A Comparison of Frontoparietal fMRI Activation During Anti-Saccades and Anti-Pointing

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1Department of Psychology and 2Department of Physiology, University of Western Ontario, London N6A 5C1; 3Advanced Imaging Labs, The John P. Robarts Research Institute; 4Departments of Radiology and Medical Biophysics, University of Western Ontario, London N6A 5K8; and 5Departments of Physiology and Ophthalmology, University of Western Ontario, London, Ontario N6A 4G5, Canada

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Connolly, Jason D., Melvyn A. Goodale, Joseph F. X. DeSouza, Ravi S. Menon, and Tutis Vilis. A comparison of frontoparietal fMRI activation during anti-saccades and anti-pointing. J Neurophysiol 84: 1645–1655, 2000. An anti-saccade, which is a saccade directed toward a mirror-symmetrical position in the opposite visual field relative to the visual stimulus, involves at least three separate operations: covert orienting, response suppression, and coordinate transformation. The distinction between pro- and anti-saccades can also be applied to pointing. We used fMRI to compare patterns of brain activation during pro- and anti-movements, to determine whether or not additional areas become active during the production of anti-movements. In parietal cortex, an inferior network was active during both saccades and pointing that included three foci along the intraparietal sulcus: 1) a posterior superior parietal area (pSPR), more active during the anti-tasks; 2) a middle inferior parietal area (mIPR), active only during the anti-tasks; and 3) an anterior inferior parietal area (aIPR), equally active for pro- and anti-movement. A superior parietal network was active during pointing but not saccades and included the following: 1) a medial region, active during anti- but not pro-pointing (mSPR); 2) an anterior and medial region, more active during pro-pointing (aSPR); and 3) an anterior and lateral region, equally active for pro- and anti-pointing (ISPR). In frontal cortex, areas selectively active during anti-movement were adjacent and anterior to areas that were active during both the anti- and pro-tasks, i.e., were anterior to the frontal eye field and the supplementary motor area. All saccade areas were also active during pointing. In contrast, a region in the dorsal premotor area, the anterior superior frontal region, and anterior cingulate were active during pointing but not saccades. In summary, pointing with central gaze activates a frontoparietal network that includes the saccade network. The operations required for the production of anti-movements recruited additional frontoparietal areas.

INTRODUCTION

An anti-saccade directs gaze toward a mirror-symmetrical position in the opposite visual field (Hallett 1978). To generate an anti-saccade, it is likely that the brain carries out at least three additional operations as compared with when generating pro-saccades: 1) attention must be oriented covertly toward the visual stimulus; 2) the pro-saccade must be suppressed; and 3) coordinates of the stimulus must be re-mapped to the new location in the opposite visual field. In this study, we used functional magnetic resonance imaging (fMRI) to compare the patterns of brain activation invoked during anti- and pro-saccades. We also carried out the first neuroimaging analysis of anti- and pro-pointing movements. This allowed us to compare the functional organization of anti- and pro-movements in two different effector systems.

Covert orienting is the redirection of attention from one spatial locus to another in the absence of eye movement. Anti-saccades require a relatively sustained covert shift toward the visual cue as compared pro-saccades. Anti-pointing while maintaining fixation requires two shifts of attention; one toward the visual cue and another toward the goal location. It is reasonable to suggest therefore that areas involved in covert orienting may be more active during an anti-task. The system for the covert orienting of visuospatial attention largely overlaps with the saccade network (for review, see Corbetta 1998). Since covert orienting is also required during pointing with central gaze, we hypothesized that the network of areas for covert orienting (and by extension the “saccade” network) would become active during pointing to one target while fixing another.

To make an anti-saccade, a pro-saccade toward the visual cue must be suppressed. Human (Braun et al. 1992; Guitton et al. 1985; Law et al. 1997; Milner 1982; O’Driscol et al. 1995; Petit et al. 1995, 1999; Sweeney et al. 1996) and monkey (Burman and Bruce 1997; Cowey and Latto 1971; Dias and Segraves 1999; Hanes et al. 1998; Schall and Hanes 1993) data suggest that the frontal eye field (FEF) is involved in saccade suppression. We expected therefore that the FEF and related saccade suppression areas would be more active during anti- as compared with pro-saccades. Also, the FEF and the other elements of the saccade network should become active during pointing to a target when gaze is maintained on another target, reflecting 1) the suppression of saccades to the pointing target, 2) the covert shift of attention to that target, or 3) both.

