Functional magnetic resonance adaptation reveals the involvement of the dorsomedial stream in hand orientation for grasping

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Submitted 8 December 2010; accepted in final form 27 July 2011

Monaco S, Cavina-Pratesi C, Sedda A, Fattori P, Galletti C, Culham JC. Functional magnetic resonance imaging (fMRI) to investigate human brain areas involved in processing hand orientation during grasping movements. Participants used the dominant right hand to grasp a rod with the four fingers opposing the thumb or to reach and touch the rod with the knuckles without visual feedback. In a control condition, participants passively viewed the rod. Trials in a slow event-related design consisted of two sequential stimuli in which the rod orientation changed (requiring a change in wrist posture while grasping but not reaching or looking) or remained the same. We found reduced activation, that is, adaptation, in the parieto-occipital sulcus (SPOC) when the object was repeatedly grasped with the same orientation. In contrast, there was no adaptation when reaching or looking at an object in the same orientation, suggesting that hand orientation, rather than object orientation, was the critical factor. These results agree with recent neurophysiological research showing that a parieto-occipital area of macaque (V6A) is modulated by hand orientation during reach-to-grasp movements. We suggest that the human dorsomedial stream, like that in the macaque, plays a key role in processing hand orientation in reach-to-grasp movements.

The wrist, which provides a large range of motion in three planes, is said to be the “most complex joint of the body” (Linscheid 1986). Not only does it integrate the arm and hand, it also enables optimal and forceful grips (Hazelton et al. 1975; Johnston et al. 2010) appropriate for the object’s orientation and affordances (particularly in case of tools) as well as task goals (Fan et al. 2006; Herbert and Butz 2010; Rosenbaum et al. 1992).

Despite the obvious importance of the wrist in hand actions, particularly in orienting the hand appropriately for the object, it has received relatively little attention compared with two other components—arm transport and hand grip—that comprise reach-to-grasp actions (Arbib 1981). While the transport component relies on extrinsic object properties (location), the grip component relies on intrinsic object properties (size and shape) (Jeannerod 1981). The visuomotor channels hypothesis of Jeannerod and colleagues (1981) suggests that the transport and the grip components are processed by different neural substrates within the dorsal visual stream: a dorsomedial versus a dorsolateral circuit, respectively. This hypothesis has received partial support from macaque neurophysiology (Jeannerod et al. 1995; Rizzolatti et al. 1998), human neuropsychology (Binkofski et al. 1998; Jeannerod 1994; Shallice et al. 2005), and human neuroimaging (Cavina-Pratesi et al. 2010b). However, recent neurophysiological findings suggest that the dorsomedial circuit is also involved in the grip component of reach-to-grasp actions. In particular, neurons in two macaque dorsomedial areas, dorsal premotor cortex and V6A, respond to grasping movements (Fattori et al. 2010; Raos et al. 2004). These discoveries convey that there might be a pure dissociation between grip and transport components in macaque dorsolateral and dorsomedial circuits. In fact, it has been suggested that while the dorsolateral circuit might integrate information about the object (such as size and shape) into the motor plan to scale an appropriate grip, the dorsomedial circuit might be a critical node for the coordination of grip and transport components to allow a skilled grasping movement (Fattori et al. 2010). Regardless of the degree of segregation of transport and grip components, the neural substrates of hand orientation during real actions remain largely unexplored in human cortex. Indeed, so far only imagined actions toward oriented stimuli have been studied with functional magnetic resonance imaging (fMRI), revealing an involvement of areas in the dorsolateral as well as the dorsomedial circuit (Jacobs et al. 2010; Johnson et al. 2002; Maragoni et al. 2011). Therefore, whether adjustments of hand orientation during action execution also involve both circuits remains an open question.

The evidence is equivocal about whether wrist orientation is processed by the dorsomedial circuit, the dorsolateral circuit, or both (Desmurget et al. 1996) and whether the wrist component is truly independent of the transport component (Lacquaniti and Soechting 1982) and the grip component (Hesse and Deubel 2009). In the macaque brain, both lesions (Battaglini et al. 2002) and neurophysiological recordings (Fattori et al. 2009) suggest that area V6A, a dorsomedial stream area located in the parieto-occipital sulcus and previously implicated in reaching, is also involved in processing wrist posture during grasping. Other macaque neurophysiological studies...
have implicated the anterior intraparietal area (AIP) of the dorsolateral stream in hand orientation for grasping movements (Baumann et al. 2009; Murata et al. 2000; Taira et al. 1990). Surprisingly, however, the human neural substrates of hand orientation during grasping have not yet been explored. Perhaps hand orientation is processed by both circuits. Indeed, mechanical and functional factors make complete independence between hand orientation and grip or transport rather unlikely. First, hand orientation can be constrained by extrinsic (orientation) or intrinsic (shape) object properties or object function. For example, grasping the handle of a mug will require a different hand orientation from grasping a glass and will also depend on the orientation of the mug. Second, the wrist shares musculature with both the arm and the hand. Specifically, flexor and extensor muscles in the wrist allow rotation, support arm movements, and enable flexion and extension of the fingers (Palastanga et al. 1989). Third, small changes in the orientation of the object can result in a major reconfiguration of the arm and wrist orientation (Stelmach et al. 1994), suggesting a functional link between the wrist orientation and the transport component. Fourth, it is likely that wrist posture and grip posture [such as the relative placement of the thumb with respect to the finger(s)] are coupled.

Here we used functional magnetic resonance imaging adaptation (FMRA) to investigate which human brain areas are involved in processing hand orientation for grasping movements. Presence of adaptation for repeated wrist postures will reveal whether the dorsomedial, the dorsolateral, or both circuits are predominantly involved in this process.

METHODS

Participants

Eleven participants took part in this study (8 men and 3 women, mean age 33 yr) and were financially compensated for their time. All participants were right-handed and had normal or corrected-to-normal visual acuity. They gave their consent prior to the experiment. This study was approved by the Health Sciences Research Ethics Board at the University of Western Ontario.

Eight additional right-handed volunteers (2 men and 6 women, mean age 33.3 yr) were recruited from Durham University to participate in a behavioral control experiment to measure kinematic parameters of the reach-to-grasp and the reach-to-touch movements in a setup similar to that used within the scanner. Informed consent was given prior to the experiments, in accordance with the University of Western Ontario Health Sciences and the Durham University Review Ethics Board.

Imaging Experiment

Experimental design. We used an fMRA paradigm (Grill-Spector et al. 2006) to investigate brain areas involved in processing orientation when it is relevant for reach-to-grasp movements. One trial consisted of a pair of sequential events, in which a rod was presented in either the same orientation (twice in a row or two orientations that differed by ~90° (Fig. 1A). We had a combination of three TASKS (Grasp, Reach, and Look) and two rod ORIENTATIONS (Same and Different) that gave rise to a 3 x 2 factorial design. Therefore we had six experimental conditions: Grasp Same orientation (GS), Grasp Different orientation (GD), Reach Same orientation (RS), Reach Different orientation (RD), Look Same orientation (LS), and Look Different orientation (LD). We looked for adaptation effects by comparing different versus same trials in Look, Reach, and Grasp conditions.

Participants were required to use the dominant (right) hand to perform one of the three tasks cued by an auditory instruction. The audio instruction consisted of a recorded voice that said “Grasp”, “Reach,” or “Look.” In the grasping conditions, participants grasped the rod by opposing the four fingers and the thumb as in a power grip. This constraint ensured that, when forming the grip appropriately for the rod orientation, participants adjusted wrist posture rather than finger posture. In the reaching conditions, participants reached out to touch the rod with the knuckles without rotating the wrist. In both reaching and grasping conditions the upper arm was restrained to prevent changes in arm posture when grasping or reaching to different orientations. At the end of each action, participants returned the hand to the starting position on the chest and kept it still between events and trials. In the looking conditions, participants passively viewed the rod without performing any action. In all conditions, participants were instructed to attend to the location of the object without moving their eyes from the fixation point. In sum, the critical difference between conditions was that the orientation of the rod required an appropriate adjustment of the hand orientation for grasping but not for reaching actions. The reaching and looking conditions served as controls for perceptual differences in rod orientation. Therefore, we hypothesized that brain areas involved in the control of hand posture would show adaptation for the same versus a different rod orientation only in the grasping condition.

