Neural Basis for the Processes That Underlie Visually Guided and Internally Guided Force Control in Humans

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Vaillancourt, David E., Keith R. Thulborn, and Daniel M. Corcos. Neural basis for the processes that underlie visually guided and internally guided force control in humans. J Neurophysiol 90: 3330–3340, 2003. First published July 2, 2003; 10.1152/jn.00394.2003. Despite an intricate understanding of the neural mechanisms underlying visual and motor systems, it is not completely understood in which brain regions humans transfer visual information into motor commands. Furthermore, in the absence of visual information, the retrieval process for motor memory information remains unclear. We report an investigation where visuomotor and motor memory processes were separated from only visual and only motor activation. Subjects produced precision grip force during a functional MRI (fMRI) study that included four conditions: rest, grip force with visual feedback, grip force without visual feedback, and visual feedback only. Statistical and subtractive logic analyses segregated the functional process maps. There were three important observations. First, along with the well-established parietal and premotor cortical network, the anterior prefrontal cortex, putamen, ventral thalamus, lateral cerebellum, intermediate cerebellum, and the dentate nucleus were directly involved in the visuomotor transformation process. This activation occurred despite controlling for the visual input and motor output. Second, a detailed topographic orientation of visuomotor to motor/sensory activity was mapped for the premotor cortex, parietal cortex, and the cerebellum. Third, the retrieval of motor memory information was isolated in the dorsolateral prefrontal cortex, ventral thalamus, anterior cingulate, and anterior cingulate. The motor memory process did not extend to the supplementary motor area (SMA) and the basal ganglia. These findings provide evidence in humans for a model where a distributed network extends over cortical and subcortical regions to control the visuomotor transformation process used during visually guided tasks. In contrast, a localized network in the prefrontal cortex retrieves force output from memory during internally guided actions.

INTRODUCTION

The process of integrating visual information from the retina through the optic nerve to the lateral geniculate nucleus and into different regions of the visual cortex is well established (Kandel and Wurtz 2000; Van Essen and Gallant 1994). Also, the primary brain regions involved in the control of movement have been known for over a century (Krakauer and Ghez 2000). Despite an intricate understanding of the neural mechanisms underlying visual and motor systems, it is still not completely understood how and where visual information is integrated into motor commands (Glickstein 2000). Thus the general purpose of this study was to examine both visually guided and internally guided motor tasks using functional MRI (fMRI) to delineate fundamental processes related to visual, visuomotor, motor/sensory, and motor memory functions.

The transfer of visual information into action is defined here as a visuomotor process. This paper confines the definition of a visuomotor process to the manual-motor system and does not include activation from oculomotor processes. A circuit controlling visuomotor processes is located in the superior parietal cortex and its connections with the premotor cortex (Caminiti et al. 1996; Johnson et al. 1996; Milner and Goodale 1993). This viewpoint was supported when the primate posterior parietal cortex was shown to transform eye-centered target locations to hand-centered target locations (Buneo et al. 2002). Other studies in both primates and humans demonstrate that the parietal cortex and its projections to the dorsal and ventral premotor cortex are involved in visuomotor processing (Burnod et al. 1992; Calton et al. 2002; Desmurget et al. 1999; Ellermann et al. 1998; Hamzei et al. 2002; Jeannerod et al. 1995; Jenkins et al. 2000; Simon et al. 2002; Tanne-Gariepy et al. 2002). In addition, direct neural recordings from the primate basal ganglia (Mushiake and Strick 1995), thalamus (van Donkelaar et al. 1999), and the cerebellum (Mushiake and Strick 1993) show task-related activation when performing visually guided pointing movements. In contrast, neuroimaging studies from humans have shown inconsistent activation in the putamen/globus pallidus, where evidence for (Toni et al. 2001) and against (Juettner and Weiller 1998) a role of the basal ganglia during visuomotor processes exist. Finally, there is evidence to suggest that the cerebellum plays a role in the visual control of movement (Stein and Glickstein 1992)—particularly through the lateral cerebellum and its output pathway through the dentate to the ventral portion of the thalamus.

Up until now, no study has recorded from the basal ganglia, thalamus, and the cerebellum during visually guided tasks while using the appropriate control conditions in which 1) subjects viewed the same visual stimulus as the visually guided motor task without producing motor output, and 2) subjects produce motor output at similar force levels as the visually guided motor task in the absence of visual feedback. Matching the level of force output is critical due to the known influence of the force level on direct neural recordings (Evarts et al. 1986; Ralston and Evarts 1970). Other studies in both primates and humans demonstrate that the parietal cortex and its projections to the dorsal and ventral premotor cortex are involved in visuomotor processing (Burnod et al. 1992; Calton et al. 2002; Desmurget et al. 1999; Ellermann et al. 1998; Hamzei et al. 2002; Jeannerod et al. 1995; Jenkins et al. 2000; Simon et al. 2002; Tanne-Gariepy et al. 2002). In addition, direct neural recordings from the primate basal ganglia (Mushiake and Strick 1995), thalamus (van Donkelaar et al. 1999), and the cerebellum (Mushiake and Strick 1993) show task-related activation when performing visually guided pointing movements. In contrast, neuroimaging studies from humans have shown inconsistent activation in the putamen/globus pallidus, where evidence for (Toni et al. 2001) and against (Juettner and Weiller 1998) a role of the basal ganglia during visuomotor processes exist. Finally, there is evidence to suggest that the cerebellum plays a role in the visual control of movement (Stein and Glickstein 1992)—particularly through the lateral cerebellum and its output pathway through the dentate to the ventral portion of the thalamus. The costs of publication of this article were defrayed in part by the payment of page charges. The article must therefore be hereby marked “advertisement” in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.
visuomotor transformation process from other types of cogni-
constant between tasks, creates dif
comparing a visually guided task to an internally guided task,
such as attention (Allen et al. 1997; McAuley 2003). Thus
1983; Stein and Glickstein 1992) and to cognitive functions
regions that are related to eye movements (Hikosaka and Wurtz
instance, the cerebellum and the basal ganglia also have re-
the visual input and the motor output constant between tasks, creates dif
visuomotor transformation process from other types of cogni-
tive and motor-related activation. Therefore our first objective
used controlled experiments to test the hypothesis that in
humans the visuomotor process occurs in the superior parietal
cortex and the premotor cortex, along with subcortical regions
that include the basal ganglia, ventral thalamus, lateral cere-
bellum, and the dentate nucleus.