To execute a spatially precise anti-movement, the coordinates that specify the location of the visual stimulus must be...
rotated through $180^\circ$ or simply mirror-reflected. Latency studies suggest that anti-saccades involve the latter (Fisher and Weber 1992). It does not follow, however, that the same mirroring underlies anti-pointing. For instance, studies that have examined reaction time for manual movements and average neuronal activity in M1 of the monkey are more consistent with rotation rather than with mirror-reflection (Georgopoulos et al. 1989). In short, if re-mapped pointing movements involve rotation and anti-saccades involve mirroring, then this might be accompanied by different patterns of activation.

FMRI allowed us to determine the amount of overlap between the networks for anti- and pro-saccades and for anti- and pro-pointing. In other words, are these independent, partially independent, or overlapping neural systems? We predicted that additional areas would be selectively activated during the anti-tasks, to subserve processes important to anti-movement. Since anti-pointing involves a different effector as compared with anti-saccades, we anticipated that the additional operations required for anti-movements of the hand would be distinct from those mediating the corresponding movements of the eyes.

**METHODS**

Seven subjects with normal vision participated in the present study after giving informed consent (4 males and 3 females, 24.8 ± 3.2 yr, mean ± SD). All subjects were right handed, as determined by the Edinburgh handedness Inventory (Oldfield 1971).

**Experimental design**

During each experimental run of saccades or pointing movements, three tasks were administered in separate blocks: central fixation (F); visually guided pro-saccades or pro-pointing (P); anti-saccades or anti-pointing (A). The order of tasks and the two replications of the

**TABLE 1. Mean Talairach coordinates for foci active during the saccade experiment**

<table>
<thead>
<tr>
<th>Pro-Saccade vs. Fixation</th>
<th>Anti-Saccade vs. Fixation</th>
<th>Total Voxels</th>
</tr>
</thead>
<tbody>
<tr>
<td>x</td>
<td>y</td>
<td>z</td>
</tr>
<tr>
<td>pSPR (L)</td>
<td>$-11 \pm 2$</td>
<td>$-73 \pm 3$</td>
</tr>
<tr>
<td>pSPR (R)</td>
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<td>mIPR (L)</td>
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<tr>
<td>aIPR (L)</td>
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<td>$-43 \pm 3$</td>
</tr>
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<td>SMA</td>
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<td>$-4 \pm 2$</td>
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<tr>
<td>FEF (L)</td>
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<td>$-7 \pm 2$</td>
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<tr>
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<td>$-5 \pm 2$</td>
</tr>
<tr>
<td>preFEF (L)</td>
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<td>$3 \pm 2$</td>
</tr>
<tr>
<td>PMv (L)</td>
<td>$-37 \pm 2$</td>
<td>$-3 \pm 2$</td>
</tr>
<tr>
<td>PMv (R)</td>
<td>$51 \pm 3$</td>
<td>$6 \pm 1$</td>
</tr>
</tbody>
</table>

Values are means ± SE. Total Voxels column represents the mean total number of active voxels (pro-saccade only + anti-saccade only + shared = total) by cortical region. Coordinates: $X$ (lateral/medial), $Y$ (anterior/posterior), and $Z$ (superior/inferior) according to Talairach and Tournoux (1988). pSPR, posterior superior parietal area; mIPR and aIPR, middle and anterior inferior parietal area, respectively; SMA, supplementary motor area; FEF, frontal eye field; PMv, ventral premotor area; L, left hemisphere; R, right hemisphere.
TABLE 2. Mean Talairach coordinates for foci active during the pointing experiment

