

What Does the Brain Do When You Fake It? An fMRI Study of Pantomimed and Real Grasping

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Króliczak G, Cavina-Pratesi C, Goodman DA, Culham JC. What does the brain do when you fake it? An fMRI study of pantomimed and real grasping. *J Neurophysiol* 97: 2410–2422, 2007. First published January 17, 2007; doi:10.1152/jn.00778.2006. Given that studying neural bases of actions is very challenging with fMRI, numerous experiments have used pantomimed actions as a proxy to studying neural circuits of real actions. However, the underlying assumption that the same neural mechanisms mediate real and pantomimed actions has never been directly tested. Moreover, the assumption is called into question by neuropsychological evidence suggesting that real actions depend on the dorsal stream of visual processing whereas pretend actions also recruit the ventral stream. Here, we directly tested these ideas in neurologically intact subjects. Ten right-handed participants performed four tasks: 1) grasping real three-dimensional objects, 2) reaching toward the objects and touching them with the knuckle without hand preshaping, 3) pantomimed grasping in an adjacent location where no object was present, and 4) pantomimed reaching toward an adjacent location. As expected, in the anterior intraparietal area, there was significantly higher activation during real grasping than that during real reaching. However, the activation difference between pantomimed grasping and pantomimed reaching did not reach statistical significance. There was also no effect of pantomimed grasping within the ventral stream, including an object-selective area in the lateral occipital cortex. Instead, we found that pantomimed grasping was mediated by right-hemisphere activation, particularly the right parietal cortex. These results suggest that areas typically invoked by real actions may not necessarily be driven by “fake” actions. Moreover, pantomimed grasping may not tap object-related areas within the ventral stream, but rather may rely on mechanisms within the right hemisphere that are recruited by artificial and less practiced actions.

INTRODUCTION

Studying real actions with the use of functional magnetic resonance imaging can be a challenge: large-amplitude movements of the hand create artifacts in the functional magnetic resonance imaging (fMRI) signal arising from distortion of the magnetic field (Culham et al. 2003) and direct viewing of real three-dimensional (3D) objects is often impossible because of the small diameter of the magnet bore. Even if all of the challenges are overcome (e.g., Culham et al. 2003, 2006), many common objects—such as tools and utensils—cannot be used in the imaging studies because they often consist of metallic parts. Consequently, early studies on neural basis of reaching and grasping simply used imagined actions (e.g., Decety et al. 1994; Grafton et al. 1996). Although considerable progress has been made since and simple grasping movements

can be successfully studied with fMRI (e.g., Binkofski et al. 1998; Culham et al. 2003), some researchers still use pantomimed actions for studies of grasping (Shikata et al. 2003; Simon et al. 2002) and tool use (e.g., Choi et al. 2001; Frey et al. 2005; Moll et al. 2000; Ohgami et al. 2004; Rumiati et al. 2004).

Importantly, the use of pantomimed tasks in the fMRI environment is based on the assumption that exactly the same neural mechanisms underlie real and pantomimed actions. However, based on observations that apraxic patients' capacity to pantomime object and tool use correlates well with their ability to use real objects and tools (De Renzi and Lucchelli 1988; Goldenberg and Hagmann 1998), this assumption has never been directly tested. Therefore we investigated whether pantomimed and real actions are mediated by the same neural mechanisms.

Contrary to the assumption that pantomimed actions are a valid proxy for real actions, behavioral and neuropsychological studies suggest that pantomimed actions and genuine actions may in fact tap different systems. For example, the behavioral kinematics of real grasping of 3D objects differ from pantomimed (spatially displaced) grasping in a location beside the object, as well as delayed (temporally displaced) grasping of a real object several seconds after viewing it (e.g., Westwood et al. 2000, 2001). Of course, in the latter two cases the action must be performed on the transformed and/or remembered representation of the object rather than on the object itself. Therefore the hand typically opens gradually to the maximum object size with little subsequent closure (observed after much wider finger aperture in real grasping) and the maximum opening of the hand is often distorted by the presence of other objects viewed earlier in the scene (Hu and Goodale 2000; Hu et al. 1999). Together, these differences indirectly suggest that real and fake grasping movements may in fact tap different neural mechanisms.