In this study, we first had subjects produce force output to a
target when using on-line visual feedback. To isolate the visuo-
motor process subjects also 1) produced force without on-line
visual feedback and 2) viewed a similar visual stimulus that
was seen during visually guided force control. These two
control conditions were separated from the fMRI activation
during visually guided force control, thereby isolating the
visuomotor process. After identifying the networks involved in
the visuomotor process and the motor/sensory process (fMRI
activation related to producing force independent of visual
feedback), our second objective examined the topographic
orientation of these two processes. An example of this topog-
raphy was shown in the primate dentate nucleus, where neu-
rons active during visually guided movements were ventral
and lateral to dentate neurons activated during internally guided
movements (Mushiake and Strick 1993). While it is important
to understand the topographic organization of individual neu-
rons within a region, it is also essential to examine how
collective regions of neural activity are topographically orga-
nized.

The third objective of the study examines the motor memory
process that involves the retrieval of force from memory. A
common method to isolate motor memory compares neural
activation during motor tasks that are internally guided to those
that are visually guided. Several studies that have examined
internally and visually guided movements suggest that the
dorsolateral prefrontal cortex, basal ganglia, and the supplemen-
tary motor area (SMA) are involved in the retrieval of
force from memory. For example, single unit recordings in
primates showed the SMA preferentially related to movements
performed without visual information (Mushiake et al. 1991).
PET in humans demonstrated that finger movements performed
without visual information activated the rostral SMA and pre-
frontal cortical regions (Jahanshahi et al. 1995). In contrast to
work by Jahanshahi et al. (1995), an fMRI study showed
similar activation in the SMA for visually triggered and inter-
nally triggered finger movement, but selective SMA activation
was found for sequenced movements versus repetitive move-
ments (Deiber et al. 1999). Furthermore, in the primate internal
globus pallidus neurons were selectively active during a move-
ment sequencing task without external cues (Mushiake and
Strick 1995).

One drawback of much of the literature examining internally
guided versus visually guided actions is that the tasks involved
overlapping processes. For instance, the internally guided mo-
tor tasks used in the primate work (Mushiake and Strick 1995;
Mushiake et al. 1991) and the neuroimaging studies on humans
(Jahanshahi et al. 1995; Jenkins et al. 2000) involved 1) the
initiation and sequencing of the motor act and 2) the retrieval
of motor memory information for producing motor output. In
particular, movement sequencing processes have been sug-
gested to occur in the basal ganglia and the SMA (Brotchie et
al. 1991). Since the tasks involved overlapping processes, it
remains unclear which regions of the prefrontal cortex, basal
ganglia, and SMA are specifically involved in the retrieval of
motor memory. The constant force task used in this study
minimized sequencing processes to isolate the retrieval of
motor memory. Therefore our third objective tests the hypo-
thesis that the motor memory process is confined to the prefrontal
cortex and that the SMA and the basal ganglia are not directly
involved. Preliminary findings of this study were presented at
the Society for Neuroscience in Orlando, FL, in November
2002.

METHODS

Subjects

We collected data on 10 right-handed subjects (range, 21–35 yr)
who all had corrected or normal vision. There were three males
and seven females. The subjects were naive to the purpose of the exper-
iment, and none of the subjects had any history of a neurological
disorder. All subjects gave informed consent to all experimental
procedures, which were approved by the local Institutional Review
Board.

Experimental design

Figure 1, A–F, shows the experimental paradigm used to examine
visuomotor and motor memory processes. During testing, subjects
pinched a specially designed apparatus (Liu et al. 2000) with their
middle finger and thumb to produce force output (Fig. 1, A and B).
The pinch grip apparatus is made of nonmetallic material (polykar-
bonate), which allows its use inside the fMRI environment. The
grasping apparatus is connected to a long nylon tube (35 ft), which
leads into an Entran (EPX-N13–250P) pressure transducer (located
outside the fMRI environment). When the pinch grip is performed,
this increases hydraulic pressure, which is sensed by the pressure
transducer. The pressure transducer output was amplified through a
pressure gauge amplifier. A PCMCI National Instruments A/D con-
verter sampled the pressure at 100 Hz. At each sampling interval, the
pressure from the transducer was displayed to the subject through the
video projector and mirror setup (Fig. 1A).