<table>
<thead>
<tr>
<th></th>
<th>Pro-Pointing vs. Fixation</th>
<th>Anti-Pointing vs. Fixation</th>
<th>Total Voxels</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>x</td>
<td>y</td>
<td>z</td>
</tr>
<tr>
<td>pSPR (L)</td>
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<td>-68 ± 2</td>
<td>38 ± 3</td>
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<tr>
<td>pSPR (R)</td>
<td>17 ± 3</td>
<td>-64 ± 2</td>
<td>41 ± 3</td>
</tr>
<tr>
<td>mlIPR (L)</td>
<td>-44 ± 3</td>
<td>-32 ± 3</td>
<td>33 ± 3</td>
</tr>
<tr>
<td>mlIPR (R)</td>
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<td>-50 ± 3</td>
<td>41 ± 4</td>
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<td>mIPR</td>
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<td>44 ± 2</td>
</tr>
<tr>
<td>aSPR</td>
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<td>-49 ± 4</td>
<td>33 ± 2</td>
</tr>
<tr>
<td>SMA</td>
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<td>50 ± 2</td>
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<tr>
<td>PreSMA</td>
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<tr>
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<td>FEF (L)</td>
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<td>45 ± 3</td>
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<td>PreFEF (R)</td>
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<td>31 ± 1</td>
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<td>PMv (L)</td>
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<td>12 ± 8</td>
<td>25 ± 2</td>
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<tr>
<td>PMv (R)</td>
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<td>10 ± 7</td>
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</tr>
<tr>
<td>PMd</td>
<td>-42 ± 3</td>
<td>-6 ± 1</td>
<td>41 ± 5</td>
</tr>
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</table>

Values are means ± SE. Total Voxels column represents the mean total number of active voxels (pro-saccade only + anti-saccade only + shared = total) by cortical region. Coordinates: X (lateral/medial), Y (anterior/posterior) and Z (superior/inferior) according to Talairach and Tournoix (1988). mSPR, aSPR, and ISPR, medial, anterior, and lateral superior parietal area, respectively; anCing, anterior cingulate; aSPR, anterior superior frontal region; PMd, dorsal premotor area; for other abbreviations, see Table 1.

saccade and pointing experiments were mirror-imaged. A total of 336 functional volumes were averaged across each of the fixation, pro-saccade, anti-saccade, pro-pointing, and anti-pointing tasks.

Visual stimuli were generated with Macromedia Director 5.0 software (San Francisco, CA) and presented using a computer connected to an NEC Multi-sync MT 800 LCD video projector (refresh rate, 72 Hz). The image was projected off a mirror onto a screen secured to the ceiling of the magnet bore. Visual cues and the fixation cross were white on black background, and each cue subtended 0.5° of visual angle. Each task began with the subject fixating the central cross. A series of 12 cues were flashed every 2 s for 200 ms. Subjects made sequential horizontal saccades (or pointed without saccades) to one of four locations with no return to center following each movement, i.e., subjects did not make pro-saccades during anti-saccade blocks, in contrast to previous studies (O’Driscoll et al. 1995; Faus et al. 1993; Sweeney et al. 1996). Cue locations were selected so that anti-movements coincided with those of the pro task (between ±6°). For example, during the anti-task when subject gaze corresponded to 6° to the left of center and a cue was flashed 9° to the left, the subject made a saccade to the 3° location. In the pro-saccade task, subjects were instructed to make a saccade toward the flashed target as soon as it appeared and to hold eye position until the next flashed target appeared. In the pro-pointing task, subjects made sequential pointing movements, without touching, using the index finger from target to target while maintaining central fixation. Subjects aligned the index finger with the cue location by rotating the hand about the wrist joint. The upper arm was immobilized throughout. An opaque barrier prevented subjects from viewing hand position during testing. In the control task, subjects maintained central fixation on a central cross as the same 12 sequential targets were flashed in the periphery at positions that controlled for retinal eccentricity. Following each “anti” block, subjects indicated whether they were looking or pointing at the expected final position and thus had completed the sequence correctly. On two occasions they were not, and the data were discarded and the experiment repeated. Order of target location was balanced across different sequences so that number, movement amplitude, rightward/leftward movement, and number of movements across the midline in a particular direction were balanced across the pro- and anti-tasks.

Preparation

All subjects were trained prior to scanning until they performed each task without error. To verify that subjects were able to suppress eye movements during fixation and the pointing tasks, horizontal eye movements were measured off-line in five subjects using an infrared eye-tracking, Eye-Trac Model 200 (Narco Systems, Houston, TX). Subjects did not make saccades during the pointing or fixation tasks, and there was no difference in mean movement amplitude for the pro- and anti-saccade tasks (t(4) = 1.63, n.s.; t(4) = 0.89, n.s., respectively). To minimize head motion during scanning, subjects were secured with J) vacuum packing of the head, neck, and shoulders via surgical positioning pillows (Olympic Medical, Seattle, WA); 2) a bite bar with an individually molded dental impression; and 3) Velcro strapping around the upper torso and right upper arm.

