 5000 ms, and ITI was pseudo-randomly chosen from periods of 4000 ms, 5000 ms and 6000 ms. Each session comprised 60 trials, with 15 presentations of the 3 occlusion time conditions, plus null events. The reason for using 3 levels of occlusion time
was to enable higher effective temporal resolution than the actual MRI scanning interval (TR) with the jittered SOA (Dale, 1999). Jittered SOA also enables lower correlations between two regressors, leading to successful separation of temporally overlapped activations. In addition, this might also minimize any anticipatory effect from subjects to the length of occlusion periods, which varied pseudo-randomly from trial to trial. Each subject undertook 2 sessions. Total scanning time of each session was 615 s.

**MRI acquisition**

Scanning was performed using a 1.5-T scanner (Magnex Eclipse 1.5 T Power Drive 250; Shimadzu Marconi). A total of 200 scans were acquired using an echo-planar T2*-weighted gradient echo sequence. Scanning parameters were as follows: TR, 3000 ms; echo time (TE), 49 ms; flip angle, 90°; field of view, 256 × 256 mm; matrix, 64 × 64; 30 axial slices; slice thickness, 5 mm; slice gap, 0 mm, covering the whole brain. T2-weighted anatomical images were also acquired for each subject. Scanning parameters were as follows: TR, 5468 ms; TE, 80 ms; flip angle, 90°; field of view, 256 × 256 mm; matrix, 256 × 256; 30 axial slices; slice thickness, 5 mm; slice gap, 0 mm, covering the whole brain.

**Analysis of behavioral data**

Cartesian coordinates of the on-screen cursor were recorded at 100 Hz using the personal computer outside the scanner. Movement distance and velocity for each trial were measured. Tracing error was defined as vertical distance between the target curve and cursor trajectory at each sampling point. This could measure the time course of motor error within a trial, and the mean value has shown a significant positive correlation with area (square measure) error between the target curve and cursor trajectory. Repeated measures analysis of variance, using the 3 occlusion periods (2500 ms, 3250 ms and 4250 ms) as intra-subject factors, was performed to identify any variations in behavioral data across occlusion time.

![Fig. 1. Time course of the experiment. At trial onset, a curved line and initial cursor position, automatically set to the starting position and alternating between left and right ends of the curve, were displayed on the screen. Participants were instructed to accurately trace the curve using a computer mouse to move an on-screen cursor as soon as the images appeared. As the subject began the tracing movement, the cursor image was occluded. The cursor image was restored at the end of the occlusion period, and the tracing path after the delay was displayed on the screen. Occlusion times of 2500 ms, 3250 ms and 4000 ms were pseudorandomly chosen.](image1)

![Fig. 2. Box-car functions that modeled task and parametric modulation with the tracing error for Events 1 and 2. Note that box-car functions for parametric modulation were mean-corrected to become orthogonal to the task functions, which therefore could have negative amplitudes. Each function was convolved with the canonical hemodynamic response function. Time points were as follows: (a) trial onset (presentation of the target curve and the initial cursor position); (b) movement onset; (c) presentation of the visual feedback of the moving cursor; (d) movement termination; (e) trial termination.](image2)
Analysis of fMRI data

SPM2 software (Wellcome Department of Cognitive Neurology, London, UK) was used for image processing and analysis. The first 6 image volumes were discarded to allow for T1 equilibration, and the remaining volumes were corrected for slice timing, realigned to the first volume. T2-weighted anatomical images, scanned in planes identical to the functional imaging slices, were then co-registered with the first functional image scan. Co-registered T2-weighted anatomical images were subsequently normalized using the stereotactic coordinate system defined by the Montreal Neurological Institute (MNI). Parameters derived from this normalization process were then applied to each functional image. Finally, volumes were spatially smoothed using an isotropic Gaussian filter of $8 \times 8 \times 10$ mm full width at half-maximum.