The task required subjects to continuously maintain their level of
force output (middle finger + thumb force) to a target force level on
the video screen or to a remembered force level (Fig. 1, D and E).
Prior to entering the magnet, the subjects participated in a 45-min
training session so the transitory portion of the motor learning process
would be removed. The fMRI experiment used a blocked design
because we were interested in closed-loop force control, and this
requires a long force production trial (Slifkin et al. 2000). The exper-
iment included one fMRI scan that lasted 570 s. Subjects produced
force at 15% of their maximal voluntary contraction (MVC) in two of
the four conditions during the scan (Fig. 1, D and E). The MVC was
estimated when the subjects initially entered the magnet, and the
MVC was calculated similarly to previous work (Vaillancourt et al.
2001a).

Figure 1, C–F, shows the stimulus conditions within the following
sequence: R – FV – R – FNV – R – V. For brevity, R is not

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performing the force production task (Fig. 1). The subjects lay supine in the fMRI scanner while viewing the visual feedback from areas related to processing the force target of the visual paradigm. This minimized the number of places on the video screen where the subject had to maintain their attention. Although processing the visual feedback is a cognitive task, the subjects experienced the same head stabilizing feedback over the course of the experiment. The subtraction technique cancels this effect, and Thulborn (1999) demonstrated that such interference is not significant in the activation maps from eye movement tasks examined at 1.5 or 3.0 T. Functional images were obtained with a T$_2$*-sensitive, single-shot, gradient-echo echo-planar pulse sequence (echo time 25 ms; repeat time 3,000 ms; flip angle 90°; field of view 200 mm; imaging matrix 64 × 64; 24 contiguous slices with 5 mm slice thickness). Slices were acquired axially to cover the whole brain. The MR scanning session ended by acquiring an anatomical image using a T1-weighted 3D inversion recovery fast spoiled gradient recalled (3DIRSPGR) pulse sequence (echo time 1.98 ms; repeat time 9 ms; flip angle 25°; field of view 220 mm; imaging matrix 256 × 256; 120 contiguous slices with 1.5 mm slice thickness).

**fMRI data analysis**

The data analysis delineated four general processes used during continuous force output based on statistical and logical comparisons. The processes were independent and by definition voxels were only assigned to one process. The critical point about the findings from this study is that the biological variance of the data, and not the statistical and logical comparisons, determined both where each process would reside and the spatial topography of one process to another.

**fMRI data acquisition**

Magnetic resonance (MR) imaging was performed using a 3 Tesla (T) scanner (General Electric Medical Systems, Milwaukee, WI) with a volume head coil. The subjects lay supine in the fMRI scanner while performing the force production task (Fig. 1). The subjects’ head was stabilized using comfortable adjustable padding and visual feedback (Thulborn 1999; Thulborn and Shen 1999). The spot of the visor parallax biofeedback system, providing information about head position, was placed at the same vertical and horizontal position as the red force target of the visual paradigm. This minimized the number of places on the video screen where the subject had to maintain their attention. Although processing the visual feedback is a cognitive task, the subjects experienced the same head stabilizing feedback over the course of the experiment. The subtraction technique cancels this effect, and Thulborn (1999) demonstrated that such interference is not significant in the activation maps from eye movement tasks examined at 1.5 or 3.0 T. Functional images were obtained with a T$_2$*-sensitive, single-shot, gradient-echo echo-planar pulse sequence (echo time 25 ms; repeat time 3,000 ms; flip angle 90°; field of view 200 mm; imaging matrix 64 × 64; 24 contiguous slices with 5 mm slice thickness). Slices were acquired axially to cover the whole brain. The MR scanning session ended by acquiring an anatomical image using a T1-weighted 3D inversion recovery fast spoiled gradient recalled (3DIRSPGR) pulse sequence (echo time 1.98 ms; repeat time 9 ms; flip angle 25°; field of view 220 mm; imaging matrix 256 × 256; 120 contiguous slices with 1.5 mm slice thickness).

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**fMRI data processing**

Functional data processing was performed using the public domain software FIASCO (Eddy et al. 1996) and AFNI (Cox 1996). The fMRI data were first processed in FIASCO by performing a baseline correction, mean correction, correcting for motion based on three-dimensional (3D) motion estimation parameters, correction for outliers, and detrending. The average displacement of head movement, averaged across volumes and subjects, was 0.78 ± 0.37 (SD) mm. This head movement was less than one-third of a voxel (voxel size =
3.125 \times 3.125 \times 5 \text{ mm). Images with greater than one-half of a voxel of head motion as detected by FIASC0 were excluded from statistical analysis, and this occurred \(< 5\%\) of the time across the 10 subjects. The exclusion of images with greater than one-half of a voxel of head motion occurred after motion correction. In FIASC0, t-maps were generated for the following comparisons (Table 1): FV-R, FV-V, FNVR, V-R, and FNV-FV. Next, we thresholded each of these five t-maps using the false discovery rate at a q of 0.05 (Genovese et al. 2002). These thresholded t-maps were then transformed into four different merged t-maps based on Table 1. These four different merged t-maps correspond to the four processes.