Imaging procedures

Images were collected with a Varian Unity Inova whole body 4 Tesla MRI system (Varian, Palo Alto, CA; Siemens, Erlangen, Germany) to measure blood-oxygen level–dependent signal changes related to brain activation (Ogawa et al. 1992). Occipital, parietal, and frontal cortices were imaged using a full head coil. Seven contiguous 8-mm slices, collected every second, were aligned parallel to the calcarine sulcus with an in-plane resolution of 3 × 3 mm (3 × 3 × 8 mm voxels; Fig. 1). Functional data were obtained using T2*-weighted segmented gradient echoplanar imaging (EPI, 7 slices, FOV: 19.2 × 19.2 cm, 64 × 64 resolution, TE = 20 ms, TR = 70 ms, flip angle = 15°, 2 segments/plane, navigator-corrected). Functional images were superimposed on high-resolution T1-weighted anatomical images (3D magnetization-prepared (MP) turbo FLASH acquisition, 64 slices, 256 × 256 resolution, T1 = 500 ms, TE = 6.0 ms, TR = 11.8 ms, flip angle = 11°) acquired in the same scan session with the same slice orientation and in-plane field of view.
Data analysis

Each scan was screened for head motion via 1) generation of a cinematic loop of the functional volumes; 2) inspection of the center of mass over time; and 3) screening for edge and ventricle artifact. In one subject, motion artifact was observed and the data discarded. All signal time courses were corrected for linear drift.

Paired sample t-tests were conducted on a voxel-by-voxel basis for each subject after the sequence of volumes was corrected for hemodynamic delay. Subtraction methodology was based on percent signal...
change for the following comparisons: 1) pro-saccades (or pointing) — fixation, and 2) anti-saccades (or anti-pointing) — fixation. The number of voxels that were activated 1) during both the pro- and anti-tasks, 2) only during the pro-task, and 3) only during the anti-task were counted for each subject for each region. An additional paired sample t-test was used to determine whether shared voxels (active during both the pro- and the anti-task) were more or less active for the anti- as compared with the pro-task.

Voxel activity for each task was compared with an average of both a preceding and succeeding baseline in which possible order effects were reduced by mirror imaging task order. Clusters consisting of six or more contiguous in-plane voxels that passed a threshold of \( P < 0.05 \) (corrected for multiple comparisons) [Stimulate (Strupp 1996)] were considered active (Forman et al. 1995; Worden and Schneider 1995). Active voxels with signal changes of \( >0.6 \) or \( >5\% \) were rejected to exclude differences related to venous drainage (Menon et al. 1993; Worden and Schneider 1995).

Functional and anatomical images were transformed to the coordinate system of Talairach and Tournoux (1988). Following transformation, functional maps were averaged across subjects and displayed on an averaged T1-weighted image set.

**RESULTS**

Talairach coordinates for each activated region for the proand anti-saccade tasks are presented in Table 1. The coordinates for pro- and anti-pointing are presented in Table 2.

Overall, more voxels were active, on average, during anti- as compared with pro-movements (means across subjects: anti-saccades = 221.1 active voxels; pro-saccades = 99.0 active voxels; anti-pointing = 387.1 active voxels; pro-pointing = 291.6 active voxels). The proportions of these voxels for each region are presented in Tables 1 and 2. More voxels were active during pointing than during saccades (means across subjects: pointing = 466.7 active voxels; saccades = 254.1 active voxels). Although there were saccade-only voxels for single subjects, in the averaged maps, areas activated during saccades were completely contained within areas activated during pointing. Thus on the basis of the averaged maps at least, it appeared as though there were no exclusively saccade-related areas.

In the majority of the single-subject maps, six distinct peaks of activity were identified within parietal cortex during the anti-pointing task. These peaks of activity were separated by inactive voxels. In those few cases where the voxels surrounding the different activity peaks were contiguous in a subject (i.e., similar to the averaged maps shown below), anatomical landmarks that separated these foci in the remaining subjects were used to partition the voxels into separate foci of activity. Three separate peaks of activity were identified in the parietal cortex for the anti-saccade task, and these coincided with three of the six peaks associated with anti-pointing.