In addition to the comparisons between experimental conditions, we also ran an independent functional localizer that allowed us to localize the anterior intraparietal sulcus (aIPS) (Culham et al. 2003) in the dorsolateral circuit and the superior parieto-occipital sulcus (SPOC) in the dorsomedial circuit. In each trial, participants performed one of three possible tasks (Grasp, Reach, or Look) toward a briefly presented three-dimensional (3D) stimulus. Unlike the experimental runs, each trial consisted only of a single presentation of a stimulus. Reaching and looking tasks were similar to those in the experimental runs; however, in the grasping conditions, participants grasped by opposing the index finger (rather than the 4 fingers) against the thumb in a standard precision grip.

Apparatus and stimuli. The stimuli were presented to the participant on the inclined surface of a black turntable placed above the participant’s pelvis (Fig. 1B). Each participant lay supine in the scanner with the head tilted, allowing direct view of the stimulus without mirrors. Participants wore headphones to hear audio instructions about the task they were to perform on the upcoming trial. Although the right forearm was free to move, the upper arm was strapped to the bed to be kept still. This helped to avoid artifacts due to the motion of the shoulder and the head (Culham et al. 2003).

The turntable was reached by the participant (from inside the bore) to perform the task and by the experimenter (from outside the bore) to change the stimulus between events. The turntable (radius = 40 cm) was mounted atop a platform, which was fixed to the bore bed through hooked feet. The turntable and the platform were made of wood and painted black. Typically the platform was located half inside and half outside the bore. However, its location could be adjusted to ensure that both the participant and the experimenter could reach it comfortably. The head of the participant was tilted by ~30–40° to allow comfortable viewing of the stimulus. The inclination of the platform could also be adjusted to improve the view and the reachability of the rod for each participant. A wooden black divider mounted perpendicularly on the turntable prevented the participant from seeing the upper rod opulus on the other side and the experimenter changing the stimulus. A rectangular surface (17 x 25 cm) on a cardboard prism was angled atop each half of the turntable to improve the visibility of the rod (see Fig. 1). The surface was covered with the “loop” layer (fuzzier side) of the Velcro fastener, while rods were mounted on Velcro with the “hook” layer facing toward the face of the prism. A lateral stopper on the circular board and on the platform prevented the turntable from being presented off-center with respect to the subject when the experimenter spun the turn-
Table and prevented it from moving during the participant’s actions. A cloth was mounted on the ceiling of the magnet bore to occlude the participant’s view of the experimenter.

For the experimental runs, the stimuli were 3D wooden rods (8.5 cm × 1.9 cm × 1.9 cm) painted white to increase the contrast with the black background. For the independent functional localizer runs, we used 3D shapes made from white plastic. They had a constant depth (0.6 cm) but varied in length (from 1.8 to 3.6 cm) and width (from 1.6 to 2.6 cm). We used 32 different shapes in total.

Except for the two sequentially illuminated presentations of the rod, subjects were in near-complete darkness throughout the length of the trial (only a small, dim light was provided for fixation). During the intertrial interval (ITI), and after the participant had performed the first event of the task, the rod was quickly replaced and the turntable was rotated by the experimenter. The experimenter also rotated the turntable when the two rods had the same orientation in both events, to prevent participants from guessing the orientation of the second rod based on the perceived rotation of the board. Black cardboard markers on the Velcro surface guided the experimenter’s placement of the rods so the location and the orientation of the rod were consistent across all trials.

Light-emitting diodes (LEDs) were used to provide a fixation point, to illuminate the workspace, and to cue the experimenter regarding stimuli on upcoming trials. The participant maintained fixation on one LED positioned ~10–15° of visual angle above the object, so that all objects were presented in the participant’s lower visual field. A bright LED (illuminator) was used to briefly illuminate the stimulus at the onset of each event of a trial. The illuminator was placed above the participant’s head and shone light onto the object. Another set of LEDs was based at the end of the platform, visible to the experimenter but not the participant, to instruct the experimenter about orientation placement of the rods in the next two events. All of the LEDs were controlled by SuperLab software (Cedrus) on a laptop PC that received a signal from the MRI scanner at the start of each trial. The windows in the scanner room were blocked and the room lights remained off such that, with the exception of the dim fixation LED that remained on continuously, nothing else in the workspace was visible to the participant when the illuminator LEDs were off.

An infrared camera (MRC Systems) recorded the performance of each participant with custom recording software (Tam et al. 2009) for off-line investigation of the errors, which were excluded from further analysis. The errors were mistakes in the performance of the task (e.g., initiating a movement in the Look condition or performing a reach in a Grasp condition). Less than 0.7% of total trials were discarded from the analyses because of subject errors.

**Fig. 1.** Schematic illustration of the setup and timing. A: for each task (Grasp, Reach, and Look) each pair of sequential events involved either 2 different rod orientations (left) or a repetition of 1 of the 2 rod orientations (right). The 2 rod orientations required different wrist orientations for reach-to-grasp but not reach-to-touch movements. The Look condition served as a control for object orientation discrimination. We hypothesized that areas involved in wrist orientation would adapt for grasping but not for reaching or looking tasks. B: the setup required participants to gaze at the fixation point (FP, marked with a star) while performing the tasks, IR cam, infrared camera. C: schematic timing of 1 trial: before each pair of events, an auditory cue instructed the participant about the task to be performed (“Grasp”, “Reach,” or “Look”). After 2 s the first rod was illuminated for 250 ms, and this represented the cue for the participant to initiate the first action; 4 s after the first presentation a second rod was illuminated, cuing the participant to perform the second action. We used an intertrial interval of 16 s.
Experimental runs: timing and experimental conditions. We used a slow event-related design to prevent contamination of the blood oxygenation level-dependent (BOLD) response by any potential artifacts generated by the hand movement, as shown in Fig. 1C. Trials were spaced every 22 s to allow the hemodynamic signal to return to baseline between trials. Each trial started with the audio cue instructing the participant about the task to be performed. After 2 s (from the onset of the audio cue), the first stimulus was illuminated for 250 ms, cuing the participant to perform the instructed task. The onsets of the first and second events were separated by 4 s, during which the participant returned the hand to the home position and the experimenter rotated the turntable to position the second rod for the next event. The brief illumination (250 ms) of the second rod was the cue for the participant to perform the instructed task. Note that the brief periods of illumination ensured that the participants performed all the actions without visual feedback (that is, in open loop).

Each run consisted of 24 trials, and each experimental condition was repeated four times in a random order. In particular, tasks and rod orientations were randomized to prevent any systematic effects of trial history. A baseline of 16 s was added at the beginning and at the end of each run, yielding a run time of ~10 min per run. Each of the four possible sequences of rod orientations ( / / / / / ) was evenly distributed through each run, with each orientation having an equal likelihood of being preceded by others. Each participant performed 4 runs, for a total of 16 trials per experimental condition.

Independent functional localizer: timing and experimental conditions. We used a slow event-related design with one trial every 18 s. A given trial started with the auditory instruction of the task to be performed: Grasp, Reach, or Look. After 2 s from the onset of the audio cue, the stimulus was illuminated for 250 ms, cuing the participant to initiate the task. Following the onset of the illumination was a 16-s interval to allow the hemodynamic response to return to baseline before the next trial began. Each localizer run consisted of 18 trials, and each condition was repeated six times in a random order for a run time of ~7 min. Each participant performed 2 localizer runs for a total of 12 trials per condition.

Session duration. A session for one participant included setup time (~45 min), six functional runs, and one anatomical scan and took ~2.5 h to be completed. We did not conduct eye tracking during the scan I because the setup time was already considerable and 2) because there are no MR-compatible eye trackers that can monitor gaze in the head-tilted configuration.