Statistical analysis was performed using the general linear model (Friston et al., 1995). The 3 occlusion time conditions were collapsed into 1 and modeled 2 temporally separated events to differentiate activations of the 2 periods of each trial, both (1) before and (2) after visual feedback was present (epochs referred to as Event 1 and Event 2, respectively). Onsets of Events 1 and 2 were time-locked to the beginning of the tracing movement and the representation of the visual feedback, respectively. Duration of each event was taken to be the period for which tracing movement continued after the start of each event. Regressors were modeled as box-car functions, convolved with the canonical hemodynamic response function. In addition, parametrically modulated regressors for tracing error were added, the heights of which were linearly related to mean tracing error occurring during each period. Fig. 2 schematically illustrates the box-car functions for each event type. To ensure that activations during either of the 2 periods did not reflect deactivations relative to the other period, activations found in categorical comparisons between the 2 events were inclusively masked with those compared with the baseline period. Results of parametric analysis were also masked inclusively with observed activated areas in categorical comparisons. The 6 movement parameters resulting from the realignment stage were also included in the design matrix as potentially confounding covariates. Before estimation, low-frequency noise was removed using a high-pass filter with a cut-off period of 128 s, and serial correlations among scans were removed with an AR (1) model implemented in SPM2. Contrast images of each subject generated with a fixed-effects model were taken into the group analysis using a random-effects model. Results were converted into Talairach coordinates (Talairach and Tournoux, 1988) using a nonlinear transform (http://www.mrc-cbu.cam.ac.uk/Imaging/Common/mnispace.shtml). Activation threshold was set at $P < 0.05$ (corrected for multiple comparisons at the cluster level) for contrasting against the baseline condition. In all other cases, threshold was set at either $P < 0.001$ or $P < 0.005$ (uncorrected) as specifically reported in the Results section, and extent threshold was set at 15 contiguous voxels.

Results

Behavioral data

Trials with no movement, during either Event 1 or Event 2 periods, were excluded from further analysis (2.0% of all trials). Fig. 3 shows the cursor trajectory of a representative subject under each condition. Note that the 0-ms condition is from a practice performed inside the scanner before actual scanning took place for reference. This demonstrates that the subject was able to correctly trace the curve when visual feedback from the moving cursor was available (Fig. 3A, solid line). Conversely, when the image of the moving cursor was occluded, tracing performance became comparatively inaccurate (Figs. 3B–D, dashed line) but returned to

Table 1

<table>
<thead>
<tr>
<th>Occlusion time [ms] (SD)</th>
<th>Tracing error [pixel]</th>
<th>Velocity [pixel/s]</th>
<th>Distance [pixel]</th>
</tr>
</thead>
<tbody>
<tr>
<td>2500</td>
<td>9.39 (2.77)</td>
<td>131.62 (11.63)</td>
<td>496.6 (23.05)</td>
</tr>
<tr>
<td>3250</td>
<td>12.38 (3.37)</td>
<td>126.37 (10.96)</td>
<td>493.76 (29.82)</td>
</tr>
<tr>
<td>4000</td>
<td>16.57 (4.27)</td>
<td>121.63 (10.04)</td>
<td>486.83 (27.72)</td>
</tr>
</tbody>
</table>

![Fig. 3. Trajectories of cursor tracing, made under each occlusion condition, for a representative subject. The circle on the right end of the curve represents starting position of the cursor. Occlusion times were as follows: (A) 0 ms; (B) 2500 ms; (C) 3250 ms; and (D) 4000 ms. Note that the 0-ms condition is from a practice performed inside the scanner before actual scanning took place for reference. Solid and dashed lines represent visible and invisible trajectories of the cursor, respectively.](http://www.mrc-cbu.cam.ac.uk/Imaging/Common/mnispace.shtml)
relatively accurate levels after visual feedback became available again (Figs. 3B–D, solid line).