**Parietal areas activated during both saccades and pointing**

There were no parietal areas that were active during saccades but not during the pointing tasks (see overview Fig. 1). Three parietal regions were activated bilaterally during the saccade and pointing tasks. Voxels anterior to the parieto-occipital sulcus, medial to the intraparietal sulcus, and posterior to the subparietal line (drawn parallel to the ascending limb of the subparietal sulcus) (Duvernoy 1991) were included within a region that we labeled the posterior superior parietal region (pSPR; Fig. 2, A and C). The second region was lateral...
to the intraparietal sulcus and posterior to the transverse parietal line (Duvernay 1991), which we call the middle-inferior parietal region (mIPR; Fig. 2, A and C). Since areas pSPR and mIPR appear contiguous in the averaged maps (Fig. 2, A and C), the voxels were demarcated based on position relative to the intraparietal sulcus (IPS). Voxels medial to the IPS were included within pSPR, and those lateral to the sulcus were included within mIPR (Fig. 2, A and C). The voxels anterior to the transverse parietal line and lateral to the intraparietal sulcus, along the postcentral sulcus, formed a third parietal area, the anterior inferior parietal region (aIPR; Fig. 2, A and C).

Area pSPR had the largest volume of all active regions and was significantly more active during the anti- as compared with the pro-tasks for both saccades and pointing. This increase involved recruiting a significantly greater number of voxels in the anti-movement tasks (Fig. 2, B and D). As well, within the shared voxels in this region (i.e., those active during both pro- and anti-movements), the level of activation was significantly greater for the anti-tasks \((P < 0.05)\). Most of the voxels activated by the pro-tasks were contained within the region activated by the anti-task (Fig. 2, A and C).

Area mIPR was only active during the anti-tasks (Fig. 2, B and D). In general, area aIPR was equally activated for anti- as compared with the pro-tasks. However, area aIPR volume increased \(\sim 130\%\) for anti-pointing as compared with anti-saccades \((\sim 1.66 \text{ cm}^3\), anti-saccades, to \(\sim 3.82 \text{ cm}^3\), anti-pointing)\).

### Parietal areas active during pointing but not saccades

Three parietal areas were activated during pointing but not saccades. All three were situated within superior parietal cortex, anterior and medial to the saccade-and-pointing foci discussed above. The first region was dorsal and anterior to area...
pMRI OF ANTI-SACCADES AND ANTI-POINTING

Saccades

[Image 6: Coronal images that illustrate activation of the dorsal and ventral premotor areas. Whereas area PMv was active only during the anti-saccade task, PMv was active during both the anti- and pro-pointing tasks. Area PMd was only active during pointing. * Significant difference in the number of active voxels for the anti- as compared with the pro-task, \( P < 0.05 \). SF, the sylvian fissure; IFS, inferior frontal sulcus.]

Medial frontal cortex

Three areas were activated within medial frontal cortex: the supplementary motor complex, the anterior superior frontal region (aSFR), and the anterior cingulate (anCing). Similar to previous studies, the supplementary motor complex was partitioned into the supplementary motor area (SMA) posterior to the vertical anterior commissural line (VAC) and the preSMA anterior to the VAC line (Fig. 4B) (Petit et al. 1998; Stephan et al. 1995). The SMA was activated during saccades and pointing, and the preSMA was activated only during pointing (Fig. 4, A and B).

Sixty-eight percent of SMA voxels were active only during the pro-saccade task. There was therefore a significant decrease in the number of active voxels in the SMA for anti- as compared with pro-saccades \( (P < 0.05) \). In contrast to the eye movement tasks, most pointing SMA voxels \( (~70\%) \) were activated by both the pro- and anti-pointing tasks. The preSMA was active only during the anti-pointing task (Fig. 4B).