Imaging parameters. All imaging was performed at the Robarts Research Institute (London, ON, Canada) with a 3-T whole body MRI system (Siemens Magnetom TIM Trio, Erlangen, Germany). The posterior half of a 12-channel receive-only head coil (6 channels) at the back of the head was used in conjunction with a 4-channel flex coil over the anterior part of the head (see Fig. 1B). The anterior part of the 12-channel coil was removed to allow the participant to see the stimuli directly and comfortably but at a cost of anterior signal loss, hence the addition of the 4-channel flex coil. The posterior half of the 12-channel coil was tilted at an angle of ~30°–40° to allow direct viewing of the stimuli. We collected IMRI volumes based on the BOLD signal (Ogawa et al. 1992). We used an optimized T2-weighted single-shot gradient echo echo-planar imaging [211-mm field of view (FOV) with 64 × 64 matrix size, yielding a resolution of 3.3 mm × 3.3 mm in plane; 3.3-mm slice thickness with no gap; repetition time (TR) = 2 s; echo time (TE) = 30 ms; flip angle (FA) = 78°]. Each volume comprised 33 slices angled at ~30° (i.e., approximately parallel to the calcarine sulcus) to sample occipital, parietal, posterior temporal, and posterior/superior frontal cortices. The slices were collected in ascending and interleaved order. During each experimental session, a T1-weighted anatomical reference volume was acquired along the same orientation as the functional images with a 3D acquisition sequence [256 × 240 × 192 FOV with the same matrix size yielding a resolution of 1 mm isovoxel, inversion time (TI) = 900 ms, TR = 2,300 ms, TE = 5.23 ms, FA = 9°].

Preprocessing. Data were analyzed with Brain Voyager QX software (Brain Innovation 1.10, Maastricht, The Netherlands). Functional data were superimposed on anatomical brain images, aligned on the anterior commissure-posterior commissure line, and transformed into Talairach space (Talairach and Tournoux 1988). Functional data were preprocessed with spatial smoothing [full-width half-maximum (FWHM) = 6 mm] and temporal smoothing to remove frequencies below 2 cycles per run. Slice time correction with a cubic spline interpolation algorithm was also performed. Functional data from each run were screened for motion or magnet artifacts with cine-loop animation to detect eventual abrupt movements of the head. In addition, we ensured that no obvious motion artifacts (e.g., rings of activation) were present in the activation maps from individual participants. Each functional run was motion corrected with a trilinear sinc interpolation algorithm, such that each volume was aligned to the volume of the functional scan closest to the anatomical scan.

Data analyses. We performed two types of analyses. First, because we had specific hypotheses about certain areas, we performed an analysis using a region of interest (ROI) approach in single subjects. The ROI approach offers the advantages that each area can be identified in individual participants regardless of variations in stereotaxic location and, moreover, specific areas are not blurred with adjacent areas due to interindividual anatomical variability (Saxe et al. 2006). For this purpose, we used data without spatial smoothing. Second, to investigate other areas within the brain that may be involved in the wrist component, we conducted a voxelwise analysis using data with spatial smooth.

For each participant, we used a general linear model (GLM) that included a predictor for each condition. Each predictor was derived from a rectangular wave function (2 s or 1 volume for the localizer runs; 6 s or 3 volumes for the experimental runs) convolved with a standard hemodynamic response function [Brain Voyager QX’s default double-gamma hemodynamic response function (HRF)]. Because the stimulus presentation and action execution components of the HRF overlapped considerably, we treated them together as one event. In the experimental runs, we chose the time window (6 s) to cover the two sequential presentations of the rod and the corresponding actions, including both the outgoing and returning phases of the second action, which did not exceed 2 s. We also ensured that the convolved hemodynamic profile of the 6-s rectangular wave function closely matched the (2-event) time courses of the Grasp, Reach, and Look conditions averaged together (to avoid any selection bias favoring one condition over another).

Errors in performance were modeled as predictors of no interest. Prior to analysis, the data were z-normalized; therefore βs were proportional to z-scores (i.e., standard deviations). In addition, the six motion parameters were added as covariates after being detrended and z-normalized.

Region of Interest Analyses

For the independent functional localizer runs, each subject’s GLM included three separate predictors: Grasp, Reach, Look. We used these runs to independently identify two ROIs for each participant. First we localized a SPOC ROI that was defined by a conjunction analysis of [Grasp > Baseline] AND (Reach > Baseline) AND (Look > Baseline)]. Recent studies have shown that SPOC is involved in the transport component of a movement (Cavina-Pratesi et al. 2010b), with grasping and pressing eliciting more activation compared with look conditions. However, it should be noted that these differences are likely weaker without visual feedback (i.e., open loop) compared to with visual feedback (i.e., closed loop) at the level of single participants, as also demonstrated by Filimon and colleagues (Filimon 2010). It follows that we were not able to identify SPOC in all subjects in our open loop paradigm using a contrast of [Grasp + Reach] > Look]. Given that the parieto-occipital cortex responds robustly to luminance transients (Bristow et al. 2005; Portin et al. 1998; Vanni et
al. 2001), the conjunction analysis we used, comparing each event type against baseline, identifies areas with strong responses to stimulus onsets across all conditions. Although the conjunction revealed additional areas, SPOC was the most reliable focus and was consistently located at the superior end of the parieto-occipital sulcus (POS).

Second, using the independent functional localizer runs, we localized an aIPS ROI by a comparison of Grasp vs. Reach, which has been typical in past studies of the region (Begliomini et al. 2007a, 2007b; Binkofski et al. 1998; Culham et al. 2003; Frey et al. 2005). In 1 of the 11 participants, it was not possible to run the independent functional localizer because of technical difficulties, so we identified SPOC and aIPS in the experimental runs using the contrasts [(Grasp > Baseline) AND (Reach > Baseline)] and [(Grasp > Reach), respectively. These criteria in the one participant, though not from an independent run, are still independent of the adaptation effects being investigated.

ROIs were defined by using a voxelwise contrast in each individual (as can be seen in Figs. 2A and 3A). First, we found the voxel with peak activation near the expected location of the ROI (superior POS for SPOC; junction of intraparietal and postcentral sulci for aIPS). Then thresholds for each subject were adjusted to obtain ROIs of comparable size compared with a (8 mm)$^3 = 512$-mm$^3$ cube centered around the peak voxel (see Table 2). The goal of this approach was to obtain ROIs in anatomically appropriate locations.

Although ROI volume was similar across subjects, thresholds varied (as shown in Figs. 2A and 3A). It should be noted, however, that because the contrast used to identify the ROIs is independent of the subsequent statistical analyses of the experimental data, if these thresholds were too liberal it would actually reduce the chance of finding significant experimental effects. For each ROI from each participant, we extracted the event-related time course of the experimental runs and calculated the percent BOLD signal change ($\%\text{BSC}$) at the peak response (average of 3 volumes) for further analysis.

Voxelwise Analyses

In the experimental runs, the group random effects (RFX) GLM included six predictors for each participant: Grasp Same orientation (GS), Grasp Different orientation (GD), Reach Same orientation (RS), Reach Different orientation (RD), Look at Same orientation (LS), Look at Different orientation (LD). Contrasts were performed on $z$-transformed beta weights ($\beta$). Statistical maps were initially generated without correction for multiple comparisons. We then flagged the areas that did not survive a cluster threshold correction (using Brain Voyager’s cluster-level statistical threshold estimator plug-in). The minimum cluster size was estimated at 10 voxels of (3 mm)$^3$ for a total volume of 270 mm$^3$. This algorithm uses Monte Carlo simulations (1,000 iterations) to estimate the probability of a number of contiguous voxels being active purely due to chance while taking into consideration the average smoothness of the statistical maps. Because map smoothness varies with contrast, different contrasts have different cluster thresholds. In cases in which activation foci did not survive cluster threshold correction (but a priori hypotheses and other contrasts suggested that the activation could very well be genuine), we indicated the regions with a star. This approach allows the rigor of correction for multiple comparisons to reduce type I errors while also identifying areas that may be vulnerable to type II errors, which often go unacknowledged (Lieberman and Cunningham 2009). For each area we extracted the $\beta$ weights for each participant in each condition for further analysis.