More direct evidence indicating that real and pantomimed grasping may be mediated by disparate neural systems and mechanisms comes from neurological patients: D.F., with visual form agnosia (Goodale et al. 1991, 1994), and I.G., with optic ataxia (Milner et al. 2001). D.F., for example, shows quite normal hand preshaping when she grasps real objects of different dimensions, even though her ability to discriminate between objects is profoundly impaired. Her performance is considerably worse, though, when she is asked to pantomime grasping movements beside a presented object or grasp an

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object after a delay. In such cases, D.F.'s anticipatory hand preshaping is then highly variable and poorly correlates with the real size of the object (Goodale et al. 1994). In short, D.F. is capable of performing real grasping as well as normal participants, but her pantomimed and delayed grasping is appreciably worse. In sharp contrast to D.F., patient I.G. is seriously impaired in real grasping, but shows a paradoxical improvement in pantomimed and delayed grasping (Milner et al. 2001).

These two cases, along with others (e.g., A.T., cf. Milner et al. 1999; see also Jeannerod et al. 1994), indicate that fake actions may involve different brain mechanisms than real actions and may in fact depend on structures that are damaged in D.F. This clear behavioral dissociation is consistent with the theoretical distinction between vision-for-perception and vision-for-action (Goodale and Milner 1992) attributed to the two visual streams—ventral and dorsal, respectively—identified earlier in the primate brain (Ungerleider and Mishkin 1982). In accordance with this model, pantomimed grasping may actually depend more on the ventral mechanisms involved in forming the perceptual representations of objects (see Goodale and Milner 1992, 2004; Milner and Goodale 1995). However, on the basis of new evidence that the dorsal stream may in fact be functionally subdivided into 1) the dorsodorsal pathway, for on-line control of actions, and 2) the ventrodorsal pathway, for motor control, action understanding, and perception of space (Rizzolatti and Matelli 2003), one may also expect some ventrodorsal contributions to pantomimed grasping.

The advent of fMRI has identified specific functional brain areas within the dorsal and ventral streams that may account for D.F.'s behavioral results. Real grasping of objects requires intact processing within one key area of the dorsal stream: the anterior intraparietal sulcus, area AIP (Binkofski et al. 1998). AIP is typically identified by contrasting brain activation for grasping with that for reaching movements of the hand (Binkofski et al. 1998, 1999; Culham et al. 2003; Frey et al. 2005). D.F.'s AIP is indeed spared and is activated during grasping, as it is in neurologically intact participants. More important, her lesions show remarkable overlap with areas in the lateral occipital cortex (LOC), as identified in neurologically intact participants (James et al. 2003). LOC is typically activated by the presentation of intact versus scrambled images of objects (Malach et al. 1995) and seems to play a major role in object recognition by integrating different visual features into coherent object representations (Grill-Spector et al. 2001). Thus the damage to LOC in D.F. not only accounts for her agnosia but could also explain her impaired performance with pantomimed and delayed grasping. Consistent with this hypothesis, Singhal et al. (2005) demonstrated that LOC is reactivated when participants grasp, but also reach toward an object, after a delay, even though no visual stimulus is present and the action is based on object features derived from memory.

Inspired by these results, we investigated whether areas typically invoked by real actions, such as AIP (and related networks) and/or LOC, would play any role during pantomimed grasping movements. Based on several previous studies from our group (Culham et al. 2003; for review see Culham et al. 2006) and others (Binkofski et al. 1998, 1999; Frey et al. 2005), we know that real grasping as opposed to real reaching

should activate dorsal stream areas, including AIP bilaterally. However, relatively little is known about the neural correlates of pantomimed grasping because the studies to date focused either exclusively on pantomimed tool use (e.g., Choi et al. 2001; Frey et al. 2005; Moll et al. 2000; Ohgami et al. 2004; Rumiati et al. 2004) or pantomimed and/or observed gestures (Fridman et al. 2006; Gallagher and Frith 2004; Lotze et al. 2006; Muhlau et al. 2005). Sporadically, when pantomimed grasping was studied, it was used instead of real grasping (Shikata et al. 2003; Simon et al. 2002) to minimize difficulties of studying real goal-directed actions in the scanner (Culham et al. 2006). As a result, there was never any direct comparison of activation during pantomimed grasping, real grasping, and their control conditions such as pantomimed and real reaching, respectively (cf. Grezes et al. 2003a,b). This is why we were interested to know whether these same areas would be activated to a similar degree during pantomimed and real grasping. Even though the literature on pantomimed tool use would indicate otherwise, based on the case of D.F., we hypothesized that LOC would be more activated during pantomimed grasping than pantomimed reaching because pantomimed grasping would rely on a stored representation of object shape.