Activation was also observed in the anCing during pointing but not saccades (Fig. 4B). There were significantly more active voxels during anti- as compared with pro-pointing (Fig. 4B, \( P < 0.05 \)). Activation was observed anterior to the preSMA and anterodorsal to the anterior cingulate, which we call the anterior superior frontal region, or aSFR (Fig. 4B). This region was activated during pointing but not saccades. Eighty-five percent of aSFR voxels were active during the pro-pointing but not during the anti-pointing task; the remainder were active during both pointing tasks. Area aSFR volume therefore significantly increased for pro- as compared with anti-pointing \( (P < 0.05) \).

Lateral frontal cortex

FEF activation was located anteromedial to M1 and borders the precentral and superior frontal sulci (Fig. 5, A and B). As in
most cortical regions, there was a significant increase in area FEF volume for anti- as compared with pro-saccades \((P < 0.05)\), and shared voxels were more active during the anti-saccade task \((P < 0.05)\).

FEF voxels activated during saccades were also activated during pointing (Fig. 5B). [This observation was based on superimposing the saccade and pointing maps.] This activation was judged distinct from M1 for the following reasons: 1) the two foci were separated by inactive voxels, with M1 activation within the anterior bank of the central sulcus and FEF activation within the anterior bank of the precentral sulcus; 2) M1 activity was entirely contralateral, whereas pointing FEF activity was bilateral; 3) FEF voxels were activated during pointing and saccades, and it is unlikely M1 would be activated by eye movements.

In contrast to the saccade tasks, there was no difference in FEF volume for pro- and anti-pointing. Sixty-three percent of active FEF voxels were shared for the two pointing tasks. Also, as was the case with the saccade tasks, shared pointing FEF voxels were significantly more active during anti-movement \((P < 0.05)\). Cortex anterior to the FEF and the VAC line was active during the anti- but not the pro-tasks (preFEF; Fig. 5B). FEF volume significantly increased for anti- as compared with pro-saccades \((P < 0.05)\) but not for anti- as compared with pro-pointing. Shared FEF voxels were significantly more active during anti-saccades and anti-pointing as compared with the respective pro-tasks \((P < 0.05)\). The preFEF was active only during the anti-tasks (Fig. 5B).

An area just anterior to the precentral sulcus, dorsal to the inferior frontal sulcus, and lateral and ventral to area FEF was activated by pointing of the contralateral limb and not by saccades, the dorsal premotor area (PMd; Fig. 6B). This area was equally active for pro- and anti-pointing, i.e., there were no differences in the number of active voxels or in the level of activation within the shared voxels. The ventral premotor area (PMv; Fig. 6, A and B) was lateral and ventral to PMd and active during the anti-saccade task and both pointing tasks. This area was situated ventral to the inferior frontal sulcus and immediately anterior to the precentral sulcus.

**Discussion**

In contrast to the results of an earlier PET study (Kawashima et al. 1996b), we found no major parietal focus devoted exclusively to saccades (see legend of Fig. 1). Indeed, in the area described as exclusively saccade related in the PET study, we found activation during our pointing tasks as well as during the saccade tasks. In our study, all areas activated during saccades were also activated during pointing, including the FEF. As noted in the introduction, the networks for covert orienting and saccade suppression overlap with significant portions of the saccade network. Since both processes are required during pointing with maintained fixation, activation during pointing may be due to the demands of covert orienting and/or suppression of saccadic eye movements.

These data suggest that the anti-movement networks include the pro-movement networks, plus additional areas that become active only during the anti-tasks. A number of areas were active during the anti- but not during the pro-pointing tasks. Some of the areas were exclusively related to anti-pointing; in other words, they were not active during either of the saccade tasks or the pro-pointing task, i.e., areas mSPR, the preSMA, and anCing (see Fig. 1). These areas are presumably involved in processes exclusive to anti-pointing. One process, for example, that is unique to the anti-pointing task is transforming the re-mapped “anti” coordinates into a hand-centered frame of reference. Perhaps these anti-pointing areas reflect this kind of transformation. An alternative possibility is that common operations are housed in different regions for saccades and pointing. This is unlikely, however, since all of the areas active during the anti-saccade task were also active during anti-pointing.

Only three areas were preferentially activated during the pro-tasks: the SMA, area aSFR, and area aSPR (see Fig. 1). Areas aSFR and aSPR showed preferential pro-movement activation only for pointing. It is noteworthy that all three of these areas were located along the medial wall of the frontoparietal cortex. It remains an intriguing question as to what processes are more important to the production of pro- than anti-movements.