Statistical Analyses

For each area, we performed an analysis of variance (ANOVA) using SPSS with 3 (TASK) $\times$ 2 (ORIENTATION) factors on either the $\%\text{BSC}$ values (ROI analyses) or the $\beta$ weights (voxelwise analyses) (see Cavina-Pratesi et al. 2010b). Post hoc contrasts were carried out for two groups of comparisons: the first one was performed to look at adaptation effects for orientation conditions within each task (GD vs. GS, RD vs. RS, LD vs. LS), while the second one was performed to look at differences among tasks within each orientation condition (GD vs. RD, GD vs. RD, RD vs. LD, GS vs. LS, GS vs. RS, RS vs. LS). We used one-tailed paired-sample $t$-tests with a Bonferroni correction for multiple comparisons: $P < 0.016$ (0.05/3) for the three comparisons in the first group and $P < 0.0083$ (0.05/6) for six comparisons in the second group. Because the predicted adaptation effects are unidirectional (Different > Same but not Same > Different), one-tailed comparisons were performed. Statistical differences are indicated on line graphs for the six conditions. To further illustrate the differences graphically with appropriate error bars for the adaptation effects, for each area we computed differences in activation between Different and Same trials for each condition (Grasp, Reach, Look), along with the 98.4% confidence limits on those difference values, such that difference scores with error bars that do not include zero indicate that the difference between the two conditions was significant at a Bonferroni-corrected level of $P < 0.016$ (3 comparisons at $P < 0.016$ for a familywise error rate of $P < 0.05$); otherwise, it is not. Given the difficulty in completing appropriate error bars for within-participants designs (Lofthus and Masson 1994) and common misconceptions about the interpretation of error bars (Belia et al. 2005), this is a straightforward way to illustrate statistical differences graphically.

For areas defined by voxelwise contrasts, where the data were not selected by independent localizers, the ANOVA and data graphs are based on nonindependent contrasts. We have opted to include these to show unequivocally the TASK $\times$ ORIENTATION interactions and to enable the reader to easily see the pattern of results, including effects that are independent of the selection criteria. Contrasts that are nonindependent are clearly indicated in square brackets.

Kinematic Control Experiment

To check whether brain activities related to the wrist rotations were associated with specific patterns of reaction time or movement time, we ran a behavioral control experiment under the same movement constraints experienced in the imaging experiments.

Procedure. Subjects lay comfortably in a mock wooden scanner, and data were collected with 1) a tilted platform similar to that used for the imaging experiments, 2) a white rod measuring 8.5 cm $\times$ 1.9 cm $\times$ 1.9 cm, 3) the head tilted, 4) liquid crystal shutter goggles (Plato System, Translucent Technologies, Toronto, ON, Canada) to control visual feedback, and 5) an upper arm immobilizer. Thus kinematic data were collected while the participants were subjected to the same movement and visual constraints experienced in the imaging experiment. Participants were asked to grasp or reach the rod, which could have one of the two orientations used in the fMRI experiment (\ or \). As for the imaging experiment, in the Grasp but not in the Reach condition the orientation of the wrist had to be adjusted to the orientation of the rod. Participants were asked to perform one action per trial for a total of 48 trials (12 trials for each task and orientation).

At the beginning of each trial the subject was instructed via headphones about the task to perform (either Grasp or Reach), and after 1–2 s the shutter goggles opened for 250 ms, cuing the participant to perform the actions. Participants were asked to fixate upon an LED placed at the center of the platform (fixation was monitored by a second experimenter via a small camera focusing on one eye). If an eye movement was detected, the trial was discarded and repeated at the end of the block. Actions were recorded by sampling the position of one marker placed on the wrist at a frequency of 100 Hz, using an electromagnetic motion analysis system (Minibird, Ascension Technology).

Data analysis. Analyses were performed on reaction time (RT) and movement time (MT). RTs were computed as the time of movement onset (the time at which the velocity of the marker rose above 50
mm/s after the opening of the goggles). MT was computed as the time interval between movement onset and movement offset, when the velocity dropped below 50 mm/s as it reached the object.

Data were analyzed with repeated-measures ANOVAs where ACTION (grasp vs. touch) and ORIENTATION (up-left vs. up-right) were used as within-subjects factors.

RESULTS

Results of Imaging Experiment

Region of interest analyses. PARIETAL DORSOMEDIAL CIRCUIT: SUPERIOR PARIETO-OccIPITAL CORTEX. For the independent functional localizer runs, the conjunction analysis comparing each of the Grasp and Reach and Look conditions vs. Baseline [i.e., (Grasp > Baseline) AND (Reach > Baseline) AND (Look > Baseline)] revealed consistent activation in the vicinity of the dorsal POS. Within the 11 participants, we localized SPOC in the left hemisphere (LH) of 10 of 11 participants and in the right hemisphere (RH) of 8 of 11 participants. The positions of the left and right SPOC are shown in the sagittal slice for each participant. In each participant, SPOC (highlighted by a yellow arrow) was identified in the vicinity of the parieto-occipital sulcus (POS).

Table 1. Average Talairach coordinates and statistical details for SPOC and aIPS in the ROI analysis

<table>
<thead>
<tr>
<th>Brain Areas</th>
<th>Average Talairach Coordinates</th>
<th>Average No. of Voxels</th>
</tr>
</thead>
<tbody>
<tr>
<td>LH SPOC</td>
<td>x = -14, y = -80, z = 32</td>
<td>483</td>
</tr>
<tr>
<td>RH SPOC</td>
<td>x = 15, y = -79, z = 35</td>
<td>512</td>
</tr>
<tr>
<td>LH aIPS</td>
<td>x = -46, y = -31, z = 43</td>
<td>354</td>
</tr>
<tr>
<td>RH aIPS</td>
<td>x = 41, y = -35, z = 44</td>
<td>430</td>
</tr>
</tbody>
</table>

Talairach coordinates and numbers of voxels have been averaged across participants. Number of participants for each region of interest (ROI): 10 for left superior parieto-occipital cortex (SPOC), 8 for right SPOC, 9 for left anterior intraparietal sulcus (aIPS), and 8 for right aIPS. LH, left hemisphere; RH, right hemisphere.
Grasp condition \( t(9) = 2.24, P < 0.05, \) corrected. In contrast, there was no adaptation for Same vs. Different orientation in the Reach condition \( t(9) = 1.126, P > 0.05, \) corrected or in the Look condition \( t(9) = 2.07, P > 0.05, \) corrected. In addition, as shown by the line graphs (Fig. 2B, left) in the Different orientation condition there was higher activation for Grasp vs. Look \( t(9) = 3.71, P < 0.05, \) corrected and for Reach vs. Look \( t(9) = 3.67, P < 0.05, \) corrected but not for Grasp vs. Reach \( t(9) = 2.75, P > 0.05, \) corrected. In contrast, in the same orientation condition there was no difference between Grasp vs. Look \( t(9) = 2.69, P > 0.05, \) corrected, Reach vs. Look \( t(9) = 2.45, P > 0.05, \) corrected, or Grasp vs. Reach \( t(9) = 0.24, P > 0.05, \) corrected. In the right SPOC we found a trend toward a significant main effect of TASK \( F(2,14) = 4.49, P = 0.07 \) but no main effect of ORIENTATION \( F(1,7) = 1.12, P = 0.32 \) and a significant TASK \( \times \) ORIENTATION interaction \( F(2,14) = 4.03, P < 0.05 \).

