Evidence for context sensitivity of grasp representations in human parietal and premotor cortices

Mattia Marangon,1 Stéphane Jacobs,1,2 and Scott H. Frey1,3

1Department of Psychology, University of Oregon, Eugene, Oregon; 2Institut National de la Santé et de la Recherche Médicale Unité 1028, Centre National de la Recherche Scientifique 5292, Lyon Neuroscience Research Center, IMPACT (Integrative, Multisensory, Perception, Action and Cognition) Team, and University Lyon I, Bron, France; and 3Lewis Center for Neuroimaging, University of Oregon, Eugene, Oregon

Submitted 16 September 2010; accepted in final form 1 March 2011

Marangon M, Jacobs S, Frey SH. Evidence for context sensitivity of grasp representations in human parietal and premotor cortices. J Neurophysiol 105: 2536–2546, 2011. First published March 2, 2011; doi:10.1152/jn.00796.2010.—Grasp-related responses in neurons of the macaque rostral inferior parietal lobule (rIPL) and the anterior intraparietal sulcus (aIPS) are modulated by task context. Event-related functional MRI was used to determine whether this is true in putative homologs of the human cortex, the rostral inferior parietal lobule (rIPL) and the anterior intraparietal sulcus (aIPS). Fifteen healthy, right-handed adults were required to select prospectively the most comfortable way to grasp a horizontally oriented handle using the cued hand (left or right). In the “no-rotation” condition, the task was simply to grasp the handle, whereas in the “rotation” condition, the goal was to plan to grasp and rotate it into a vertical orientation with the cued end (medial or lateral) pointing downward. In both conditions, participants remained still and indicated their grip preferences by pressing foot pedals. As in overt grasping, participants’ grip preferences were significantly influenced by anticipation of the demands associated with handle rotation. Activity within the aIPS and rIPL increased bilaterally in both the rotation and no-rotation conditions. Importantly, these responses were significantly greater in the rotation vs. no-rotation condition. Similar context effects were detected in the presupplementary motor area, caudal intraparietal sulcus/superior parietal lobule, and bilateral dorsal and left ventral premotor cortices. Grasp representations within the rIPL and aIPS are sensitive to predicted task demands and play a role in context-sensitive grip selection. Moreover, the findings provide additional evidence that areas involved in the sensorimotor control of grasp also contribute to feedforward planning.

inferior parietal lobule; grasping; action selection; functional magnetic resonance imaging; feedforward planning

THE CHOICE OF HOW TO GRASP an object (e.g., over- vs. under-hand) depends on sensory information concerning the state of the body (e.g., current posture, range of motion) and the target object (e.g., location, orientation), as well as anticipation of forthcoming task demands (e.g., intended object rotation) (Johnson-Frey 2004). For instance, when grasping a handle with the intention to rotate it, participants may select a less comfortable initial grip to end in a more comfortable posture (Rosenbaum and Jorgensen 1992). Although much is currently understood about the neural mechanisms involved in online sensorimotor control, comparatively little is known about brain mechanisms that enable anticipated future task demands to influence the selection of movements, including object-oriented grasping.

Neurophysiological studies in monkeys have identified several areas in parietal and premotor cortices that are involved in grasp-related sensorimotor transformations (Gardner et al. 2007; Rizzolatti and Luppino 2001). These include the rostral inferior parietal lobule (rIPL) within the lateral bank of the intraparietal sulcus (area AIP), area V6A (Fattori et al. 2009), ventral premotor (area F5), and the forelimb sector of dorsal premotor (area F2) cortices (Raos et al. 2004). Neurons along the lateral convexity of the rIPL (areas PF/PFG), which show increased activity during reach to grasp, are also sensitive to the larger action context in which these movements are embedded; i.e., they are influenced by prediction of forthcoming task demands. More precisely, a majority of neurons studied responded differentially depending on whether the reach-to-grasp movements were to be followed by bringing the object to the mouth or placing it in a container (Fogassi et al. 2005; Fogassi and Luppino 2005). Likewise, responses within AIP show selective premovement responses depending on the type of grasp that the animals are instructed to perform during a forthcoming movement (Baumann et al. 2009). It remains unknown whether responses in other regions [e.g., dorsal (PMd) and ventral premotor cortices (PMv)] implicated in sensorimotor control of grasp display such context sensitivity.

Similarly to studies in monkeys, human neuroimaging studies of visually guided grasping demonstrate consistent activation in rIPL, extending into the anterior part of the intraparietal sulcus (aIPS) (Binkofski et al. 1998; Culham et al. 2003; Frey et al. 2005). Likewise, transcranial magnetic stimulation over this region can disrupt sensorimotor control of grasp (Rice et al. 2006, 2007; Tunik et al. 2005). Increased activity in premotor cortex also has been reported during some studies of grasp execution (Binkofski et al. 1999; Ehrsson et al. 2000, 2001; Grafton et al. 1996).

In contrast to our understanding of the sensorimotor control of grasp, comparatively little is known about the neural mechanisms involved in selecting actions on the basis of anticipated task demands. Parietal and premotor regions show increased activity when participants prospectively decide whether it would be more comfortable to grasp a handle, appearing in various orientations, in an over- or underhand grip despite the complete absence of overt hand movements (Johnson et al. 2002). More recently, volunteers were trained to grasp objects in many orientations with the hands or a novel mechanical tool. Subsequent functional magnetic resonance imaging (fMRI)
testing revealed increased activity within and along the IPS [including aIPS and caudal IPS (cIPS)], left vPMC, and dPMC during prospective grip selection (Jacobs et al. 2010). Behavioral data provided strong evidence that these decisions were based on accurate, effector-specific internal representations. Interestingly, increases in neural activity were the same regardless of the side (left or right) or effector (hand or tool) on which grip selection decisions were based. These findings suggest that at least some of the parietal and premotor regions involved in the online control of grasping also participate in forming effector-specific representations of grasping actions that are sensitive to anticipated task demands. Whether, like cells in monkey rIPL and AIP, responses in one or more of these areas might be influenced by anticipation of the demands of a movement subsequent to grasping the object is unknown.