**Parietal areas active during both saccades and pointing**

A network extending into inferior parietal cortex was active during saccades and pointing. Area mIPR was active only during anti-movements. This region has been found to be active during prism-adaptation while reaching (Clower et al. 1996). Presumably, visuo-motor space is “updated” during such adaptation. This same area may perform similar operations for anti-movements, i.e., transform the visual cue location into the anti-target location. Since this area was selectively active during both the anti-tasks, one possibility is this area transforms the cue location into the anti-target location within a common frame of reference.

Area pSPR was more active during the anti-tasks. It is noteworthy that this area is active during tasks of covert orienting (for review, see Corbetta 1998). We expected that anti-pointing would induce the most activation in areas implicated in covert shifts of attention. This is because, for the anti-pointing task, not only was the subject required to orient covertly toward the visual cue, but also toward the target of the anti-pointing movement. Consistent with this reasoning, area pSPR volume was maximal during anti-pointing.

A final area lateral to the most anterior portion of the IPS was active during all four tasks, area aIPR. This is the first study to report activation of this anterior “pointing” focus during an oculomotor task. Talairach coordinates \((X = -44 Y = -32 Z = 33)\) are consistent with foci active during hand movements \((X = -42 Y = -36 Z = 46)\) (Kawashima et al. 1998) and grasping \((X = -46 Y = -39 Z = 37)\) (Grafton et al. 1996a) \((X = \text{medial/lateral}, Y = \text{anterior/posterior}, Z = \text{dorsal/ventral})\).

**Parietal areas active during pointing but not saccades**

This is the first study to report three functionally distinct parietal activation peaks: the middle, anterior, and lateral superior parietal regions, i.e., areas mSPR, aSPR, and lSPR, respectively. These regions are well situated to contain cortex homologous to monkey areas MIP, MDP, and 7m (for review, see Johnson et al. 1997), as well as the parietal reach region (Snyder et al. 1997). These regions constitute most of the monkey superior parietal lobule and are related to limb move-
ment in this species (for reviews, see Andersen et al. 1997; Colby and Goldberg 1999; Johnson et al. 1997).

Area mSPR was more active during anti- as compared with pro-pointing. In contrast, aSPR was more active during pro-pointing. As described above, inferior parietal area mIPR was selectively active during both anti-tasks. Whereas neurons in this area may transform the visual cue location into the anti-target location, area mSPR may transform “anti” coordinates into a hand-centered frame of reference.

Area ISPR is adjacent to area aIPR but is instead medial to the intraparietal sulcus. Since the fMRI activity peaks are on opposite sides of the sulcus, Talairach coordinates likely under-estimate the distance between these two peaks. Previous imaging studies of limb movement have also reported greater contralateral activity in this area (Kawashima et al. 1996b; Kertzman et al. 1997; Weinstein et al. 1997).

**Medial frontal cortex**

With the exception of SMA proper, all medial frontal areas, i.e., the preSMA, the anCing, and area aSFR, were active only during pointing movements. As was the case in the parietal lobe, medial areas appear to be involved more in mediating pointing than generating saccades.

The preSMA was active only during anti-pointing, and the absence of eye-movement activation in this area is consistent with the report that this region contains only a forelimb representation (Kurata 1992). Moreover, about 30% of monkey preSMA neurons exhibit activity when the arm is moved away from a preceding movement target, a paradigm similar to the anti-pointing task (Matsuzaka and Tanji 1996). In both monkey and human, the preSMA is active during tasks involving spatial working memory and shifts of attention, observations that are also consistent with its select activation during anti-pointing (D’Esposito et al. 1998; Nagahama et al. 1998; Petit et al. 1998). Select activation of this region during anti-pointing but not during anti-saccades raises the possibility that at least one of these processes has a distinct representation for the purposes of guiding re-mapped hand movements.