METHODS

Participants

Five males and five females, ranging in age from 22 to 32 yr (mean age = 27 yr) participated in this study and were compensated financially for their time. Participants were right-handed and had normal or corrected-to-normal visual acuity. Before testing, they gave their informed consent. All ten participants were tested at least with four functional runs and one anatomical scan. The experiment was approved by The Health Sciences Research Ethics Board at the University of Western Ontario and was carried out in accordance with the principles of the 1964 Helsinki Declaration.

Apparatus, stimuli, and viewing conditions

A metal-free device called the "grasparatus" was used to present 3D stimuli inside an fMRI scanner (for further details see Culham 2004; Culham et al. 2003). The grasparatus consists of an octagonal rotatable drum on which an object can be placed in one of four different locations along each of the drum faces. Eight 3D rectangular blocks, made of white translucent plastic, with a constant width (1.6 cm) and depth (0.6 cm), but with varying length (from 1.6 to 5 cm), were used. One object of variable size, chosen at random, was put on each of the eight faces of the drum, just left of the center, with the only restriction that its orientation (either vertical or oblique) was such that it could be comfortably grasped with a precision grip. The grasparatus was set nearly 10 cm above the participant's pelvis and thus the objects were within a natural grasping distance. Importantly, because participants laid supine with the torso and head tilted at an angle of around 30°, the front face of the grasparatus and, as a result, the presented objects could be seen directly without a mirror.

Because testing took place in complete darkness, the presented object was flashed briefly (for 150 ms) with a superbright red light-emitting diode (LED, 12 cd/m²) located inside the drum of the grasparatus, just beneath its front surface. Before each trial, the drum was rotated to the subsequent face with a computer-controlled pneumatic system. Throughout the experiment, participants were asked to look at LEDs mounted on the ceiling of the magnet bore that served as fixation points and cues for the upcoming task (see following text). The LEDs were masked by a 0.1° aperture and were positioned nearly 10° of visual angle above the grasparatus. The positioning of the

fixation LEDs placed the stimuli in the participant's lower visual field, a typical configuration for everyday interactions with objects. Importantly, it prevented the eye strain that would occur with continual gazing downward in the direction of the grasparatus. The color of the fixation LEDs indicated the task to be performed on a given trial (for further details, see *Task procedures*).

To minimize head motion caused by the reach-to-grasp movement, the participant's right upper arm was supported and restrained by a hemicylindrical arm brace, tied with Velcro straps. The arm brace entirely immobilized the shoulder, allowing a limited motion at the elbow—enough to move the hand from the starting position around the navel toward the stimuli—but did not limit the motion of the wrist. Thus any object presented on the front face of the grasparatus could be reached toward and/or grasped quite comfortably. All the hardware (e.g., a pneumatic piston rotating the drum of the grasparatus, LEDs) and the software (VisionShell) were controlled by a Macintosh G4 computer, which at the beginning of each trial received a trigger from the computer controlling the acquisition of the functional data by the MRI scanner.

Task procedures

We used a slow event-related design with trials spaced every 18 s to allow a hemodynamic signal to return to baseline between events. Each trial began with a brief illumination of the object for 150 ms. Before target illumination, a colored fixation point indicated for 16 s which of the tasks a participant was to perform on the upcoming trial (see Fig. 1). When the fixation point was green, the participant grasped the object with the index finger and thumb along its long axis. When the fixation point was red, the participant's task was to reach toward the object and touch it with the knuckles, without preshaping the hand. Because the objects were firmly attached to the drum, they could not be lifted on the grasping trials, and thus movement durations were comparable for grasping and reaching trials (Cavina-Pratesi, Goodale, and Culham, unpublished observations). When the fixation point was blue, a participant pantomimed the grasping movement. In