Presently, we investigated this issue through use of a task in which participants were required to choose whether an under- or overhand power grip would be most natural to grasp a visually presented handle while undergoing whole brain, blood oxygen level-dependent (BOLD) fMRI. No overt movements were performed in this prospective planning task, and grip preferences were instead expressed through button presses using the feet. Critically, we varied the intended goal of the movement. In the “no-rotation” condition, participants were required to simply select what would be the most natural grip for engaging the handle, whereas in the “rotation” condition, the task involved choosing the grip that they would prefer in order to rotate the handle to a cued orientation once in hand. On the basis of past research, we expected that in the no-rotation condition, participants would prefer the less awkward overhand grip with either hand (Johnson 2000) but that in the rotation condition, they would select the grip that would allow them to complete the handle rotation in a comfortable posture within the middle of their range of forearm supination-pronation. This “end-state comfort effect” is well-established in overt motor performance (Rosenbaum and Jorgensen 1992) and is evidence of context sensitivity in action selection.

In accordance with neurophysiological evidence from monkeys indicating context sensitivity, we predicted that the lateral convexity of the rIPL (Fogassi et al. 2005) and aIPS (Baumann et al. 2009) would show increased activity when participants performed the rotation vs. no-rotation condition of the prospective grip selection (PGS) task during BOLD fMRI. As reviewed earlier, human left vPMC and bilateral dPMC and cIPS are also implicated in the prospective selection of grasp (Jacobs et al. 2010). To the extent that representations in these areas are sensitive to anticipated task demands that extend beyond prehension of the target handle, they should also show greater activity during the rotation vs. no-rotation condition.

To our knowledge, the end-state comfort effect has not been investigated in a prospective planning task. We therefore undertook a preliminary behavioral experiment (experiment 1) to establish the effects of anticipated handle rotation on overt grip selection (OGS), using a design similar to that of the main neuroimaging study (experiment 2). These results would then serve as a standard against which the accuracy of PGS preferences expressed during fMRI testing could be compared.

METHODS

Experiment 1: overt grip selection task. Participants were asked to grasp a handle using either an over- or under-hand power grip under two instructional conditions. The hand used varied from trial to trial. In the no-rotation control condition, participants simply used the cued hand to grasp a horizontally oriented handle. In the rotation condition, they were instructed to grasp the handle and rotate it 90°, placing the cued end of the handle downward. We expected that subjects would show a strong preference for the overhead grip in the no-rotation condition. In the rotation condition, we expected that participants would show an increased preference for underhand grips when the medial end (pointing rightward on left hand trials and leftward on right hand trials) of the handle was cued. This increased preference for the underhand grip would be considered evidence for context sensitivity of grip selection.

This project was reviewed and approved by the Institutional Review Board at the University of Oregon. Thirteen healthy participants (8 females), ages 26 ± 3.8 yr (SD), gave informed consent to undertake the study. All participants were consistently right-handed according to the Edinburgh Handedness Inventory (Oldfield 1971) and had normal or corrected-to-normal vision. None had a history of neurological or psychiatric illness.

Apparatus. Both experiments 1 and 2 were controlled with a laptop computer running Presentation software (Neurobehavioral Systems; http://nbs.neuro-bs.com/). A wooden rack was positioned within reach of the participant, and the distance was adjusted to accommodate each participant’s arm length. The rack was centered along the participant’s midsaggital line. A 2-in.-diameter wooden handle (10-in. length) was suspended horizontally on the rack with the square end pointing toward the left or right, depending on the trial. A wooden 2 × 2 × 0.5-in. square was attached to one end of the handle, and a 2-in.-diameter, 0.5-in.-thick circle was centered on the opposite end. Lying horizontally on the tabletop, directly in front of the rack, was a 20-in. flat LCD computer monitor fitted with a clear Lexan cover.

Procedure. Every participant performed 144 trials divided into 3 blocks. Each block consisted of 4 repetitions of the 12 different trial types presented in pseudorandom order: 2 hand cues (left or right) × 2 dowel orientations (square end pointing toward the left or right) × 3 target shapes (square, circle, or triangle). Figure 1A illustrates the graphic stimuli used in experiment 2. These are similar to actual handles and targets used in experiment 1, with the exception that the handles in experiment 1 were unpainted.

Participants sat on a chair with their forearms resting on the tabletop and their left and right index fingers depressing left and right response buttons, respectively. They wore a pair of liquid crystal goggles (Translucent Technologies, Toronto, ON, Canada). At the beginning of a run, the participant viewed a left- or rightward arrow that served to indicate which hand would be used on the subsequent trial. The goggles then became opaque, preventing vision of the display. The experimenter placed the handle on the rack with the square pointing to the left or right, according to the trial list, and depressed a key on the keyboard. The goggles became transparent from the onset of vision until the response button was depressed.
selecting the overhand grip for each condition was then calculated end was pointing away from the midline. The mean probability of pointing toward the participant’s midline. On lateral trials, the cued orientation on rotation trials. Medial trials were those in which the cued end of the handle (square or circular, depending on the target shape) was videotaped, and grip preferences were coded off-line. The entirety of each run became opaque and the process was repeated. The entirety of each run sequence during a PGS trial in experiment 2. Participants were instructed to decide whether it would be more comfortable to place the thumb side of their cued hand (as indicated by the arrow) on the pink or tan end of the handle if grasping it in a power grip. If the target was a circle or square, they were to base their grasp selection on consideration of the need to rotate the handle to align the corresponding end of the handle (rotation condition). If, as shown, the target was a triangle, then they were instructed to decide on which end of the handle they would place their thumb if simply grasping the handle without the intention to rotate it (no-rotation condition). C: biomechanical constraints governing pronation-supination of the left and right hands are mirror symmetrical (i.e., 180° out of phase). To directly compare grip selection preferences across left and right hands, rotation trials were therefore organized according to whether the end of the handle cued by the target shape was pointing toward (medial) or away from (lateral) the participant’s midline. Grip preferences are illustrated for both the overhand (top) and underhand (bottom) possibilities. released. After each trial was completed, participants returned their hand to the response button. This triggered the appearance of the 500-ms hand cue for the next trial, after which the goggles again became opaque and the process was repeated. The entirety of each run was videotaped, and grip preferences were coded off-line.