**Lateral frontal cortex**

The lateral frontal areas activated during saccades and/or pointing include areas FEF, preFEF, PMv, PMd, and M1. The FEF was active during both the pointing and the saccade tasks and was more active during the anti-tasks. These are the first data to suggest that the FEF becomes active during pointing to a peripheral location while maintaining fixation of a central visual cue. Talairach coordinates (X 27 Y 2 Z 46) are consistent with previous studies of anti-saccades (X 28 Y 5 Z 49) (average coordinates of O’Driscoll et al. 1995; Paus et al. 1993; Sweeney et al. 1996). These previous studies also found more activation in this region during the anti-tasks. Although FEF volume increased for anti- as compared with pro-saccades, there was no increase in FEF volume for anti- as compared with pro-pointing (and most pointing FEF voxels were shared). No increase in pointing FEF volume supports the idea that the FEF is part of a saccade suppression network.

In contrast, the preFEF was selectively active during the anti-tasks. In human imaging studies, cortex anterior to the FEF and the vac line, which probably corresponds to what we are calling the preFEF, has been found to be active during tasks of spatial working memory (Courtney et al. 1996, 1998; Owen 1997; Smith et al. 1996) and during the covert orienting of attention (Corbetta 1998). These processes could account for the pattern of activation observed during the performance of the anti-tasks, to encode the visual stimulus location as the anti-movement vector is computed. Since this area was active during both anti-tasks, it likely encodes information important to both eye and hand movement.

The ventral premotor area (PMv) was active during both pointing tasks and during the anti-saccade task. These are the first human data that suggest that this area becomes active during a saccade task. Other researchers have proposed that this area is homologous to monkey PMv (Fink et al. 1997; Grafton et al. 1996b; Weinstein et al. 1997). In monkey, single-cell activity is modulated by arm and hand movements (Fogassi et al. 1992; Gallese et al. 1996; Gentilucci et al. 1983; Graziano et al. 1997; Murata et al. 1996), and forelimb movements are elicited by microstimulation of PMv (Ghosh and Gattara 1995). The Talairach coordinates (X 45 Y 6 Z 25) are consistent with foci that have been found to be active during finger movement (X 54 ant 2 sup 24) (Sadato et al. 1997), arm movement (X 56 Y 7 Z 23) (Kawashima et al. 1996a), and manual aiming (X 55 Y 7 Z 25) (Weinstein et al. 1997). Nevertheless, consistent with activation during anti-saccades, an oculomotor-specific subpopulation exists within monkey PMv, in which stimulation induces saccades with anti-saccade velocities (Fujii et al. 1998).

**Summary**

The pattern of activation in the posterior parietal cortex suggests that it may be divided into two related networks: 1) an inferior network involved in both eye and hand movements and 2) a superior network primarily involved in pointing movements (see Fig. 1). The inferior network may generate a target representation for both classes of movement, as well as shifts of covert attention to the target and to the anti-target position. It is possible, however, that this network, particularly areas pSPR and mIPR, may also be involved in the coordinate transformations required to generate anti-movement. In contrast to the inferior network, the superior network appears to be primarily involved in higher-order coordinate frameworks (i.e., head- and/or limb-centered coordinates) required for pointing.

In frontal cortex, a number of patterns of activation were observed. Some of these foci could be separated anatomically by the vac into two functional groups (see Fig. 1). Indeed, with the exception of area aSFR, all regions anterior to the vac (i.e., the preFEF, preSMA, and anCing) were active only during the anti-tasks. This suggests that there may be a common organizing scheme within frontal cortex, with anti-only foci situated directly anterior to shared pro- and anti-foci. Similar to the parietal lobe, frontal pointing-only areas are medial to the shared saccade-and-pointing foci, and these areas include PMd, the anCing, the preSMA, and aSFR.

The organizational scheme observed in the present study is consistent with anatomical tracer studies in monkey. The superior network in the parietal cortex (active during pointing but not saccades) may be homologous with SPL in the monkey, which projects to medial frontal regions (Cavada and Goldman-Rakic 1989; Pandya and Kuypers 1969; Petrides and
Pandya 1984; Strick and Kim 1978). The inferior network in the parietal cortex, in contrast, may correspond to monkey IPL, which projects to lateral frontal and dorsolateral prefrontal cortex. In summary then, these data suggest that 1) a common organizational scheme exists in the human that parallels the monkey, with areas involved in eye and hand processes situated lateral to those selectively involved in hand movement; 2) additional brain areas become active during the anti-tasks, to process additional operations important to cognitively mediated movements; and 3) anti-pointing involves additional areas as compared with anti-saccades.

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