Each voxel was assigned to one of the four processes or to nothing at all. Each voxel was assigned to a particular process based on the positive (+) and negative (−) signs. NA corresponds to not applicable. For a voxel to be assigned to a process, it had to meet all of the requirements from each of the t-maps of Table 1. A voxel was assigned to the visual merged t-map if it was significant during the condition of seeing the visual stimulus compared with rest. A voxel was assigned to the motor/sensory merged t-map if the same voxel was active in all of the FV-R, FV-V, and FNVR comparisons. This confirmed that the voxel was related either to producing force or processing the sensory feedback from the digits touching the grasping apparatus. Similarly, a voxel was assigned to the visuomotor process if and only if 1) the voxel was significantly active during the FV-R and the FV-V conditions, and 2) the same voxel was not significantly active during the FNV-R and the V-R t-maps. If a voxel was consistently active in these t-maps, the mean t-value from these t-maps was taken and replaced in the merged t-map. Finally, the motor memory merged t-map was constructed by assigning voxels that were significant in both the FNV-R and FNV-FV comparisons.

Next, analysis of the active regions that were consistent across subjects was performed. To determine the consistent activation across subjects (i.e., form a group map) the Fisher test statistic was performed on each of the motor/sensory, visuomotor, visual, and motor memory merged t-maps (Fisher 1950). This group test statistic has been recommended when raw data are not available, which is the case in this study because of the transformation to the process t-maps (Lazar et al. 2002). The Fisher method transforms the t-values into P values and performs the following test statistic

\[
T_F = -2 \sum_{i=1}^{i} \log \frac{P_i}{k_i}
\]

where P is the P value, and log is the natural logarithm. The $T_F$ value is compared with a χ² distribution with 2k degrees of freedom. Large values of $T_F$ relative to the χ² distribution lead to a rejection of the null hypothesis that there is no activation. The group maps were thresholded at a χ² value of 56, which approximates a t-value equal to 4.

R E S U L T S

F o r c e o u t p u t m e a s u r e s

An example of a single subject’s block of force output is shown in each of the four conditions in the bottom panels of Table 1.

<table>
<thead>
<tr>
<th>Comparison</th>
<th>Visual</th>
<th>Motor/Sensory</th>
<th>Visuomotor</th>
<th>Motor Memory</th>
</tr>
</thead>
<tbody>
<tr>
<td>FV-R</td>
<td>na</td>
<td>+</td>
<td>+</td>
<td>na</td>
</tr>
<tr>
<td>FV-V</td>
<td>na</td>
<td>+</td>
<td>−</td>
<td>+</td>
</tr>
<tr>
<td>FNVR</td>
<td>na</td>
<td>+</td>
<td>−</td>
<td>+</td>
</tr>
<tr>
<td>V-R</td>
<td>+</td>
<td>na</td>
<td>−</td>
<td>na</td>
</tr>
<tr>
<td>FNV-FV</td>
<td>na</td>
<td>na</td>
<td>na</td>
<td>+</td>
</tr>
</tbody>
</table>

na, not applicable; +, included voxel; −, excluded voxel.

Fig. 1, C–F. During the rest (R) and visual (V) conditions (Fig. 1, C and F), the subject did not produce force, but the subject did produce force during the force with vision (FV) and in the force without vision (FNV) time periods (Fig. 1, D and E). To examine subjects’ performance, the mean and standard deviation (SD) of force was calculated during the force output intervals. Mean force output was not different between the vision and no vision conditions ($P > 0.05$). The SD of force was greater in the no vision condition compared with the vision condition ($P < .001$). That force variability was higher without visual feedback is consistent with previous behavioral work (Vaillancourt et al. 2001a,b) and shows that the subjects performed the task inside the magnet similarly to outside the magnet.

A c t i v i t y r e l a t e d t o v i s u a l m o t i o n

During a visuomotor task, neurons process visual information, and this results in fMRI activation within the visual cortex. This study ran a control condition where subjects viewed an almost identical visual stimulus to that observed during the visuomotor force output task (Fig. 1F) to parse out the visual from the visuomotor processing network. The visual control condition elicited activity in the middle temporal (MT) region that has previously been attributed to the detection of motion from visual stimuli (Zeki et al. 1991). Both the left and right middle occipital gyrus and the left and right middle temporal gyrus were activated by the task (Table 2). The Fisher test did not reveal neuronal activity in the frontal eye fields or the supplementary eye fields. Through an eye monitoring system, the experimenter watched the subjects, and eye movements were infrequently observed during the scan. This strengthens the assertion that the activity in the premotor regions is related to visuomotor processes and not the processes related to saccadic or volitional eye movement control (Rosano et al. 2002).

L o c a t i o n o f t h e m o t o r / s e n s o r y a n d v i s u o m o t o r p r o c e s s e s

Table 2 shows the motor/sensory and visuomotor processes from the across subject Fisher test. The motor/sensory process included bilateral activation in the medial frontal gyrus (SMA), precentral gyrus (premotor cortex and primary motor cortex), and the postcentral gyrus (somatosensory cortex). There was additional ipsilateral activation for the lateral cerebellum on the left side, and for the right side, there was activation in the superior frontal gyrus, inferior frontal gyrus, the middle frontal gyrus, and the lateral cerebellum. The visuomotor process was more widespread and distributed. The visuomotor process included bilateral activation in the middle and inferior frontal gyrus (anterior prefrontal cortex), precentral gyrus (premotor), postcentral gyrus (somatosensory cortex), insular cortex, inferior parietal lobule, intermediate cerebellum, and the lateral cerebellum. On the left hemisphere, there was additional activation in the putamen and the thalamus. Most of the activity in the thalamus was primarily in the ventral and posterior regions (Fig. 2). In the right hemisphere, there was additional activation in the superior parietal lobule, precuneus, and the dentate nucleus. Figure 2 depicts the activation from the motor/sensory and visuomotor process, and Topography of the visuomotor process and the motor/sensory process describes their detailed topography.
TABLE 2. Visual, motor/sensory, visuomotor, and motor memory activation