The t-tests showed that there was adaptation for Same vs. Different orientation but only for the Grasp condition \( t(7) = 2.83, P < 0.05, \) corrected. In contrast, there was no difference in the response for Same vs. Different orientation in both the Reach condition \( t(7) = 1.091, P > 0.05, \) corrected and the Look condition \( t(7) = 1.86, P > 0.05, \) corrected. In the Different orientation condition there was no difference for Grasp vs. Look \( t(7) = 2.75, P > 0.05, \) corrected, Reach vs. Look \( t(7) = 1.94, P > 0.05, \) corrected, or Grasp vs. Reach \( t(7) = 2.72, P > 0.05, \) corrected. Similarly, in the Same orientation condition there was no difference between Grasp vs. Look \( t(7) = 1.44, P > 0.05, \) corrected, Reach vs. Look \( t(7) = 1.03, P > 0.05, \) corrected, and Grasp vs. Reach \( t(7) = 1.48, P > 0.05, \) corrected.

PARIETAL DORSOLATERAL CIRCUIT: ANTERIOR INTRAPARIETAL SULCUS. For the independent functional localizer runs, using a contrast of (Grasp > Reach) for the 11 participants, we identified aIPS in the left hemisphere of 9 participants and in the right hemisphere of 8 participants. In particular, a focus of activation was found near the junction of the intraparietal sulcus and the inferior segment of the postcentral sulcus. Averaged Talairach coordinates (see Table 1) are in agreement with previous fMRI experiments that also used real 3D stimuli (Castiello and Begliomini 2008; Culham et al. 2003; Frey et al. 2005; Kroliczak et al. 2007). Results for left and right aIPS are shown for each participant in Fig. 3, and the Talairach coordinates and the number of voxels are specified in Table 1.

For the experimental runs, left and right aIPS showed higher responses for Grasp vs. Reach and Reach vs. Look regardless of the orientation of the rod. Specifically, in the left aIPS, we found a main effect of TASK \( F(2,16) = 92.45, P < 0.001 \) but no main effect of ORIENTATION \( F(1,8) = 0.001, P = 0.97 \) and only a trend toward a significant TASK \( \times \) ORIENTATION interaction \( F(2,16) = 4.21, P = 0.07 \). There was a higher response for Grasp vs. Reach \( t(8) = 4.83, P < 0.05, \) corrected and Grasp vs. Look \( t(8) = 11.95, P < 0.05, \) corrected as well as for Reach vs. Look \( t(8) = 8.78, P < 0.05, \) corrected. Similarly, right aIPS showed a main effect of TASK \( F(2,14) = 18.29, P < 0.001 \) but no main effect of ORIENTATION \( F(1,7) = 0.42, P = 0.54 \) or TASK \( \times \) ORIENTATION interaction \( F(2,14) = 0.67, P = 0.53 \). In particular, there was a higher response for Grasp vs. Reach \( t(7) = 4.01, P < 0.05, \) corrected as well as for Grasp vs. Look \( t(7) = 4.67, P < 0.05, \) corrected but not for Reach vs. Look \( t(7) = 2.81, P > 0.05, \) corrected.

Voxelwise analyses (averaged data). We hypothesized that areas involved in processing wrist orientation would show adaptation for same orientation in the grasping but not in the reaching and looking conditions. Such areas should thus show significant activation for both the TASK \( \times \) ORIENTATION interaction as well as the contrast GD > GS. As shown in Fig. 4A, numerous regions within the medial dorsal visual stream showed both these effects with full or partial overlap. Because interactions can occur for many reasons (and in some cases seemed to be driven in part by unhypothesized effects such as LS > LD), we chose to extract the data from the areas identified by the more specific GD > GS contrast for further analysis. We also examined two additional contrasts, (LD > LS) and (RD > RS), which showed no differences in the positive direction (although some areas showed repetition enhancement, Same > Different).

The activation map for the contrast (GD > GS) showed two areas located medially in the parietal lobe of both hemispheres: one posterior, located at the superior end of the parieto-occipital sulcus (SPOC) and a second one more anterior, located in the posterior intraparietal sulcus (pIPS). We also found a third area in the frontal cortex of the left hemisphere, where the precentral sulcus and the superior frontal sulcus intersect. Because of its characteristic location, we suggest that this is dorsal premotor cortex (dPM) (Fig. 4). Note that the foci of SPOC in the right hemisphere and dPM in the left hemisphere were too small to survive cluster threshold correction, as indicated by a star. However, given that both areas also appeared in the interaction contrast and survived its cluster threshold correction, the correction may be overly conservative. Talairach coordinates and number of voxels for each area are reported in Table 2.

To determine whether the adaptation effect was truly specific to hand orientation for grasping (GD > GS), we also examined whether the interaction effect was significant and whether there was adaptation for the reaching (RD > RS) and looking (LD > LS) tasks in which no adjustment of hand orientation was required. In fact, all areas showed an interaction and no areas showed adaptation for Different vs. Same orientation in Reach and Look conditions, suggesting that the hand orientation was the critical factor. Another way to consider the interaction is that in all areas, except dPM, a difference between grasping and reaching was observed only when the orientation changed between events but not when the orientation remained the same. Statistical values of the post hoc t-tests for each area are reported in Table 3.

Relative action/visual activation within subdivisions of the superior parieto-occipital cortex. Given that clear responses for seeing objects and for performing grasping, reaching, and wrist movements have been recorded within specific subdivisions of the dorsomedial cortex of macaques (Galletti et al. 1999, 2003), we checked whether it was possible to isolate similar subdivisions within SPOC in humans. In particular, to allow a comparison between the functional properties of human SPOC and those of macaque area V6, showing visual properties (Galletti et al. 1999), and V6A, also showing motor properties (Galletti et al. 2003), we looked at the relative contribution of action execution and visual stimulation in averaged data using the localizer runs. Following previous results by Cavina-Pratesi et al. (2010b), we hypothesized that the more anterior division of SPOC (likely corresponding to macaque area V6A, particularly the V6Ad subdivision) would show a preference for action execution (Grasp and Reach) over...
passive viewing (Look), while the more posterior division of SPOC (likely corresponding to macaque V6 or the V6Av subdivision of V6A) would show more comparable levels of activation for all three conditions (Grasp, Reach, and Look).

As indicated in Fig. 5A, left, two zones showed a gradient between action execution and visual stimulation. In particular, SPOC and the precuneus have a more anterior division showing activation predominantly for action execution and a more posterior division showing activation for both action execution and visual stimulation. In contrast, primary motor cortex (M1) and the cingulate sulcus show activation predominantly for action execution. To ensure that the patterns revealed qualitatively by the relative contribution maps were statistically valid, we also did a direct contrast, shown in Fig. 5A, right. Specifically, while a large swathe of activation was observed around SPOC for all three conditions [(Grasp and Reach) > Look], only the more anterior portion of SPOC, anterior to the POS, showed higher activation for the action conditions than the visual condition in a contrast of [(Grasp and Reach) > Look]. We selected regions of (8 mm)³ from the anterior and posterior divisions of SPOC (aSPOC and pSPOC, respectively), using the localizer scans. We then investigated the pattern of weights in these two areas for the experimental runs (Fig. 5B).

Consistent with these observations and with neurophysiological findings by Fattori et al. (2010), aSPOC showed a clear involvement in wrist orientation for grasping, while pSPOC showed only a trend. In particular, aSPOC showed a main effect of TASK $[F_{(2,18)} = 63.507, P < 0.001]$ as well as a significant TASK × ORIENTATION interaction $[F_{(2,18)} = 8.04, P < 0.01]$ but no main effect of ORIENTATION $[F_{(1,9)} = 4.096, P = 0.099]$. As shown by the difference score graphs (Fig. 5B, bottom left), there was higher adaptation for Same vs. Different orientation, but only in the Grasp condition $[r(9) = 3.26, P < 0.05, corrected]$. In contrast, there was no adaptation for Same vs. Different orientation in the Reach condition $[r(9) = 0.678, P > 0.05, corrected]$ or in the Look condition $[r(9) = 1.72, P > 0.05, corrected]$. In addition, as shown by the line graphs (Fig. 5B, top left), in the
Different orientation condition there was higher activation for Grasp vs. Reach \(t(9) = 4.22, P < 0.05\), corrected, Grasp vs. Look \(t(9) = 13.65, P < 0.05\), corrected, and Reach vs. Look \(t(9) = 6.26, P < 0.05\), corrected. In contrast, in the Same orientation condition there was higher activation for Grasp vs. Look \(t(9) = 5.72, P < 0.05\), corrected\] and Reach vs. Look \(t(9) = 7.28, P < 0.05\), corrected\] but not for Grasp vs. Reach \(t(9) = 0.4, P > 0.05\), corrected\]. Interestingly, pSPOC showed only a main effect of TASK \(F_{(2,18)} = 20.26, P < 0.001\) but no main effect of ORIENTATION \(F_{(1,9)} = 1.97, P = 0.191\) and only a trend toward a TASK × ORIENTATION interaction \(F_{(2,18)} = 3.34, P = 0.056\). The main effect of TASK was driven by a higher activation for Grasp vs. Look \(t(9) = 4.56, P < 0.05\), corrected\] and for Reach vs. Look \(t(9) = 4.98, P < 0.05\), corrected\] but not for Grasp vs. Reach \(t(9) = 0.18, P > 0.05\), corrected\].