Tracing error was analyzed to investigate the effects of online visual information on ongoing movements. Because tracing errors were dependent on curvature of the target curve, which was pseudo-randomized for each trial, raw data were averaged to determine whether online correction occurred after the presentation of visual feedback, excluding the effects of the curvature. Fig. 4 shows mean tracing error (A) and standard deviation (SD) (B) for the period of the trial. Tracing error and SD increased when visual feedback was unavailable, whereas the presence of visual feedback reduced both. Table 1 summarizes behavioral results. Tracing error increased significantly with increasing occlusion time \( F(2,30) = 57.8, P < 0.001 \). Movement distance and velocity also showed the significant effects of occlusion time (distance, \( F(2,30) = 3.7, P < 0.05 \); velocity, \( F(2,30) = 28.7, P < 0.001 \)). However, when 3 occlusion conditions were collapsed, differences in movement velocity between Events 1 and 2 were not significant (Event 1: 121.63 pixels/s; Event 2: 129.07 pixels/s; \( t(15) = 1.40, P = 0.18 \)). Analysis of linear regression of the mean tracing error within each trial versus the number of trials did not show any significant change in tracing error for either session (Session 1, \( t(44) = 0.23, P = 0.82 \); Session 2, \( t(44) = 1.38, P = 0.17 \)).

Fig. 4. Tracing error series against time. Horizontal axis indicates trial time. Vertical axis indicates mean (A) and standard deviation (SD) (B) of the tracing error. Each plot shows 3 levels of occlusion duration (2500 ms, 3250 ms and 4000 ms).

In red: activated areas when Event 1 versus Event 2 \( P < 0.001 \) uncorrected) was inclusively masked with Event 1 versus baseline \( P < 0.05 \) corrected). In green: activated areas when Event 2 versus Event 1 \( P < 0.001 \) uncorrected) was inclusively masked with Event 2 versus baseline \( P < 0.05 \) corrected). L, left hemisphere; R, right hemisphere. Talairach coordinates of the activated foci are reported in Table 2.

Fig. 5. In red: activated when Event 1 versus Event 2 \( P < 0.001 \) uncorrected) was inclusively masked with Event 1 versus baseline \( P < 0.05 \) corrected). In green: activated when Event 2 versus Event 1 \( P < 0.001 \) uncorrected) was inclusively masked with Event 2 versus baseline \( P < 0.05 \) corrected). L, left hemisphere; R, right hemisphere. Talairach coordinates of the activated foci are reported in Table 2.
fMRI data

Specific activations during Event 1

Event 1 versus Event 2 ($P < 0.001$ uncorrected) was inclusively masked with Event 1 versus baseline ($P < 0.05$ corrected) to reveal specific activations during Event 1. Significant activation was found bilaterally in the basal ganglia, centered in the putamen; mesial motor areas, peaking in the presupplementary motor area (pre-SMA) and extending caudally into the supplementary motor area (SMA) and dorsal caudal cingulate zone (CCZ); thalamus; brainstem; and ventral premotor cortex (PMv). Significant activation was also found in the left hemisphere in the postcentral gyrus, extrastriate cortex and medial cerebellum (Figs. 5 and 6; Table 2A).

Specific activations during Event 2

Event 2 versus Event 1 ($P < 0.001$ uncorrected) was inclusively masked with Event 2 versus baseline ($P < 0.05$ corrected) to reveal specific activations during Event 2. Significant activation was found bilaterally in the lateral cerebellum, postcentral gyrus and inferior parietal lobule (IPL) extending from the intraparietal sulcus (IPS) to the temporo-parietal junction (TPJ), and the middle temporal gyrus, occipito-temporal cortex and middle and inferior frontal gyri in the right hemisphere (Fig. 5; Table 2B).