Data analysis. As illustrated in Fig. 1C, to enable direct comparisons of grip preferences between hands, we recoded handle orientation on rotation trials. Medial trials were those in which the cued end of the handle (square or circular, depending on the target shape) was pointing toward the participant’s midline. On lateral trials, the cued end was pointing away from the midline. The mean probability of selecting the overhand grip for each condition was then calculated separately for every participant and submitted to 2 (hand: left, right) × 3 (cue type: lateral, medial, control) repeated-measures ANOVA. A significance level of \( P < 0.05 \) was used for all statistical tests.

Trials with response times (RT) ± 2 SD from the mean were defined as outliers and removed. Excluded trials constituted 4% of the total number.

RESULTS AND DISCUSSION

As expected, differences in grip preferences between hands were nonsignificant \( (F < 1.0) \). There was a main effect of the target (medial, lateral, control) \( [F(1,11) = 28.08, \text{mean square error (MSE)} = 773.314, P < 0.001] \). As shown in Fig. 2A, participants showed a strong preference for the overhand grip when the lateral end of the handle matched the target \( (97.8 \pm 10.3\%) \). This response pattern did not differ significantly from that of the control condition \( (99.31 \pm 9.64\%) \) \( [t(12) < 1.0] \). As expected, subjects were less likely to select the overhand grip in the rotation condition when the medial end of the handle was cued \( (41.91 \pm 24.21\%) \) compared with either use of the lateral end \( [t(12) = 5.614, P < 0.001] \) or control condition \( [t(12) = 5.611, P < 0.001] \) (Fig. 2A). Response times did not differ significantly between hands or target types \( (P < 0.20) \).

Adopting an overhand grip in the lateral cue condition and an underhand grip in the medial cue condition allowed partic-
participants to complete handle rotations in a comfortable posture in the middle of their range of hand pronation-supination. The fact that the current grip preferences exhibited this pattern is further evidence that grip selection involves anticipation of forthcoming task demands (Rosenbaum and Jorgensen 1992). Because participants continued to prefer an overhand grip in the lateral cue condition, this result cannot be attributed to merely choosing overhand in the no-rotation condition and underhand in the rotation condition.

Experiment 2: fMRI prospective grip selection task. As expected on the basis of previous findings (Rosenbaum et al. 1992; Rosenbaum and Jorgensen 1992), participants in experiment 1 adapted their grip preferences to the anticipated demands of a forthcoming handle rotation. In experiment 2, we asked whether this end-state comfort effect would also be exhibited when participants were asked to decide how they would grasp the handle in both rotation and no-rotation conditions while remaining still; i.e., in a purely PGS task that lacks overt movement and associated sensory feedback (John- son 2000). If so, then participants should again show an increased preference for underhand grips in the rotation condition when the medial, but not the lateral, end of the handle is cued. To the extent that this is the case, we reasoned that fMRI data acquired during performance of this PGS task could be used to identify regions showing context sensitivity during the planning of reach-to-grasp movements.

On the basis of earlier findings regarding prospective planning of grasp (Jacobs et al. 2010; Johnson et al. 2002), we expected that PGS in both the no-rotation and rotation conditions would be associated with increased activity within and along the IPS (including aIPS and cIPS), dPMC, and left vPMC. Furthermore, results showing context sensitivity in monkey rIPL (Fogassi et al. 2005; Fogassi and Luppino 2005) and AIP (Baumann et al. 2009) suggest that putatively similar areas in the human (rIPL and aIPS) might, in particular, show greater increases in activity during rotation vs. no-rotation conditions. The reason for this expectation is that grip selection in the rotation condition involves anticipating the additional demands that would be associated with rotating the handle once in hand. Our use of whole brain imaging also provided the opportunity to assess whether other regions implicated in sensorimotor control and prospective planning of grasp (cIPS, dPMC, and left vPMC) might also show similar context sensitivity. If so, then these findings could serve as an impetus for future single-unit investigations in monkeys.

METHODS

Fifteen healthy participants (9 females), ages 24 ± 4.3 yr, took part in the study after giving written informed consent. None had participated in experiment 1 or had a history of neurological or psychiatric illness. All participants were consistently right-handed according to the Edinburgh Handedness Inventory (Oldfield 1971) and had normal or corrected-to-normal vision.

Procedure. Stimuli consisted of two graphically rendered handles, each with a square end and a round end (Fig. 1A). For one handle, the half with the square end was colored pink and the other, tan; the second handle had these colors reversed. Each handle appeared in two orientations, one with the square end on the left and the other with the square end on the right. The handles were realistically shaded to give the appearance of three-dimensionality. As detailed below, on a given trial one of these four handle permutations (2 handles × 2 orientations) was paired with one of three different target objects, a circle, square, or triangle.