<table>
<thead>
<tr>
<th>Talairach Coordinates</th>
<th>RL</th>
<th>AP</th>
<th>IS</th>
<th>Mean T</th>
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<tbody>
<tr>
<td>Visual</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Left middle occipital gyrus</td>
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<td>15</td>
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<td>49</td>
<td>-63</td>
<td>3</td>
<td>5.14</td>
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<td>Right middle temporal gyrus</td>
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<td>-83</td>
<td>6</td>
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<td>Left medial frontal gyrus</td>
<td>-3</td>
<td>-1</td>
<td>56</td>
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<td>4.89</td>
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<td>4.96</td>
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<td>-68</td>
<td>-29</td>
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<td>Visuomotor</td>
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<td>4</td>
<td>15</td>
<td>4.58</td>
</tr>
<tr>
<td>Right insula</td>
<td>39</td>
<td>0</td>
<td>12</td>
<td>4.80</td>
</tr>
<tr>
<td>Right cingulate gyrus</td>
<td>9</td>
<td>-2</td>
<td>47</td>
<td>4.27</td>
</tr>
<tr>
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<td>2</td>
<td>-18</td>
<td>50</td>
<td>5.02</td>
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<tr>
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<td>30</td>
<td>-15</td>
<td>59</td>
<td>4.57</td>
</tr>
<tr>
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<td>59</td>
<td>-25</td>
<td>35</td>
<td>5.01</td>
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<tr>
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<td>-48</td>
<td>47</td>
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<tr>
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<td>37</td>
<td>-52</td>
<td>56</td>
<td>4.85</td>
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<tr>
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<td>12</td>
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<td>4.25</td>
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<tr>
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<td>Right int. cerebellum</td>
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<td>-16</td>
<td>4.96</td>
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<tr>
<td>Right precuneus</td>
<td>17</td>
<td>-68</td>
<td>52</td>
<td>4.63</td>
</tr>
</tbody>
</table>

Motor memory

| Left medial frontal gyrus | -11 | 60  | 3  | 4.34   |
| Left middle frontal gyrus | -27 | 51  | -10 | 4.43  |
| Left anterior cingulate | -7  | 45  | 8  | 4.38   |
| Left anterior cingulate | -4  | 36  | 1  | 4.24   |
| Left insula               | -35 | 5   | 12 | 4.01   |
| Right middle frontal gyrus | 43  | 33  | 33 | 4.23   |

Topography of the visuomotor process and the motor/sensory process

In Fig. 2, each coronal slice is depicted starting at 5 mm posterior to the level of the anterior commissive (VCA line) in Talairach coordinates and working posteriorly in steps of 5 mm. In slice A, there is visuomotor and motor/sensory activity in the bilateral SMA and visuomotor activity in the ventral and dorsal premotor (PMd) areas. This activity is posterior to the anterior commissure, and it constitutes the SMA proper, whereas pre-SMA activity is anterior to the anterior commissure. On the dorsal and lateral surface, PMd proper (Picard and Strick 1996, 2001), there is visuomotor activity contralateral to the hand producing force output, but there is very little motor/sensory activity. At this point, there is no evidence of bilateral activity in the PMd. Contralateral to the hand producing force, there is visuomotor activity in the putamen for slice A. There was no consistent evidence that ipsilateral putamen was involved in the visuomotor process.

In slice B, ventral and lateral motor/sensory activities are observed in the ipsilateral and contralateral premotor areas, and in primates, this region has been identified as the arm region of the ventral premotor area (Picard and Strick 1996, 2001). Slice B shows motor/sensory and visuomotor activity bilaterally in the SMA proper, and there is contralateral motor/sensory activity in the PMd proper. When comparing the motor/sensory and visuomotor activity superior to the lateral ventricles, the visuomotor activity is more lateral and ventral to the motor/sensory activity.

In slice C, the visuomotor activity in PMd proper is again lateral and ventral to the motor/sensory activity. The bilateral SMA proper activity is still present, and there is ventral thalamic activity. In the lateral and ventral premotor area, there is still bilateral motor/sensory activity. Slice D also shows the thalamic visuomotor activity (Table 2). Moreover, the motor/sensory processes did not activate the putamen, which suggests that only the visuomotor process used the basal ganglia (Table 2). Compared with slices A, B, and C, slice D has less volume of SMA proper activity for both the motor/sensory and visuomotor processes, and in slice E, the SMA proper activity is no longer present. This is significant because it demonstrates where SMA proper activity ends and the primary motor cortical activity begins (slice D, 20–25 mm, to slice E, 25–30 mm). Slice E now has enhanced motor/sensory activity in the ipsilateral primary motor cortical region, although the volume of activity is much less than the contralateral motor/sensory and visuomotor activity. Again the visuomotor activity was still lateral and ventral to the motor/sensory activity, and this topography was preserved for both ipsilateral and contralateral regions.

Compared with slice E, slice F shows a reduction in motor/sensory and visuomotor activity in the hand region of the ipsilateral and contralateral motor cortex. It is evident from the left panel of Fig. 2 that slices F–H border the central sulcus, and the volume of motor/sensory activity declines posteriorly through these regions. The pattern of ventral and lateral visuomotor to motor/sensory activity is not as strong in slices F–H as in slices B–E, as the two processes are now merged together.