Table 2
Results of categorical comparisons between conditions

<table>
<thead>
<tr>
<th>Region</th>
<th>BA</th>
<th>Voxels</th>
<th>Talairach coordinates</th>
<th>t value</th>
</tr>
</thead>
<tbody>
<tr>
<td>(A) Event 1 vs. Event 2 inclusively masked with Event 1 vs. baseline</td>
<td></td>
<td></td>
<td>x</td>
<td>y</td>
</tr>
<tr>
<td>L Thalamus</td>
<td>340</td>
<td>−4</td>
<td>−16</td>
<td>1</td>
</tr>
<tr>
<td>L Putamen</td>
<td>655</td>
<td>−26</td>
<td>−2</td>
<td>2</td>
</tr>
<tr>
<td>R Putamen</td>
<td>402</td>
<td>26</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>R PMv</td>
<td>6, 9, 44</td>
<td>383</td>
<td>51</td>
<td>5</td>
</tr>
<tr>
<td>M Pre-SMA</td>
<td>6</td>
<td>1149</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>L PMv</td>
<td>6, 9, 44</td>
<td>934</td>
<td>−53</td>
<td>6</td>
</tr>
<tr>
<td>M CCZ</td>
<td>24, 31, 32</td>
<td>122</td>
<td>10</td>
<td>18</td>
</tr>
<tr>
<td>M SMA</td>
<td>6</td>
<td>565</td>
<td>−14</td>
<td>−5</td>
</tr>
<tr>
<td>L Extrastriate cortex</td>
<td>18</td>
<td>206</td>
<td>−28</td>
<td>−78</td>
</tr>
<tr>
<td>L Postcentral gyrus</td>
<td>2</td>
<td>47</td>
<td>−50</td>
<td>−19</td>
</tr>
<tr>
<td>L Cerebellum</td>
<td>42</td>
<td>−40</td>
<td>−26</td>
<td>23</td>
</tr>
<tr>
<td>M Brainstem</td>
<td>19</td>
<td>0</td>
<td>−25</td>
<td>−31</td>
</tr>
<tr>
<td>(B) Event 2 vs. Event 1 inclusively masked with Event 2 vs. baseline</td>
<td></td>
<td></td>
<td>x</td>
<td>y</td>
</tr>
<tr>
<td>L Cerebellum</td>
<td>335</td>
<td>−36</td>
<td>−62</td>
<td>−34</td>
</tr>
<tr>
<td>L Cerebellum</td>
<td>29</td>
<td>−40</td>
<td>−73</td>
<td>−18</td>
</tr>
<tr>
<td>R Middle temporal gyrus</td>
<td>37</td>
<td>41</td>
<td>−59</td>
<td>−54</td>
</tr>
<tr>
<td>R Middle occipital gyrus</td>
<td>19</td>
<td>72</td>
<td>46</td>
<td>−77</td>
</tr>
<tr>
<td>M Postcentral gyrus</td>
<td>3</td>
<td>119</td>
<td>−12</td>
<td>−35</td>
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<tr>
<td>R Cerebellum</td>
<td>30</td>
<td>22</td>
<td>−67</td>
<td>−29</td>
</tr>
<tr>
<td>R Inferior parietal lobule</td>
<td>40</td>
<td>65</td>
<td>44</td>
<td>−40</td>
</tr>
<tr>
<td>R Middle temporal gyrus</td>
<td>39</td>
<td>29</td>
<td>48</td>
<td>−65</td>
</tr>
<tr>
<td>R Middle frontal gyrus</td>
<td>9</td>
<td>27</td>
<td>38</td>
<td>30</td>
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<tr>
<td>R Middle frontal gyrus</td>
<td>8</td>
<td>49</td>
<td>38</td>
<td>24</td>
</tr>
<tr>
<td>R Supramarginal gyrus</td>
<td>40</td>
<td>28</td>
<td>59</td>
<td>−47</td>
</tr>
<tr>
<td>R Inferior frontal gyrus</td>
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<td>31</td>
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<tr>
<td>L Inferior parietal lobule</td>
<td>40</td>
<td>28</td>
<td>−55</td>
<td>−43</td>
</tr>
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</table>

BA, Brodmann area; PMv, ventral premotor area; pre-SMA, presupplementary motor area; SMA, supplementary motor area; CCZ, caudal cingulate zone; L, left; R, right; M, medial.