Every trial consisted of six consecutive phases optimized for event-related fMRI testing (Fig. 1B): 1) hand cue: for 500 ms a left- or rightward pointing arrow was presented centrally to inform the participant on which hand (left or right) they should base their upcoming grip selection decision; 2) oversampling interval: a variable delay of 500, 1,000, 1,500, or 2,000 ms was time-locked to the acquisition of a volume of functional MRI data (Miezin et al. 2000); 3) grip selection cue: for 2,500 ms a handle stimulus was presented centrally above 1 of 3 different targets (square, circle, or triangle); 4) variable delay interval: 500, 1,000, 1,500 ms; 5) response cue: for a 2,000-ms duration, colored squares indicated which foot pedal (left or right) represented the pink or tan option on that particular trial. Subjects were instructed to press the pedal whose color corresponded to where the thumb side of their hand would be on the handle if grasped. Trial-by-trial variation in the identity of the pedals forced participants to wait for this response cue before indicating their choice. This enabled separation of activity associated with grip selection (our focus) from response button selection and execution. 6) An intertrial interval (1,500, 2,000, 2,500, 3,000, 3,500, or 4,000 ms) was adjusted to bring each trial to an equal 10-s duration. The ordering of events within trial was necessarily fixed, due to the sequential relationship between hand preparation, grip selection, and response execution. However, oversampling and jitter interval durations occurred equally often for each trial type; i.e., 2 hands (left, right) × 2 conditions (rotation, no rotation). For a randomly selected 50% of the trials within each run, the left foot pedal was used to indicate the “pink” response, and for the remainder this pedal indicated the “tan” response.

A centrally presented white cross remained visible throughout the entirety of each functional run, and subjects were instructed to maintain fixation. Each participant performed six functional runs. Each run consisted of 32 10-s-long experimental trials (16 rotation trials: 2 hand cues × 4 stimulus handles × 2 targets; 16 no-rotation trials: 2 × 2 hand cues × 4 stimulus handles), plus an additional 8 null trials of equal duration during which no stimuli were presented. The doubling of the no-rotation trials was necessary to achieve equity with the total number of rotation trials, making the identity of the forthcoming trial unpredictable. Within each run, these 40 trials (16 rotation, 16 no rotation, and 8 null) were presented in pseudorandom order, subject to the constraint that no more than 3 trials of any single type could occur sequentially.

The PGS task was similar to experiment 1 except that no overt hand movements were involved. Instead, in both the no-rotation and rotation conditions, participants were instructed to identify whether they would prefer to place the thumb side of their cued hand on the pink or tan side of the handle if grasping it in a power grip. This enabled us to code whether they preferred an over- or underhand grip for each trial. In the rotation condition, the shape of the target matched one end of the dowel (square or circular target). The task was to select the grip that would be preferred if intending to rotate the handle downward with the indicated hand, placing the cued end on the target. Again, participants were not asked to
consider aligning the cued end and target shape. On no-rotation trials (triangular target), the task was to select the grip that would be preferred if intending simply to grasp the handle with the cued hand and put it down lengthwise. Target objects appeared centrally below each stimulus dowel (Fig. 1A). Again, half of the total number of trials consisted of the no-rotation control condition, whereas the remainder was equally split between lateral and medial rotation trials.

Before the start of the scanning session, participants practiced the PGS task both outside the scanner and inside an MRI simulator scanner (80 trials in each session). During both mock and actual fMRI testing, participants were lying supine in the scanner with their arms extended at their sides with the palms oriented vertically. They were unable to see their hands.

Stimuli were projected onto a screen at the back of the scanner oriented vertically. They were unable to see their hands. Participants were instructed to select the appropriate grip from two rectangular options, one of which was the correct grip for that trial and the other of which was incorrect. The grips were presented with the appropriate alignment for each hand (Fig. 1C). In addition, pink and tan responses on all trials were recoded as over- or underhand. The mean probability of selecting the overhand grip for each condition was then calculated separately for each participant and submitted to 2 (hand: left, right) × 3 (cue type: lateral, medial, control) repeated-measures ANOVA. Response times were not analyzed because they included not only the time to select a grip but also the variable delay and response cue intervals.

**MRI data acquisition.** Functional images were acquired on a Siemens Allegra 3T MRI system (Siemens, Erlangen, Germany) equipped with echo planar imaging (EPI) capabilities, using a standard birdcage coil for radiofrequency transmission and signal reception. BOLD-sensitive functional images were acquired using a single-shot gradient EPI sequence (TE/TR = 30/2000 ms, flip angle = 80°, 33 axial slices, voxel size = 4.0 × 4.0 mm; field of view = 200 mm, thickness = 3.0 mm). A double-gradient echo sequence was used to acquire a field map that was used to correct EPI distortions. Two high-resolution anatomic images were acquired using a three-dimensional MP-RAGE pulse sequence (TE/TR = 4.38/2500 ms; flip angle = 8.0°, 176 contiguous axial slices, thickness = 1.0 mm, voxel size = 1.0 × 1.0 × 1.0 mm; field of view = 256 mm). Siemens’ AutoAlign scout and TrueFISP sequences were executed for each participant at the beginning of each functional data collection run to ensure that slices were prescribed in exactly the same positions across runs. DICOM image files were converted to NIfTI format using MRICronvert software (http://lcni.uoregon.edu/~jolinda/MRICronvert/).