The superior part of slice I traversed the inferior parietal lobule where both visuomotor and motor/sensory activation occurred. Slice I marks the final evidence of motor/sensory activity, because in slice J, the motor/sensory activity has all but disappeared. Slice J demonstrates bilateral visuomotor activity in the parietal cortex, and ipsilateral activation is also evident in slice L. Table 2 reveals the specific regions of the parietal cortex utilized in visuomotor processes, and it is clear that both inferior and superior lobules of the parietal cortex are involved. In the parietal cortex, there is no longer motor/sensory activity, and coupled with the results from slices A and B, this reveals that the visuomotor process bounded the motor/sensory processes anteriorly in the PMd proper and posteriorly in the parietal cortex.

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Slice H shows a small amount of visuomotor activity in the medial and dorsal portion of the cerebellum, and slice I shows the first evidence for both motor/sensory and visuomotor activity in the cerebellum. In the cerebellum, the volume of motor/sensory activity is even more pronounced in slice J, and the visuomotor activity is lateral and ventral to the main motor/sensory component. However, in the cerebellum, slice K shows both medial and lateral visuomotor activity relative to the motor/sensory activity. Slice L depicts medial visuomotor activity compared with the motor/sensory activity. This is important because it directly shows that in the cerebellum the visuomotor process surrounds the motor/sensory activity.

**Motor memory processes**

Figure 3 and Table 2 show the regions active for the motor memory process. In Fig. 3, the anterior portion of the anterior cingulate cortex is significantly active (highlighted by cross-bar), and in the sagittal plane, there is additional prefrontal activity anterior to the anterior cingulate cortex. The additional regions that were consistently active across subjects included the right dorsolateral prefrontal cortex, left insular cortex, the anterior portion of the left medial gyrus, and the anterior portion of the left middle frontal gyrus. In general, the motor memory activity was medial to the visuomotor and motor/sensory activity in the prefrontal regions (Table 2). Also, the motor memory activity was ipsilateral to the motor/sensory activity in the primary motor cortex. The concentration of activity in the prefrontal regions and overall lack of activity found in the basal ganglia suggest that the motor memory process during continuous force production is confined to the prefrontal network. There was no evidence found for motor memory processes in the parietal cortex, SMA, basal ganglia, thalamus, or in the cerebellum. The scanning procedures were unlikely to be a limitation to detecting activity in these regions because visuomotor activity was found in these same regions during the same scan.

**DISCUSSION**

The first objective of this study examined the visuomotor process to determine if this transformation mechanism occurs
in the human basal ganglia, ventral thalamus, lateral cerebellum, and the dentate nucleus. Evidence was obtained from fMRI in humans that during a continuous force control task the putamen, ventral thalamus, lateral cerebellum, and the dentate nucleus were directly involved in the visuomotor process. This activation occurred even when experimental conditions controlled for the visual input and motor output. The second objective established the topography of the visuomotor process and the motor/sensory process in the premotor cortex, parietal cortex, and the cerebellum. Finally, our third objective determined if the retrieval of motor memory information was isolated in the prefrontal cortex, or if this process extended to the SMA and the basal ganglia. The results demonstrated that the motor memory process was confined to the prefrontal cortex. These findings provide evidence for both localized and distributed processes used during visually guided and internally guided motor tasks.

Task versus process approach

An important distinction between this study and other studies of visually guided and internally guided motor control is the difference between task and process approaches to experimental design and data analysis. An example of a task approach involves an experimental paradigm where subjects produce movement while in the presence or absence of on-line visual feedback. The typical analysis then examines neural data (Mushiake and Strick 1993, 1995; van Donkelaar et al. 1999) or neuroimaging data (Deiber et al. 1999; Jahanshahi et al. 1995) by comparing the activation in specific regions between visually guided and internally guided tasks. Therefore the activation measured during a visually guided task represents all of the functional processes within the visual, visuomotor, and motor systems, along with attentional and memory-related mechanisms. On the other hand, a process approach segregates visuomotor activity as only those regions that are active when performing a visuomotor task, while excluding activity related to seeing the visual stimulus, producing the motor output, and activation due to somatosensory processes. This approach has recently been applied in the parietal cortex to separate processes such as grasping, attention, saccadic eye movement, and mental calculation (Simon et al. 2002), and to separate eye movement from hand movement–related activity in the cerebellum (Miall et al. 2001) and the SMA (Fujii et al. 2002). Each experimental paradigm has important merits, but for the purpose of this study, the process approach was used.

Visuomotor process

Because the task required fixation of the retina at the force target while the force cursor moved in the central visual field, it was expected that the visual process would include activity in the middle temporal (MT) region. Our findings were consistent with previous work showing that the MT area responded to the motion of visual stimuli across the retina (Table 2) (Zeki et al. 1991). Once visual information leaves the visual cortex, Glickstein (2000) suggested that little is known about how visual information and motor output are connected. Next, we outline the regions found in this study that are directly involved in the visuomotor transformation process.