Next, we wondered how the aSPOC and pSPOC areas identified in this analysis related to the area we defined in individual subjects in the ROI analysis. Recall that ROIs were defined in individuals based on the conjunction of all three localizer tasks versus fixation because the motor-specific contrast, (Grasp + Reach) > Look, was not reliable enough in

<table>
<thead>
<tr>
<th>Talairach Coordinates</th>
<th>No. of Voxels</th>
</tr>
</thead>
<tbody>
<tr>
<td>LH SPOC</td>
<td>388</td>
</tr>
<tr>
<td>RH SPOC</td>
<td>151</td>
</tr>
<tr>
<td>LH pIPS</td>
<td>378</td>
</tr>
<tr>
<td>RH pIPS</td>
<td>503</td>
</tr>
<tr>
<td>LH dPM</td>
<td>104</td>
</tr>
</tbody>
</table>

Area abbreviations as in figure legends. pIPS, posterior intraparietal sulcus; dPM, dorsal premotor area.
Table 3. Statistical details for post hoc t-tests in the voxelwise analyses

<table>
<thead>
<tr>
<th>Area</th>
<th>Interaction TASK × ORIENTATION</th>
<th>Interaction TASK × ORIENTATION</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>r-Tests (P &lt; 0.016) D &gt; S</td>
<td>r-Tests (P &lt; 0.0083) S</td>
</tr>
<tr>
<td>LH SPOC</td>
<td>G: 0.001 R: 0.125 L: 0.106</td>
<td>G &gt; R: 0.004 G &gt; L: 0.001 R &gt; L: 0.001</td>
</tr>
<tr>
<td>RH SPOC</td>
<td>G: 0.001 R: 0.128 L: 0.031</td>
<td>G &gt; R: 0.002 G &gt; L: 0.001 R &gt; L: 0.5</td>
</tr>
<tr>
<td>LH pIPS</td>
<td>G: 0.001 R: 0.138 L: 0.327</td>
<td>G &gt; R: 0.003 G &gt; L: 0.005 R &gt; L: 0.478</td>
</tr>
<tr>
<td>RH pIPS</td>
<td>G: 0.001 R: 0.104 L: 0.421</td>
<td>G &gt; R: 0.001 G &gt; L: 0.173 R &gt; L: 0.5</td>
</tr>
<tr>
<td>LH dPM</td>
<td>G: 0.001 R: 0.108 L: 0.327</td>
<td>G &gt; R: 0.001 G &gt; L: 0.001 R &gt; L: 0.5</td>
</tr>
</tbody>
</table>

Area abbreviations as in figure legends. G, Grasp; R, Reach; L, Look; D, Different; S, Same. Significant values (Bonferroni corrected) are indicated in boldface. Contrasts and values listed in square brackets are expected given the criteria used to select the region (i.e., nonindependent).

Fig. 5. Gradient of motor specificity within SPOC in voxelwise analyses. A, left: activation maps show the relative contribution between action execution and passive view conditions in the group voxelwise analysis shown on the group-average anatomical image. For each voxel in which the action and passive view predictors together accounted for a significant proportion of the variance \((R^2 > 0.35)\), the figure shows the relative contribution index, computed as \((\text{Grasp} - \text{Reach} - \text{Look}) / (\text{Grasp} + \text{Reach} + \text{Look})\). Voxels with greater responses to the action tasks (grasping and reaching) than passive viewing appear dark green, while voxels with comparable responses to the action tasks as passive viewing appear in the intermediate range of the spectrum (light green–yellow). No voxels showed higher responses for passive viewing than the action tasks (which would have appeared red). Right: maps show significant effects in the contrast \([\text{Grasp and Reach}] > \text{Look} \) in blue and in the conjunction analysis \([\text{Grasp and Baseline}] \ AND \ (\text{Reach and Baseline}) \ AND \ (\text{Look and Baseline})\) in orange. All areas shown survived correction for multiple comparisons. The minimum cluster size was estimated at 36 voxels of (3 mm)\(^3\) for a total volume of 972 mm\(^3\) in the contrast and at 15 voxels of (3 mm)\(^3\) for a total volume of 405 mm\(^3\) in the conjunction analyses. B: bar graphs show the difference in \(\beta\) weights between key conditions. Line graphs indicate the \(\beta\) weights for the 6 experimental conditions in the 5 areas. *Significant statistical differences among conditions for \(P < 0.05\), corrected. Error bars indicate 98.4% confidence intervals. Areas have been selected by using a cube of (8 mm)\(^3\) = 512 mm\(^3\). aSPOC, anterior SPOC; pSPOC, posterior SPOC; ROI SPOC, ROI in the SPOC based on average coordinates from individual subjects SPOC in the ROI analysis.
Table 4. Summary of kinematic control results

<table>
<thead>
<tr>
<th>Rod Orientation</th>
<th>Average, ms</th>
<th>ANOVA P Values</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Grasp</td>
<td>Reach</td>
</tr>
</tbody>
</table>
| RT, reaction time; MT, movement time.

Results of Kinematic Control Experiment

RT and MT were not affected by the type of task to be performed [RT: \( F_{(1,7)} = 3.014, P = 0.123 \); MT: \( F_{(1,7)} = 0.205, P = 0.7 \)], the orientation of the rod [RT: \( F_{(1,7)} = 0.665, P = 0.4 \); MT: \( F_{(1,7)} = 5.26, P = 0.06 \)], or their interaction [RT: \( F_{(1,7)} = 1.4, P = 0.3 \); MT: \( F_{(1,7)} = 2.7, P = 0.1 \)], showing that low-level movement factors could not account for the pattern of activation found with the fMRI experiment. Averages are reported in Table 4.

DISCUSSION

Our results demonstrate the involvement of the dorsomedial circuit in processing wrist orientation for grasping in humans. In particular, SPOC and pIPS selectively adapted to repeated object orientation during grasping, which required an adjustment of the orientation of the hand and the wrist, but not during reaching and looking, which did not require any adjustment of the hand and the wrist orientation. In addition, a similar pattern was suggested in dPM, indicating that in addition to being sensitive to grip and transport (Cavina-Pratesi et al. 2010b), it may also be involved in coding hand orientation and maybe coordinating different components of reach-to-grasp movements.

Our finding that human SPOC codes hand orientation corroborates the proposal that human SPOC and the macaque V6/V6A complex are likely homologs. Several studies have already suggested this (Cavina-Pratesi et al. 2010b; Filimon 2010; Gallivan et al. 2009; Pitizalis et al. 2006; Prado et al. 2005; Quinlan and Culham 2007) based on functional similarities as well as on the similarity in anatomical location. Consistent with the recent discovery by Fattori and colleagues (Fattori et al. 2009) that macaque V6A neurons are tuned to wrist orientation, our fMRA results now suggest that human SPOC neurons share this property, thus bolstering the argument for homology. Lesions to macaque parietal cortex (Faugier-Grimaud et al. 1978, 1985), and specifically to V6A (Battaglini et al. 2002), lead to profoundly awkward wrist and hand postures during grasping. Our results explain previous findings showing that lesions to human SPOC lead not only to reaching errors (optic ataxia; Jakobson et al. 1991; Jeannerod 1986) but also to difficulties in achieving an appropriate wrist posture (Karnath and Perenin 2005; Perenin and Vighetto 1988, Wood et al. 2009). Further studies in patients with lesions that include SPOC or studies using transcranial magnetic stimulation (TMS) to temporarily inactivate SPOC could also address whether the three components can be dissociated by examining each one separately (see Cavina-Pratesi et al. 2010a).