**fMRI processing and analysis.** fMRI data were preprocessed using the FSL toolbox version 4.0.2 (http://www.fmrib.ox.ac.uk/fsl) (Smith et al. 2004). Pre-statistical processing was applied as follows: EPI dewarping was done using PRELUDE and FUGUE (Jenkinson 2003, 2004), motion correction was performed using MCFLIRT (Jenkinson et al. 2002), volumes were smoothed with a Gaussian kernel of 5 mm (FWHM) to reduce the noise, and intensity was normalized and filtered with a nonlinear high-pass temporal filter (70.0 s). Skull and surrounding tissue were removed using a brain extraction tool (Smith 2002). Registration to high-resolution structural and/or standard space images was carried out using FLIRT (Jenkinson et al. 2002; Jenkinson and Smith 2001).

Each fMRI run for a given subject was modeled separately at the first level. For each run, we created a model with four explanatory variables (EVs) and their temporal derivatives to encode the conditions under which grip selection decisions were performed in our 2 (hand: left, right) × 2 (goal: no rotation, rotation) factorial design. These EVs were time-locked to the onset of the handles and target objects (phase 3 above) and included the subsequent 3000-ms (2500-ms stimulus duration plus the shortest delay interval of 500 ms, Fig. 1B). A fifth EV coded the 10-s null trials that were used as resting baseline. Orthogonal contrasts were used to test for differences between each of the four experimental conditions and resting baseline.

Higher level analyses were performed using FLAME Stage 1 (Beckmann et al. 2003; Woolrich et al. 2004) to model and estimate random-effects components of mixed-effects variance. The resulting first-level contrasts of parameter estimates (COPEs) served as inputs to second-level analyses (within subjects across runs). COPEs from the second-level analyses then served as inputs to third-level analyses (across participants). Z-statistic (Gaussianized T/F) images were thresholded using Z > 2.3 and a (corrected) cluster significance threshold of P = 0.05 (Worsley 2001).

**fMRI ANOVA.** Next, a more targeted 2 (hand: left, right) × 2 (goal: no rotation, rotation) repeated-measures ANOVA was carried out only on those voxels from the initial whole brain analysis that showed evidence of being modulated by the task at the group level; i.e., significant increases in activity within at least one of the four experimental conditions relative to rest (Z > 2.3, corrected cluster significance threshold of P = 0.05).

Anatomical localization was undertaken by manual comparison with an atlas (Duvernoy 1991) and by overlaying activation maps on the population, landmark, and surface-based atlas.
of Van Essen (2005) using Caret 5.5 software (Van Essen et al. 2001).

Descriptive region-of-interest analysis. Regions-of-interest (ROIs) were defined post hoc within bilateral rIPL/aIPS, dPMC, and left vPMC. Spherical ROIs (5-mm radius) were centered on the mean x, y, z coordinates obtained by averaging across the four conditional peaks in each area (Table 1). For every participant, mean percent signal change (PSC) relative to the resting baseline was calculated separately within every ROI for each condition. Mean PSC was computed for each individual and condition by taking the ratio of the COPEs (experimental condition > rest) and mean voxel intensity and then scaling by the peak height of a regressor formed by convolving an isolated 3-s event with the double gamma hemodynamic response function (Mumford 2007). Subject conditional means were then submitted to separate repeated-measures ANOVAs for each ROI with hand and condition as within-subjects factors. A Bonferroni-corrected threshold of P < 0.05 was used in significance tests.

RESULTS AND DISCUSSION

Behavioral data on prospective grip selection. Similar to results of the OGS task in experiment 1, no difference was detected between hands (F < 1.0), and data were therefore pooled across this variable (Fig. 2B). As expected if PGS preferences were context sensitive, there was again a significant main effect of target (medial, lateral, control) [F(1,14) = 43.687, MSE = 695.945, P < 0.001]. As in experiment 1, participants showed a strong preference for overhand grips when the lateral end of the handle was cued (82.3 ± 10.54%) that did not differ from that of the control condition (84.3 ± 11.32%) [t(14) = 1.409, P = 0.181]. Importantly, in the medial cue condition (28.08 ± 26.60%), participants again displayed a significantly lower preference for overhand grips compared with either the lateral cue condition [t(14) = 6.65, P < 0.001] or the no-rotation control [t(14) = 6.85, P < 0.001]. This suggests that despite the absence of overt movements and associated sensory feedback, prospectively chosen grips involved accurately anticipating the demands associated with the intended handle rotations.

Direct comparisons between the OGS (experiment 1) and PGS tasks (experiment 2) failed to detect a significant difference in grip preferences between tasks (F < 1.0) (cf. Fig. 2, A and B). Likewise, the variable task did not interact with the hand involved (F < 1.0).

Post hoc, paired comparisons also failed to reveal any significant differences between specific conditions of the PGS and OGS tasks (P > 0.20 in all cases). This suggests that despite the absence of overt movements and associated sensory feedback, prospectively chosen grips accurately anticipating the demands associated with the intended handle rotations. As with OGS, grips were chosen that would allow participants to complete the required actions in a comfortable posture, i.e., they demonstrated the end-state comfort effect (Rosenbaum et al. 1992; Rosenbaum and Jorgensen 1992). Results of fMRI testing provide insights into the neural mechanisms involved in this prospective planning.

Neural activity associated with PGS. To identify brain regions whose activity was modulated by the PGS task, each of the four experimental conditions [2 (hand: left, right) × 2 (goal: no rotation, rotation)] were separately contrasted against resting baseline. Consistent with earlier results on PGS (Jacobs et al. 2010; Johnson et al. 2002), very similar patterns of activity were found across all conditions (Fig. 3). Areas showing increased activity included regions within and along the intraparietal sulcus (including the aIPS, rIPL, and cIPS), dPMC, superior parietal lobule (SPL), presupplementary motor area (pre-SMA), and the lateral cerebellum. Likewise, activity in the posterior middle temporal gyrus (pMTG) and vPMC only reached significance in the left hemisphere (Jacobs et al. 2010).