PARIETAL AND PREMOTOR CORTEX. There are numerous studies supporting the hypothesis that visual signals are transferred into motor commands through neural activity in the parietal and premotor cortical network (Caminiti et al. 1996; Johnson et al. 1996; Milner and Goodale 1993). We isolated visuomotor activity to the superior and inferior parietal lobule along with the dorsal and ventral premotor cortex. An implication from these findings relates to the previously suggested grasping and pointing visuomotor channels in the inferior and superior parietal cortex (Jeannerod et al. 1995). The current results demonstrate that, because activation of both of these parietal regions occurred during a visuomotor precision grip force task, the possibility is raised that, in humans, the visuomotor channel for grasping may be related to both inferior and superior parietal regions rather than a strict dichotomy between grasping and reaching tasks. It is important to note that the task employed in this study heavily relied on feedback control, and the mapping of the visuomotor process may be different under visually guided motor output that uses more feedforward con-
control processes (e.g., grasping different sized objects based on visual cues) (Toni et al. 2001). A final point regarding our finding of ventral and dorsal premotor visuomotor activity is that each of these regions plays important roles during visually guided tasks. Hanzei et al. (2002) postulated that the PMv plays a minor role (if any) during visuomotor processes, but our findings agree more with the hypothesis that both the ventral and dorsal premotor regions are involved in visuomotor control (Passingham 1993).

SMA. In the SMA, most of the previous evidence suggests that this region is more involved with internally guided movements rather than visually guided movements (Jahanshahi et al. 1995; Mushiake et al. 1991; Passingham 1987), but there is also evidence counter to this hypothesis (Deiber et al. 1999; Remy et al. 1994). In particular, Deiber et al. (1999) showed similar fMRI activation in the SMA during visually triggered and internally triggered finger movement, but different activation was found preferentially for sequential rather than repetitive movements. Moreover, during visually guided movements, a substantial number of neurons consistently responded during the task (Mushiake et al. 1991). The current findings showed activation in the SMA for the visuomotor process but not for the motor memory process. Also, consistent activation was found for the motor/sensory process, which occurred when subjects produced force in the presence or absence of visual feedback. Therefore, our findings are consistent with the idea that a strict functional dichotomy does not apply for only internally guided movement being present in the SMA (Mushiake et al. 1991).

LATERAL CEREBELLUM, DENTATE NUCLEUS, AND VENTRAL THALAMUS. The output from the cerebellar dentate nucleus and its connections with the ventral and posterior thalamus has been implicated as a circuit involved in the visual control of movement (Stein and Glickstein 1992). In the primate, examination of internally guided versus visually guided movement following temporary inactivation of different regions of the primate thalamus suggested a specific role for nucleus X (which mostly receives cerebellar input) during the visual control of movement (van Donkelaar et al. 2000). In support of the findings on primates, we have shown that in humans the visuomotor process occurred in the ventral and posterior portions of the thalamus, which included the expected location of nucleus X. There was no evidence to suggest that anterior thalamic regions were involved in the visuomotor process. There was also specific activation in the lateral cerebellum related to visuomotor processes and to motor/sensory processes. From the lateral cerebellum, there are projections to the dentate nucleus where visuomotor activity was found. There was no evidence of motor/sensory activation in the dentate nucleus. Thus our findings support the hypothesis in humans that the lateral portion of the cerebellum, dentate nucleus, and the ventral and posterior thalamus are involved in the visuomotor transformation process. Because the thalamus receives heavily interdigitated inputs from both the cerebellum and the basal ganglia (Middleton and Strick 2000), the ventral thalamic activation observed in this study most likely includes inputs from the basal ganglia (see Putamen).

PUTAMEN. While there is some evidence to suggest that the basal ganglia may be involved during visually guided movement (Mushiake and Strick 1995), most of the literature has focused on its role during internally guided actions (Flowers 1976; Glickstein and Stein 1991; Hore et al. 1977; Jueptner and Weiller 1998). The current findings provide direct evidence for the visuomotor process in the putamen. Because of the known anatomical connections between basal ganglia output and the ventral thalamus, the ventral thalamic activation for the visuomotor process may be associated with the visuomotor activation in the putamen. Previous work from primate electrophysiology showed preferential activation of pallidal neurons during a visually guided movement task (Mushiake and Strick 1995). Also, patients with Parkinson’s disease have been shown to have difficulties at adapting their visuomotor output to distortions in visual gain (Teulings et al. 2002), and patients have an increased visuomotor feedback gain response in the 1- to 2-Hz band of force output (Vaillancourt et al. 2001a). The current finding that the visuomotor process occurred in the putamen suggests a possible neural mechanism for the behavioral deficits that patients with Parkinson’s disease experience during visually guided tasks.

ANTERIOR PREFRONTAL CORTEX. The prefrontal cortex has been associated with movement-related activation when external cues are not present (Passingham 1993). The current findings on the motor memory process (see Motor memory process) support that hypothesis. In addition, recent evidence from PET and fMRI demonstrates that the learning of a visually guided task specifically involves the connectivity between the striatum and the prefrontal cortex. For example, when humans learn to position the hand with certain visual cues, the network included changes in the striatum and prefrontal cortex (Toni et al. 2001, 2002). Anatomical evidence from primates supports the notion that visual input does reach the prefrontal cortex (Webster et al. 1994) and that the premotor cortex has projections to these anterior prefrontal regions (Matelli et al. 1986). Also, in the primate, the prefrontal cortex was related to an association between sensory cues and the appropriate motor response (Asaad et al. 1998). Thus, our findings provide further support in humans for the idea that the anterior prefrontal cortex may be associated with visuomotor transformations.