Table 3
Results of parametric analysis of tracing error

<table>
<thead>
<tr>
<th>Region</th>
<th>BA</th>
<th>Voxels</th>
<th>Talairach coordinates</th>
<th>t value</th>
</tr>
</thead>
<tbody>
<tr>
<td>(A) Negative correlation with tracing error during Event 1</td>
<td></td>
<td></td>
<td>x</td>
<td>y</td>
</tr>
<tr>
<td>M Pre-SMA</td>
<td>6</td>
<td>169</td>
<td>−4</td>
<td>8</td>
</tr>
<tr>
<td>L Precentral gyrus</td>
<td>4</td>
<td>70</td>
<td>−32</td>
<td>−17</td>
</tr>
<tr>
<td>(B) Positive correlation with tracing error during Event 2</td>
<td></td>
<td></td>
<td>x</td>
<td>y</td>
</tr>
<tr>
<td>R Inferior parietal lobule</td>
<td>40</td>
<td>20</td>
<td>−44</td>
<td>−38</td>
</tr>
</tbody>
</table>

BA, Brodmann area; pre-SMA, presupplementary motor area; L, left; R, right; M, medial.

Discussion

Behavioral data

Behavioral data demonstrated that absence of visual feedback increased the size and variability of tracing error, whereas the presence of visual feedback reduced both. This indicates that internal guidance of movements gradually became inaccurate, and online visual feedback is used to correct subsequent movements. Quantitative analysis of tracing errors showed a significant increase in tracing errors with increased occlusion time. In addition, movement distance and velocity were significantly increased with increased occlusion time. However, when 3 conditions were collapsed as in fMRI analysis, movement velocity was not significantly different during Events 1 and 2 and was thus comparable between the 2 events. Finally, linear regression analysis indicated no significant variation in tracing error within sessions, meaning that no learning effect was present.

Activations involved in movements without visual feedback (Event 1)

Activations specific to Event 1 were analyzed to investigate the activations involved in movements without visual feedback. During Event 1, significant activation was found bilaterally in the basal ganglia, thalamus, brainstem, PMv and mesial motor areas, in addition to the postcentral gyrus, extrastriate cortex and...
medial cerebellum in the left hemisphere. In addition, activation in the pre-SMA was negatively correlated with tracing errors, indicating that the pre-SMA is important for motor performance in the absence of visual feedback.

These results suggest that both the basal ganglia and premotor cortex have a greater involvement in internal generation of movement than visual feedback control. Previous studies have shown that the basal ganglia, mainly the putamen, are predominantly concerned with selection or planning of movements, rather than sensory feedback processing (Jueptner and Weiller, 1998; Liu et al., 1999). A recent study by Seidler et al. (2004) also indicated involvement of the putamen in feedforward rather than feedback processes. Neurophysiological studies in monkeys have found that a large number of premotor neurons show greater activations during preparation periods (set-related activity) in visually guided movements (Kurata, 1989). These studies are compatible with the current results that the basal ganglia and premotor cortex are primarily unrelated to visual feedback control.

The pre-SMA is known to represent a high-level motor control area, independent of effectors in use and sensory modalities (Picard and Strick, 2001). Another study has also shown that the pre-SMA is involved in movements when visual feedback is unavailable (Hamzei et al., 2002). The pre-SMA activation observed here is unlikely to be related to increased demand for proprioceptive feedback control due to visual occlusion, for 2 reasons. First, contrasting with the SMA or M1, which receive afferent somatosensory inputs, the pre-SMA has no inputs from the somatosensory area (Luppino et al., 1993). Second, the pre-SMA is activated in motor imagery without any proprioceptive feedback due to actual movements, whereas the more caudal part (the SMA proper) is related to motor execution (Gerardin et al., 2000; Hanakawa et al., 2003). In addition, Deiber et al. (1998) showed

Fig. 6. Activated areas in the subcortical regions when Event 1 versus Event 2 ($P < 0.001$ uncorrected) was inclusively masked with Event 1 versus baseline ($P < 0.05$ corrected). L, left hemisphere; R, right hemisphere; A, anterior. Talairach coordinates of activated foci are reported in Table 2.