Fig. 3. Areas of the brain showing significant increases in activity relative to resting baseline for the 4 experimental conditions. Group average data (Z ≥ 2.3, P < 0.05, cluster-based correction for multiple comparisons) are overlaid onto the partially inflated population-average, landmark-, and surface-based atlas in Caret 5.5 software using the multifiducial mapping procedure. Areas showing significant activation after multifiducial mapping are represented in warm hues. Pale green areas were significantly activated in the group FSL analysis but did not survive the multifiducial correction for intrasubject anatomic variability. Note the similarity of increases across all 4 conditions and the left cerebral asymmetries in rostral posterior parietal and premotor regions.
Next, a 2 (hand: left, right) × 2 (goal: rotation, no rotation) repeated-measures ANOVA was performed across all voxels that showed significantly increased activity relative to resting baseline in at least 1 of the 4 conditions (see Fig. 3). Table 1 provides details on the coordinates used to center these 5-mm-radius spherical regions of interest (ROIs). No areas showed a significant effect of hand. However, premotor and parietal regions, including rostral inferior parietal lobule (rIPL) and anterior intraparietal sulcus (aIPS), did show significantly greater increases when grip selection involved considering the demands associated with handle rotation compared with no rotation. These effects were bilateral within the rIPL and in dorsal premotor cortex (dPMC) but were restricted to the left cerebral hemisphere in the posterior middle temporal and ventral premotor cortices (vPMC; see text for details). No regions showed the opposite effect. At bottom, the same data group results are displayed on neurologically-oriented, axial slices of the group-average, T1-weighted structural scan (L, left; R, right). Graph insets show results of descriptive ROI analyses (see METHODS). These post hoc tests provide some evidence for responses that are affected by the hand involved in planning. Right aIPS and right dPMC both showed significantly greater activity when planning involved the contralateral (left) vs. the ipsilateral (right) hand. With the exception of left dPMC, all ROIs showed a significant interaction between hand and goal, reflecting greater increases in activity when choosing a grip for the contralateral hand with the goal of handle rotation (see text for details).

**Fig. 4.** Results of the 2 (hand: left, right) × 2 (goal: rotation, no rotation) repeated-measures ANOVA. This more targeted analysis included voxels that were activated significantly relative to resting baseline in at least 1 of the 4 conditions (see Fig. 3). Table 1 provides details on the coordinates used to center these 5-mm-radius spherical regions of interest (ROIs). No areas showed a significant effect of hand. However, premotor and parietal regions, including rostral inferior parietal lobule (rIPL) and anterior intraparietal sulcus (aIPS), did show significantly greater increases when grip selection involved considering the demands associated with handle rotation compared with no rotation. These effects were bilateral within the rIPL and in dorsal premotor cortex (dPMC) but were restricted to the left cerebral hemisphere in the posterior middle temporal and ventral premotor cortices (vPMC; see text for details). No regions showed the opposite effect. At bottom, the same data group results are displayed on neurologically-oriented, axial slices of the group-average, T1-weighted structural scan (L, left; R, right). Graph insets show results of descriptive ROI analyses (see METHODS). These post hoc tests provide some evidence for responses that are affected by the hand involved in planning. Right aIPS and right dPMC both showed significantly greater activity when planning involved the contralateral (left) vs. the ipsilateral (right) hand. With the exception of left dPMC, all ROIs showed a significant interaction between hand and goal, reflecting greater increases in activity when choosing a grip for the contralateral hand with the goal of handle rotation (see text for details).
GENERAL DISCUSSION

As introduced earlier, the ways that we grasp objects are influenced by the movements that we intend to perform once they are in hand, i.e., the ultimate goals of the action. Although much is currently known about the neural mechanisms involved in online sensorimotor control of grasping, little is understood about the neural mechanisms responsible for the context sensitivity of this fundamental behavior. The current work yielded two main insights. We found that even in the complete absence of movement and associated sensory feedback, prospectively selected grips (experiment 1) were highly consistent with those expressed during a similar task involving overt movements (experiment 2). Importantly, grip preferences in both circumstances showed clear evidence of being influenced similarly by the anticipated demands of a forthcoming handle rotation. In the rotation condition, participants chose grips that would have allowed them to complete the required action in a comfortable posture in the middle of their range of motion. To our knowledge, this is the first demonstration of an end-state comfort effect in an action selection task that involves only planning and no movement. The presence of this end-state comfort effect in the PGS task is consistent with the hypothesis that context sensitivity, as manifest in the selection of the macroscopic aspects of grasp (e.g., under- vs. overhand), can arise in a purely feedforward manner (Frey 2010). Critically, these behavioral results allowed us to pursue the primary objective of this work, to evaluate the presence of context-sensitive grasp representations in the rIPL.

As predicted based on evidence from single-unit recordings in macaques (Baumann et al. 2009; Fogassi et al. 2005), we detected greater increases in rIPL/aIPS during the rotation vs. no-rotation condition of the PGS task. This suggests that these regions participate in the formation of context-sensitive representations of grasp in the human brain. We now consider these neurophysiological findings, as well as evidence for context sensitivity of grasp representations in other brain regions, in greater detail.

Context-sensitive grasp representations in the IPL. A considerable body of evidence implicates the IPL of macaques (Gardner et al. 2007) and humans (Castiello and Begliomini 2008) in constructing sensorimotor representations of grasp. Grasp-related activity of neurons in macaque AIP (Baumann et al. 2009) and rIPL (Fogassi et al. 2005) further show sensitivity to the context in which these movements are performed. That is, activity within these regions of the IPL is modulated according to the actions that the animal is instructed to perform once the object is in hand. We found that human aIPS and rIPL both showed increased activity during PGS relative to resting baseline. Importantly, these increases were significantly greater in the rotation vs. no-rotation condition (Fig. 4). This suggests that these areas of the human brain participate in context-sensitive representations of grasp.