Despite the suggested homology between human SPOC and the V6/V6A complex, homologies between subregions of the complex have not yet been clearly established. In the macaque, functional and anatomical differences exist not only between V6 and V6A but also between subregions of area V6A: ventral V6A (V6Av) and dorsal V6A (V6Ad) (recently overviewed in Gamberini et al. 2011). In particular, while the majority of neurons in V6Av have clear visual responses, a larger proportion of somatomotor neurons predominate in V6Ad (Fattori et al. 2001, 2004; Breveglieri et al. 2002). These functional differences are also reflected in the anatomical connections of these two areas: while V6Av receives inputs mainly from visual areas, V6Ad receives inputs from associative areas in the parietal cortex (Gamberini et al. 2009; Passerelli et al. 2011). These findings suggest a motor to visual preference in macaque V6Ad-V6Av-V6 neurons. Our results provide clear evidence of the presence of a similar gradient also in human SPOC (Fig. 5), showing a stronger motor than visual response in aSPOC compared with pSPOC. These findings reinforce the potential of a homology between aSPOC and macaque area V6A and pSPOC and macaque area V6 (see also Cavina-Pratesi et al. 2010b, discussion). Consistent with the finding of wrist selectivity in V6A (Fattori et al. 2010), particularly V6Ad (Gamberini et al. 2011), we see wrist selectivity in aSPOC.

Our results may clarify some discrepancies we observed in previous experiments about the selective involvement of the parieto-occipital cortex in grasping actions. In some studies, we have found higher responses for grasping versus reaching in the vicinity of SPOC (Cavina-Pratesi et al. 2007; Culham et al. 2003; Krollczak et al. 2007), while in others we have not (Cavina-Pratesi et al. 2010b; Gallivan et al. 2009). Interestingly, all the studies that found a grasping-selective effect in SPOC were run with a setup that required wrist rotations for grasping but not reaching (Table 5). In fact, in these setups the 3D objects were often presented with a rightward or a leftward orientation, and therefore they required participants to rotate their wrist for grasping (as compared with reaching). Therefore, SPOC activation during grasping (vs. reaching) may have arisen from the involvement of the wrist, when present, rather than the other aspects of the grip.

Interestingly, the voxelwise analyses revealed bilateral SPOC activation, although that in the right hemisphere did not survive cluster threshold correction. The bilateral activation could be due to the fact that participants evaluated grasping affordances with both hands prior to movement execution. Indeed, a study by Johnson (2000) has nicely shown that participants evaluate grasps with both their dominant and nondominant hand when they need to make a selection based on the orientation of a dowel and on the awkwardness of the resulting grasp with both hands. Although no selection option was given in the present study, it is possible that the two orientations of the rod in the fMRI setup could have been...
grasped comfortably with both hands, lacking any clear preference for one hand over another and, therefore, eliciting affordances judgments for the two rod orientations with both hands.

We investigated only one of several degrees of freedom for adjusting hand orientation. Because of the movement constraints of the fMRI environment, the wrist movements employed here involved a twisting of the wrist (radial/ulnar deviation) rather than lifting of the wrist (extension/flexion) or rotation of the forearm (pronation/supination). As such, our movements involved relatively distal musculature rather than proximal musculature, making it even more notable that they are processed in the dorsomedial stream, which is typically associated with proximal musculature (Cavina-Pratesi et al. 2010b). Combined with the findings that macaque V6A neurons are tuned for pronation/supination (Fattori et al. 2009), it seems likely that V6A/SPOC codes the final angle of the wrist rather than the specific musculature employed. Another possibility is that rather than coding the wrist orientation per se, SPOC coordinates the arm transport and the wrist orientation as a whole to achieve the appropriate arm configuration for grasping. Recall that we deliberately had subjects employ a grasp with the four fingers opposing the thumb (rather than a precision grip with just the index finger vs. the thumb) such that the postural adjustments would largely involve wrist rotations rather than changes to finger placement. Nevertheless, it is quite possible that changes to rod orientation also invoked minor adjustments in the positioning of the digits (such as the positioning of the thumb relative to the fingers). That said, we speculate that the effects on SPOC of our paradigm are more likely to have arisen from the role of the wrist than the fingers. Specifically, if digit positioning was a key factor in our paradigm, we would have predicted it to have a greater effect on pIPS (which is thought to be more strongly involved in finger movements) than SPOC (which does not appear to be affected by other changes to digit positioning such as varying object size; Monaco et al. 2010). Moreover, the putative homolog of SPOC, V6A, has clearly been implicated in wrist posture. Either way, however, our results implicate SPOC in the control of overall hand orientation regardless of the specific musculature involved.

Although pIPS has not clearly been assigned to either the dorsomedial or dorsolateral circuit, the present results suggest that it works together with areas of the dorsomedial circuit for coordination of wrist orientation for grasping. Indeed, similarly to SPOC, pIPS shows a selective involvement in the wrist component. Our pIPS may correspond to the caudal intraparietal area (CIP), which has been shown to be involved in object manipulation (Faillenot et al. 1999), discrimination of texture orientation (i.e., slant) (Faillenot et al. 1999; Shikata et al. 1997; Kroliczak et al. 2008).

### Table 5. Summary of SPOC foci from the present experiment and other published papers

<table>
<thead>
<tr>
<th>Studies</th>
<th>LH SPOC</th>
<th>RH SPOC</th>
<th>Comparison Conditions</th>
<th>Properties of the Area</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present results</td>
<td>−14 −80 32 15 −79 35</td>
<td>[G vs. Baseline AND (R vs. Baseline) AND (L versus Baseline)]</td>
<td>Wrist orientation (ROI)</td>
<td></td>
</tr>
<tr>
<td>de Jong et al. 2001</td>
<td>2 −65 29</td>
<td>R with target selection vs. R with finger selection</td>
<td>Representation of external space for R</td>
<td></td>
</tr>
<tr>
<td>Prado et al. 2005</td>
<td>−18 −79 43 16 −79 43</td>
<td>[R to peripheral target vs. S) vs. (R to foveal target vs. S)]</td>
<td>R to peripheral targets</td>
<td></td>
</tr>
<tr>
<td>Filimon et al. 2010</td>
<td>−9 −73 42 13 −73 41</td>
<td>Visual R vs. nonvisual R</td>
<td>Visually guided R</td>
<td></td>
</tr>
<tr>
<td>Cavina-Pratesi et al. 2010b</td>
<td>−7 −80 36</td>
<td>R Far vs. R Near</td>
<td>Transport component for G and R</td>
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</tr>
<tr>
<td>Kroliszak et al. 2008</td>
<td>None</td>
<td>None</td>
<td>G &gt; R</td>
<td>Stereotyped, less object-dependent movements</td>
</tr>
<tr>
<td>Kroliszak et al. 2010b</td>
<td>None</td>
<td>None</td>
<td>G &gt; R</td>
<td></td>
</tr>
</tbody>
</table>

### A. Our results

#### B. Past activations for reaching

<table>
<thead>
<tr>
<th>Studies</th>
<th>LH SPOC</th>
<th>RH SPOC</th>
<th>Comparison Conditions</th>
<th>Properties of the Area</th>
</tr>
</thead>
<tbody>
<tr>
<td>Culham et al. 2003</td>
<td>−17 −73 32</td>
<td>G &gt; R</td>
<td>Wrist in G</td>
<td></td>
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<tr>
<td>Cavina-Pratesi et al. 2007</td>
<td>−12 −84 20</td>
<td>G &gt; R</td>
<td>Wrist in G</td>
<td></td>
</tr>
<tr>
<td>Kroliszak et al. 2007</td>
<td>21 −83 27</td>
<td>Pantomimmed G &gt; pantomimed R</td>
<td>Stereotyped, less object-dependent movements</td>
<td></td>
</tr>
<tr>
<td>Kroliszak et al. 2008</td>
<td>None</td>
<td>None</td>
<td>G &gt; R</td>
<td></td>
</tr>
</tbody>
</table>