Fig. 7. Activation in the presupplementary motor area (pre-SMA) and left primary motor area (M1) was significantly negatively correlated with tracing error during Event 1 ($P < 0.001$ uncorrected). L, left hemisphere; R, right hemisphere. Talairach coordinates of the activated foci are reported in Table 3.
that the pre-SMA is related particularly to visuomotor imagery, which involves motor imagery using visual coordinates (Jean-nerod, 1995). In the present study, subjects had to visually estimate current on-screen cursor position to trace the curve accurately when visual feedback was unavailable. The current study suggests that the pre-SMA is involved in visuomotor imagery for the internal guidance of effector movements. This pre-SMA might differ from internal prediction with the forward model suggested by the predictive control model (Wolpert and Ghahramani, 2000), as forward prediction should be active regardless of the absence or presence of visual feedback to compensate for delays inherent in feedback loops. The forward model has been indicated to be contained in the PPC or the cerebellum (Blakemore and Sirigu, 2003; Kawato et al., 2003), whereas no such reports have indicated that the pre-SMA is related to the forward model. Further study is necessary to investigate relationships between visuomotor imagery and the forward model.

Activations involved in visual feedback control (Event 2)

Activations specific to Event 2 were analyzed to investigate the activations involved in visual feedback control. During Event 2, bilateral activation in the PPC was observed. Among these regions, only the right PPC along the IPS showed positive correlations with tracing error after visual feedback became available. This indicates that the right PPC is involved in evaluating visuomotor error using online visual feedback. Previous studies have shown increased activation in the PPC accompanied by distorted visual feedback causing large visuomotor errors (Inoue et al., 1997; Ghilardi et al., 2000) and decreased activation as learning proceeded (Graydon et al., 2005). This PPC activation is located in the anterior part of the IPS and is close to the human homolog of the medial intraparietal area (MIP) (Johnson et al., 2002; Simon et al., 2002), which is involved in spatially directed hand movements by constructing spatial representations of effector location that are dynamically updated in conjunction with self-generated movements (Colby, 1998). Desmurget and Grafton (2003) suggested that the PPC computes a "dynamic motor error" to update the ongoing movements by building an internal representation of effector location. These findings are in congruent with the current results that indicate involvement of the PPC in online error evaluation. However, the online correction in the current study differs from those in previous studies (Desmurget et al., 1999, 2001) in 2 respects. First, previous studies focused on non-visual feedback, which may consist of efferent motor signals or proprioceptive feedback, whereas online error correction in the current study was based on visual feedback from moving effectors. Second, error correction in previous investigations remained an unconscious, subliminal process, in contrast to the conscious and intentional process of the current study. The differences in reporting of left- and right-lateralized activation between previous studies and the present investigation could be explained by this distinction. The right PPC is generally involved in visuospatial perception (Milner and Goodale, 1995), and previous studies using a visuomotor discrepancy have induced right-lateralized activation in the PPC (Inoue et al., 1997; Ghilardi et al., 2000). The current study suggests that the right PPC is involved in conscious error evaluation based on online visual feedback from effectors.