An earlier investigation provided evidence that transcranial magnetic stimulation delivered soon after movement initiation over aIPS interferes with the ability to update motor programs on the basis of sensory feedback (Tunik et al. 2005). Subsequent results suggest that these effects are related to the execution, rather than the planning, phase of the grasping movement (Rice et al. 2006). However, there is also evidence that aIPS codes the goals, rather than movements, of observed grasping actions (Hamilton and Grafton 2006), and a recent investigation of PGS involving the hands or a recently mastered tool found that aIPS participates in grasp planning even in the complete absence of movements (Jacobs et al. 2010). The present study extends these observations by showing further increases in aIPS (and rIPL) activity when grip selection decisions involve representing the demands of a subsequent object rotation. This finding is consistent with the hypothesis that the aIPS (and we would add the rIPL) participates in representing actions’ intended goals (Tunik et al. 2007). Furthermore, we provide evidence that context sensitivity is not peculiar to aIPS/rIPL but also is found in a number of other regions known to be involved in sensorimotor control of grasp.

Context-sensitive responses in other brain regions. As introduced earlier, in addition to rIPL and AIP, single-unit recordings reveal that neurons in PMv, PMd, and V6a exhibit grasp-related responses. Very recent findings also indicate context-sensitive response during movement preparation in some grasp-related neurons located in the macaque rostral ventral premotor cortex (area F5) (Bonini et al. 2010; Fluet et al. 2010). Together with an interconnected subdivision of the rIPL (area PFG), F5 may play a key role in the organization of sequential, goal-directed actions (Bonini et al. 2010). Similarly, despite the complete absence of movement, we found increased activity in human left vPMC, located along the inferior portion of the precentral sulcus and extending rostrally into both the inferior and middle frontal gyri. This is consistent with earlier work on PGS with the hands or a recently learned tool (Jacobs et al. 2010) and could be taken as evidence for a putatively homologous circuit for goal representation in the human brain that is strongly left lateralized (further discussion follows). Likewise, our whole brain coverage identified context-sensitive responses in bilateral dPMC and cIPS/SPL during PGS both in both this study and our previous work (Jacobs et al. 2010; Johnson et al. 2002) (Fig. 4). This suggests that context sensitivity during planning is a widespread property of parietopremotor grasp representations.

Our grasp selection tasks demand that participants choose the most comfortable hand orientation (under- vs. overhand) for grasping the stimulus object. Cells in V6a (Fattori et al. 2009) and the distal forelimb sector of dorsal premotor cortex (area F2) (Raos et al. 2004) code wrist (hand) orientation during grasping. Increased activity in cIPS (extending into the POS and SPL) and dPMC in all conditions of the present investigation might reflect similar coding within the human brain (Fig. 4). Importantly, the fact that these increases occurred in the absence of movements suggests their involvement in feedforward processing. As suggested below, along with aIPS/rIPL and left vPMC, these areas may be involved in representing the state of the effectors during internally simulated movements. Greater involvement during the rotation vs. no-rotation condition would seem consistent with this hypothesis.

It is known that in macaques, pre-SMA (F6) is richly interconnected with prefrontal regions, plays a role in pre-movement processes including selection and preparation (Lupino et al. 1991; Lupino and Rizzolatti 2000), and may serve similar functions in humans (Picard and Strick 1996, 2001). The fact that pre-SMA activity shows evidence of context sensitivity in this study suggests that its role must also include representing the different demands of the rotation and no-rotation conditions. One possibility is that pre-SMA plays a...
role in the internal simulation of movements. Increased pre-SMA activity is commonly found in a wide range of motor-cognitive tasks in human neuroimaging studies that involve dynamically imagining or planning movements (Frey and Gerry 2006; Gerardin et al. 2000; Johnson et al. 2002). This region could be important for updating parietopremotor representations of the effectors’ states over time. We will return to the issue of state estimation shortly.

Despite a high degree of similarity between stimulus displays, an unexpected increase in left pMTG was also found for the rotation vs. no-rotation comparison. This area has been shown to increase activity during tasks that involve identification of familiar tools (Chao et al. 1999; Martin et al. 1996) and shows a particular sensitivity to the motions of tools and utensils (Beauchamp et al. 2002). Yet, the present task involved neither familiar tools nor moving stimuli. Because both rotation and no-rotation conditions involved identical objects, this difference also cannot be attributed to the coding of objects’ structural properties, as has been reported in adjacent lateral occipital complex (Krolizak et al. 2008). Alternatively, left pMTG might be activated during the internal simulation of grasping movements. As introduced below, PGS may involve the use of feedforward processes to predict the sensory consequences associated with each grip option. Perhaps increased activity in pMTG reflects the processing of predicted visual sensory feedback that would accompany grasping movements. By this account, the greater response in the rotation condition would reflect more complex movements than in the no-rotation condition.

Areas involved in grip selection but not affected by context. Compared with rest, all experimental conditions were associated with increased activity along the left middle frontal gyrus (MFG), and the rotation condition for the left hand also involved increases in the right hemisphere (Fig. 3). Increases in left rostral MFG were also detected in all conditions of an earlier study of prospective grip selection (Jacobs et al. 2010). In contrast to all other regions, however, MFG did not show evidence of context sensitivity, i.e., responses did not differ significantly between the rotation vs. no-rotation conditions. This suggests that MFG is involved in a processing component that is common to all grip selection conditions, yet unaffected by the additional demands of planning for handle manipulation. Based on previous findings (Schluter et al. 2001), a likely candidate is the choice between the two grip options after the costs associated with each option have been computed.