#### C. Past studies of grasping vs. reaching

<table>
<thead>
<tr>
<th>Studies</th>
<th>LH SPOC</th>
<th>RH SPOC</th>
<th>Comparison Conditions</th>
<th>Properties of the Area</th>
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<tr>
<td>Gallivan et al. 2009</td>
<td>−1 −76 26</td>
<td>L at reachable vs. unreachable objects</td>
<td>Encoding object reachability</td>
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<tr>
<td>Quinlan and Culham 2007</td>
<td>−8 −83 27 9 −83 31</td>
<td>Near vs. far vergence (Exp. 1)</td>
<td>Near vergence (Exp. 1)</td>
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<tr>
<td>Pitzalis et al. 2006</td>
<td>−9 −78 37</td>
<td>Retinotopic mapping</td>
<td>Retinotopically organized</td>
<td></td>
</tr>
<tr>
<td>Pitzalis et al. 2010</td>
<td>−9 −78 34 9 −78 34</td>
<td>Retinotopic mapping and functional localizers</td>
<td>Motion sensitivity</td>
<td></td>
</tr>
</tbody>
</table>

### D. Past activations for other tasks
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ences in results from parietal cortex may be due to meth-
in other experiments (Boynton and Finney 2003). Differ-
that code multiple stimulus dimensions (Scannell and
fMRA are difficult to interpret, particularly in areas like V1
(CIP (Shikata et al. 2001, 2003). As with aIPS, null results in
(Rice et al. 2007; Valyear et al. 2006) as well as aIPS and
adaptation to orientation in the Look condition. Previous
implicating the dorsomedial stream in wrist coding.
Regardless of the
objects (i.e., tools). Indeed, the lack of adaptation in aIPS,
extrinsic feature of the object. Therefore, it is not surprising
find the involvement of the dorsomedial circuit only.
Indeed, the results could be different for tasks in which the
orientation of the wrist was driven by intrinsic features of
objects (i.e., tools). Indeed, the lack of adaptation in aIPS,
which is implicated in planning and executing grasping
actions, suggests that the overall effects we see are not due
to a nonspecific higher demand of grasping over reaching or
grasping different versus same orientation conditions. If
this had been the case, aIPS would have likely shown adaptation
for grasping but not reaching conditions. Regardless of the
uncertainty in aIPS, fMRA was observed in SPOC, clearly
implicating the dorsomedial stream in wrist coding.

Similar interpretational caveats apply to the absence of
adaptation to orientation in the Look condition. Previous
fMRI studies have suggested coding of orientation in other
brain areas, including V1 (Kamitani and Tong 2005; Larsson et
al. 2006) and the lateral parieto-occipital junction (Rice et
al. 2007; Valyear et al. 2006) as well as aIPS and
CIP (Shikata et al. 2001, 2003). As with aIPS, null results in
fMRA are difficult to interpret, particularly in areas like V1
that code multiple stimulus dimensions (Scannell and
Young 1999) and have failed to show orientation selectivity
in other experiments (Boyton and Finney 2003). Differ-
ences in results from parietal cortex may be due to meth-
odological differences: whereas Shikata and colleagues used
two-dimensional (2D) textures and Valyear and Rice and
colleagues used 2D pictures of tools, here we employed real
but simple 3D objects.

Another possible way to interpret the data is that the adap-
tation effect observed in the grasping but not the reaching
condition was due to the recalculation of the motor plan in the
former but not the latter task. One could argue that when part-
icipants performed the same movement twice in a trial, they
needed to plan it only once, as the motor program could
be buffered and re-executed. That is, it could be that while the
Grasp Same, Reach Same, and Reach Different orientation
conditions required planning only one movement, the Grasp
Different orientation condition required planning two move-
ments. However, the crucial variable changing during the
replanning involved selectively the orientation of the wrist, as
the configuration of the fingers remained constant across Dif-
ferent and Same orientation conditions. While this argument
is possible, there is debate about the merits of storing and retrieving
movement plans vs. recalculating them based on current
parameters (see discussion in Kroliczak et al. 2008). Moreover,
fMRA effects in different brain areas may depend on the
attributes that change between trials. Indeed, recent data from
our lab suggests that SPOC shows adaptation for some aspects
of object-directed grasping movement, such as object location,
but not others, such as object size (Monaco et al. 2010).
Admittedly, this argument relies on a failure to detect differ-
ences (e.g., SPOC did not show significant adaptation when the
condition required planning two different-sized grasps; Mon-
aco et al. 2010), which may be due to limitations in sensitiv-
ity. Nevertheless, the argument that SPOC codes orientation
(and location but not size) rather than just any action that
requires planning is parsimonious, consistent with predictions
from other literature, and could be further examined with other
methods (such as multivoxel pattern analysis or TMS).

Wrist orientation selectivity was also present in left dPM
(although the activation did not survive a cluster threshold
correction). Area dPM is involved in the transport and grip
components of grasping movements (Cavina-Pratesi et al.
2010b, corroborated by the present data). Here we also
suggest its involvement in the wrist component. These
results are consistent with the findings that stimulation to
dPM in humans can disrupt changes in wrist orientation,
particularly at later stages of processing (Taubert et al.
2010) and that neurons in macaque dPM are tuned to a
combination of grip and wrist postures (Raos et al. 2004).
Given its involvement in all three components, dPM may be
a critical area for their integration. After all, once the
opposition axis for the fingers on the object has been
selected, the transport and the wrist components must be
adjusted accordingly to achieve the most effective and
forceful grip on the object. Indeed, the selection of wrist
orientation is often based on task goals and past associa-
tions, two cognitive factors processed in dPM (Chouinard
and Paus 2006). Our results confirm and extend previous
findings showing the involvement of dPM and superior
parietal lobule in grip and wrist orientation selection for
imagined movements toward an oriented stimulus using a
prehension grip (Johnson et al., 2002) or a tool (Jacobs
et al., 2010). Indeed, we show that these areas are also in-
volved during the execution of the movement, suggesting

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that the orientation of the hand during the actual movement execution, in addition to the selection of the wrist posture in the planning phase, is a critical factor.

In summary, our results show the strong involvement of the dorsomedial circuit in processing wrist orientation. In particular in human SPOC, the putative equivalent of the macaque V6/V6A complex (Galletti et al. 2003), and in dPM. These areas are strongly interconnected in macaques (Caminiti et al. 1999; Galletti et al. 2001; Gamberini et al. 2009; Luppino et al. 2005; Matelli et al. 1998; Shipp et al. 1998) and seemingly also in humans (Grol et al. 2007). Our fMRI results indicate coadaptation of these two areas within the dorsomedial circuit during the processing of wrist orientation for grasping actions. Despite the existence of connections between the dorsomedial and dorsolateral circuits, these connections are substantially weaker than those within the dorsomedial circuit (Gamberini et al. 2009), perhaps contributing to the absence of an effect in dorsolateral areas such as aIPS and ventral premotor cortex. Area pIPS also showed a clear involvement in selecting the wrist posture for grasping, suggesting that this area works together with areas of the dorsomedial circuit and it deserves attentive investigation of its role in coordination of different components during hand actions.

ACKNOWLEDGMENTS

We are grateful to Adam McLean and Joy Williams for assistance with fMRI data collection and Haitao Yang for assistance with hardware development. We thank Jason Gallivan for comments on an earlier draft of this manuscript and for providing valuable insights. We also thank Daniel Wood for helpful discussions.

GRANTS

This work was supported by an operating grant from the Canadian Institutes of Health Research (Grant MOP 84293) to J. C. Culham.

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

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