The previous work by Seidler et al. (2004) found no PPC activations related to feedback process. This difference might be due to 2 reasons. First, they used simple pointing movements to targets at the same location, whereas our study employed the tracing of variable curves, which requires more visual feedback of effectors. Second, their study used a blocked design and
manipulated overall task difficulty by changing target size with full vision of both the target and effector, whereas our study directly manipulated vision of the effector and used ER-fMRI to investigate activations specific to visual feedback control of this effector. Activations during Event 2 in the present study were thus specific to online visual feedback control of moving effectors. The PPC is also known to be related to eye movement control (Andersen et al., 1997), and PPC activation observed here may reflect saccadic or smooth pursuit eye movements when visual feedback of the on-screen cursor is available. However, the parietal eye field is in mid-posterior lateral IPS (lateral intraparietal area; LIP), which is located approximately 20 mm posterior to the activation observed here (Kawashima et al., 1996; Berman et al., 1999). In addition, activations were observed in neither the frontal eye field (FEF) (Paus, 1996) nor the supplementary eye field (SEF) (Grosbras et al., 1999). Therefore, it is unlikely that the PPC activation observed here was related to eye movements. The possibility also exists that neural activations associated with Event 2 may be related to movement termination, as Event 2 preferentially occurs near movement termination. Few previous studies have investigated motor termination, and 1 study involving finger movements found that movement termination was predominantly related to the SMA and M1 (Toma and Nakai, 2002). Activations associated with Event 2 are thus unlikely to be related to movement termination.

The right TPJ is known to be involved in the sense of agency, which could be based on a comparison between movement prediction and visual feedback of consequences (Farrer et al., 2003; Jackson and Decety, 2004), and abnormal activity in this region leads to passivity phenomena, which could be accounted for as an incorrect attribution of self-movement to consequential visual feedback (Spence et al., 1997; Farrer et al., 2004). In addition, right TPJ activity correlates positively with motor performance when visual feedback is delayed, with subjects having to properly integrate internal predictions and visual feedback (Ogawa et al., in press). These previous studies indicate that the right TPJ plays an important role in the integration of effector motor-related signals and reafferent visual information. TPJ activity observed during Event 2 might reflect this process.

We also observed significant activity in the right hemisphere during Event 2 in the occipito-temporal cortex and middle and inferior frontal gyri. The occipito-temporal regions observed here are located near the human homologue of MT+, which is specifically involved in the visual motion analysis (Dumoulin et al., 2000). The observed occipito-temporal activity may therefore be related to the processing of visual feedback for motion in general. The prefrontal cortex is related to top-down attentional control (Kastner and Ungerleider, 2000) and anticipation of visual stimulus presentation (Liang et al., 2002). In the current study, participants could anticipate the presentation of visual feedback during movements, even though occlusion duration varied. The observed frontal activations may thus be related to such anticipatory effects.

Bilateral lateral cerebellar activity was also observed in Event 2. Previous studies using visuomotor tracking tasks have shown selective activations in the cerebellum during visual feedback control, indicating that the cerebellum makes a particularly important contribution to movements under visual direct control (Inoue et al., 1998; Miall et al., 2000). The lateral cerebellum receives abundant inputs from the PPC (Middleton and Strick, 1998), and Desmurget and Grafton (2000) suggested that the cerebellum converts dynamic error signals computed by the PPC into appropriate corrective motor commands. The current results agree with these previous studies, suggesting that the cerebellum is involved in correcting ongoing movements based on visual feedback. The cerebellum is also involved in motor learning with acquisition of the internal model (Wolpert and Miall, 1996; Imamizu et al., 2000). Although error-dependent learning was not observed in the current study, sufficient time may not have been available in our experiment for improvement of motor performance. The observed PPC and cerebellum activity could therefore also be related to motor learning processes. The PPC is also involved in visuomotor learning (Clower et al., 1996; Inoue et al., 1997; Inoue et al., 2000), and a study by Graydon et al. (2005) showed a learning-dependent transition from early activation of the PPC to later distributed cortico–subcortical–cerebellar responses. Roles of the PPC and cerebellum in motor learning should be clarified in further studies.

Conclusion

This study aimed at dissociating the neural correlates of internally guided and visual feedback control by temporal manipulation of visual feedback of moving effectors. ER-fMRI revealed that activation in the pre-SMA displayed a negative correlation with motor error during which visual feedback was unavailable. Results also showed that activation in the right PPC activity was positively correlated with tracing error after the presentation of visual feedback. The results suggest that the pre-SMA is involved with internally guided movements when visual feedback is unavailable, and that the PPC is related to visual feedback control by evaluating online visuomotor error.

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