The lateral cerebellum also showed bilateral increases in activity for all conditions in this study and in our previous investigations of PGS (Jacobs et al. 2010; Johnson et al. 2002). However, responses were unaffected by the goal manipulation (Fig. 4). There is a considerable body of evidence suggesting that the cerebellum may support internal models that predict the sensory consequences of movements based on a copy of the motor command (see reviews by Shadmehr and Krakauer 2008; Wolpert and Flanagan 2001). These predictions are viewed as extending over relatively brief periods of time, slightly in advance of actual sensory feedback. Involvement of the cerebellum in this and other prospective planning tasks (Jacobs et al. 2010; Johnson et al. 2002) raises the possibility of this structure being involved in forecasting movements’ longer range sensory consequences for use in action selection (Frey 2010). The fact that cerebellar activity does not increase further when planning involves handle rotation, however, suggests that other areas may be involved in representing the sensory consequences of these predictions (Fig. 4). More precisely, it may be that the parietal and premotor regions that do show context sensitivity are involved in maintaining and updating representations of how the state of the limbs would be impacted by these predictions arising from internal models supported in the cerebellum.

Left cerebral asymmetries in vPMC. Previous work revealed a strong left cerebral asymmetry in vPMC during PGS regardless of the limb (left or right) or effector (hand or novel tool) on which these judgments were based (Jacobs et al. 2010). We replicated this result and also showed that grasp-related responses within left vPMC are sensitive to the task context (Fig. 4). The significance of this cerebral asymmetry in prospective grasping planning is unclear. Together, these findings point to the fact that the laterality within the sensorimotor system extends to motor-cognitive planning functions (Willems et al. 2009). This is consistent with previous findings on the specialized role for the left hemisphere in motor selection and attention processes in healthy right-handed participants (Haaland and Harrington 1996; Rushworth et al. 1997, 1998; Schluter et al. 2001) and in stroke patients (Laimgruber et al. 2005).

Hand-independent responses. It is important to stress that although participants’ behavioral responses showed strong evidence of taking into account the unique constraints of the two hands (i.e., hand dependence), our analyses focusing on areas involved in PGS failed to detect any regions showing hand-dependent neural activity. The only indications of effector specificity came from post hoc ROI analyses showing an advantage for the contralateral hand in right aIPS and right dPMC. The failure to detect evidence of effector specificity in statistical parametric maps is consistent with earlier results (Jacobs et al. 2010). It is tempting to interpret this as evidence for limb-independent levels of motor representation. However, as stated earlier, our behavioral data clearly show that PGS decisions were based on internal representations that took into account the biomechanical constraints specific to each upper limb. Together with the behavioral findings, these results thus demonstrate that common patterns of neural activity across different effectors are a necessary, but not sufficient, source of evidence for effector-independent levels of action representation. It is known that both effector-specific and effector-nonspecific responses can be found in both parietal (Hyvarinen 1982) and premotor regions (Rizzolatti et al. 1988). This intermixing may lead to indistinguishable fMRI responses.

Limitations of the current work. One limitation of the current project is that during fMRI, participants were required to plan, but not to execute, grasping actions. Whether activity would be the same during the premovement planning phase of an actual grasping end-state task remains to be shown. However, there is evidence indicating that in similar grip selection tasks, macroscopic aspects of grasp (e.g., hand orientation) are chosen before movement onset (Stelmach et al. 1994). The prospective task might involve processes, such as visual or kinesthetic/motor imagery, that may not be engaged when planning forthcoming movements (Walsh and Rosenbaum 2009). Although we cannot rule out these possibilities, we did not detect any increases in visual areas of the brain that were greater in the rotation vs. no-rotation condition, as would be expected if these conditions differed in their demands on visualization. Engage-
ment of the pre-SMA is consistent with involvement of kinesi-thet/motor imagery (Gerardin et al. 2000; Stephan et al. 1995). It is also possible that the rotation condition was more demanding of spatial attention than the no-rotation control. Attentional demands might account for some of the increased activity in the posterior parietal and even frontal cortex during the rotation condition (Shulman et al. 2002). However, attentional processing alone cannot account for the effector- and goal-specific behaviors exhibited in this study. Finally, it is tempting to interpret these results in terms of evidence for functional homologies between monkey rIPS/AIP and human rP1/ aIPS. However, care must be exercised when drawing such conclusions, especially in light of evidence for differences between species in some IPS functions (Orban et al. 2004).

In conclusion, we present evidence that the human rIPS/ aIPS is involved in forming context-sensitive grasp representations. Despite the complete absence of overt movements, this region shows increased activity when selecting how best to grasp a handle for subsequent rotation. These findings complement earlier observations of context-sensitive units in the macaque rIPS and AIP. Furthermore, we find evidence for context sensitivity in a number of other regions that have previously been implicated in sensorimotor control of grasping and/or action planning, including cIPS, dPMC, left vPMC, and pre-SMA. Additional work is needed to determine the precise relationship between these regions and context-sensitive behavior.

ACKNOWLEDGMENTS

M. Marangon and S. H. Frey designed the experiment. M. Marangon and S. Jacobs analyzed the data. S. H. Frey and M. Marangon wrote the article. Experiment 1 fulfilled part of the requirements of a MA thesis submitted to the University of Oregon by Evan Lohele-Conger.

Present address of M. Marangon: Department of General Psychology, University of Padua, Padua, Italy.

GRANTS

This work has been supported by National Institute of Neurological Disorders and Stroke Grant NS053962 to S. H. Frey and by Army Research Laboratory Grant ARO/ARL 49581-LS. S. Jacobs held a grant from the Fyssen Foundation during a portion of this work.

DISCLOSURES

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

REFERENCES