Topographic orientation of visuomotor and motor/sensory processes

The findings (Table 2; Fig. 2) on the visuomotor and motor/sensory processes suggested several rules regarding their topographic organization. In the PMd proper, the visuomotor process was more ventral and lateral relative to motor/sensory processes. The ventral and lateral visuomotor to motor/sensory pattern was not observed in the posterior portion of the PMd proper. One explanation for this finding is that in the posterior portion of the PMd proper lies the central sulcus, and this region is more associated with the execution of force (Dettmers et al. 1995; Georgopoulos et al. 1992). Indeed, the findings showed that motor/sensory processes occurred in the primary motor cortex and primary somatosensory cortex. Visuomotor processes in the PMd proper were anterior to the motor/sensory processes, and in the parietal cortex, the visuomotor process was posterior to the motor/sensory processes. Finally, in the cerebellum ipsilateral to the hand producing force, the visuomotor process was diffusely organized around the motor/sensory processes. While this finding may seem contrary to previous work in the primate dentate nucleus (Mushiake and
Strick 1993), it is important to consider that the present study examined collective regions spatially larger than the previous work from single unit dentate neurons.

**Motor memory process**

The retrieval of motor memory is frequently used without visual information (Baddeley 1986; Ghez et al. 1990; Goldman-Rakic 1987; Vaillancourt and Russell 2002). This study identified the motor memory process by comparing force without visual feedback to force with visual feedback. The motor memory process was active in the prefrontal regions, including the anterior portion of the anterior cingulate, dorsolateral prefrontal cortex, and ventral prefrontal cortex (Table 2) (Jenkins et al. 2000). Most of the neuronal activity for the motor memory process was ipsilateral to the activity found in the primary motor cortex. Within the prefrontal cortex, the motor memory process was more medial compared with the motor/sensory and visuomotor processes (Table 2; Fig. 3). An important note is that previous work demonstrates that the anterior cingulate is important for error monitoring (Carter et al. 1998; Cohen et al. 2000). It is therefore possible that a portion of the anterior cingulate activation during the motor memory process could have also been due to the monitoring of errors made without visual information. In summary, these findings on the retrieval of memory for force output agree with other findings from cognitive neuroscience describing the prefrontal cortex and its role in other forms of working memory (Baddeley 1986; Goldman-Rakic 1987; Passingham 1993; Rowe et al. 2000).

The novel contribution here was that motor memory processes were not found in the SMA or in the basal ganglia. The activity found in the SMA corresponded to the visuomotor process and to the common motor/sensory activation that was independent of visual feedback. The previous work showing SMA and basal ganglia activity examined tasks that involved both movement sequencing and memory function, making it difficult to isolate motor memory processes (Jahanshani et al. 1995; Jenkins et al. 2000; Mushiake and Strick 1995; Mushiake et al. 1991). In contrast, the current study minimized sequencing processes by using a constant force production task. Our current findings isolated the motor memory process to the dorsolateral prefrontal cortex, ventral prefrontal cortex, and anterior cingulate.

The lack of neuronal activity in the basal ganglia when visual information was absent has implications for understanding the mechanisms underlying internally guided motor deficits in patients with Parkinson’s disease. Previous behavioral work has shown that when visual information is removed, patients with Parkinson’s disease have a greater deficit in their ability to control motor output compared with control subjects (Cooke et al. 1978; Flowers 1976), and this was hypothesized to be related to memory processes (Gentilucci and Negrotti 1999; Vaillancourt et al. 2001b). Because patients with Parkinson’s disease suffer from a basal ganglia deficit, one might have expected the basal ganglia to be directly involved in the motor memory process. However, anatomical work has shown that the basal ganglia have projections to the prefrontal cortex (Middleton and Strick 2002), and we found that the motor memory process was located in the dorsolateral and ventral prefrontal cortex. Furthermore, an fMRI study has shown reduced activation in patients with Parkinson’s disease in the dorsolateral prefrontal cortex during an internally guided sequential movement task (Sabatini et al. 2000). Thus in patients with Parkinson’s disease, we suggest that the increased inhibitory globus pallidus output acts as a modulator to cause dysfunction in the prefrontal cortex, which in turn has adverse effects on the ability to use motor memory, and this leads to difficulties for patients in performing internally guided tasks.

**Conclusions**

This study separated a task-related network used during continuous force output into four distinct processes spanning multiple brain regions that merge motor, sensory, and cognitive domains. The findings showed that the visuomotor process spanned beyond the parietal-premotor network and also included the SMA, anterior prefrontal cortex, ventral thalamus, putamen, intermediate cerebellum, lateral cerebellum, and the dentate nucleus. These findings support a model of visuomotor control where distributed nodes transform visual signals into motor commands. This distributed model interpretation further suggests that visuomotor processes occur in both medial (e.g., SMA, basal ganglia) and lateral (e.g., lateral cerebellum, lateral premotor cortex) channels. Another significant finding included a systematic visuomotor to motor/sensory topography located in the premotor cortex, parietal cortex, and the lateral cerebellum. It should be noted that the processes identified in this study were in the context of a constant precision grip force task, and tasks that include more dynamic proprioceptive and motor output signals may reveal additional or even different regions of activation. Finally, the retrieval of motor memory information was isolated to the dorsolateral prefrontal cortex, anterior cingulate, and the ventral prefrontal cortex. In summary, this study isolated the visuomotor and motor memory processes into distributed and localized networks, respectively, that underlie the control of visually guided and internally guided actions.

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**Disclosures**

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