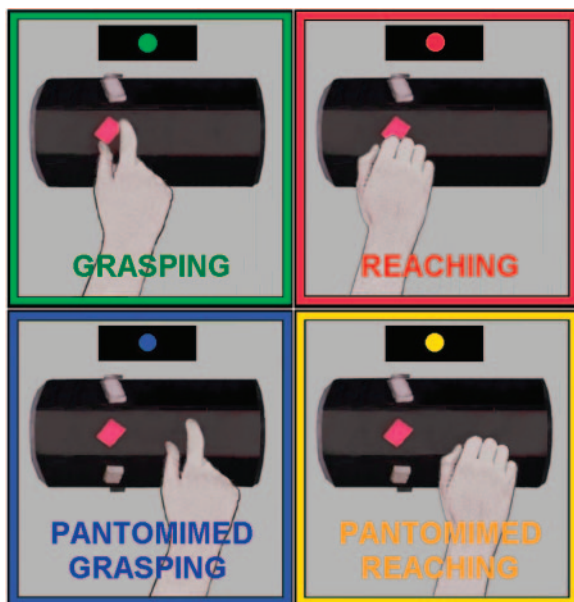


FIG. 1. Display, stimuli, and the different conditions used in the study. After the object on the front surface of the grasparatus was illuminated by an underlying ultrabright red light, the participant performed a task associated with the color of the fixation point (as shown in the picture). Grasparatus with the objects and a fixation point are shown from the participant's perspective. Except for the brief illumination of the object (150 ms), trials were performed in darkness.

such a case, the index finger and thumb were to be scaled to the size of the object and the wrist adjusted according to object orientation, but, instead, the fingers touched the surface of the drum in an adjacent location, approximately 8 cm to the right of the target object. When the fixation point was yellow, the task was to pantomime the reaching movement by adjusting the wrist according to the object orientation, but touching the nearby surface to the right of the object with the knuckles only.

In addition, in the last six of ten participants, a passive viewing condition was added. The participant passively viewed the presented object when two LEDs—blue and red—were lit simultaneously. This was done to make it easier to identify AIP because AIP, unlike S1, responds to visual stimuli. (The passive viewing condition is not shown in the graphs because it was examined only in a subset of participants.)

In the functional runs, each of the tasks (grasping, reaching, pantomimed grasping, pantomimed reaching, and, if present, passive viewing) was repeated five times in a pseudorandom order, constrained such that these trial types were fairly evenly distributed through the run. The only exceptions to the number of trial repetitions were on a few occasions when, because of technical difficulties, the run was prematurely aborted by the scanner and as a result consisted of only four repetitions of each trial. Each participant was typically tested on average with six runs (not fewer than four). Four different orders of trials within runs were established and participants received each run order at least once in a random sequence. Participants who completed more than four runs had some of the orders repeated once.

Imaging parameters

A 4-Tesla whole body MRI scanner (Varian, Palo Alto, CA; Siemens, Erlangen, Germany) at the Robarts Research Institute (London, Ontario, Canada) was used to perform the imaging. In all experiments, a transmit–receive, cylindrical birdcage radiofrequency head coil was used. In addition to functional runs, each session also consisted of a high-resolution anatomical scan. Functional volumes sensitive to the blood oxygenation level–dependent (BOLD) signal (see Ogawa et al. 1992) were collected using an optimized, T2*-weighted, segmented gradient echo echoplanar imaging [field of view (FOV) = 19.2 cm, with 64×64 matrix size for an in-plane resolution of 3 mm, repetition time (TR) = 1 s, with two segments/planes for a volume acquisition time of 2 s; time to echo (TE) = 15 ms, flip angle (FA) = 45°, navigator-corrected]. Depending on the size of the participant's head, each functional volume constituted 15–18 contiguous slices of 6-mm thickness (to cover the same brain areas in each participant). The slices were angled at about 30° from axial to sample occipital, parietal, posterior temporal, and posterior/superior frontal cortices. There was no gap left between the slices and their acquisition order was noninterleaved. During each experimental session, a T1-weighted anatomical reference volume was acquired along the same orientation as the functional images using a 3D acquisition sequence ($256 \times 256 \times 64$ matrix size, in-plane resolution of 0.75 mm, 3.0 mm slice thickness, TI = 600 ms, TR = 11.5 ms, TE = 5.2 ms, FA = 11°).

Data analysis

PREPROCESSING. Brain Voyager software (2000 and QX; Brain Innovation, Maastricht, The Netherlands) was used for data analysis. All the data were preprocessed with linear trend removal and temporal high-pass filtering (to remove frequencies below three cycles per run). The functional data were then superimposed on anatomical brain images transformed into Talairach space (Talairach and Tournoux 1988). We did not perform spatial smoothing on the functional data because AIP is adjacent to somatosensory areas and smoothing typically obscures the distinction, particularly in individual subjects.

Because we used multishot imaging to improve the signal-to-noise ratio, slice scan time correction was not possible.

As the result of hand movements, the distortion of the magnetic field in the form of positive and/or negative spikes $\leq 1\%$ of signal change occurred sometimes during the first two acquisition volumes at the onset of the movement (compare Birn et al. 1999; Culham 2006). Because such artifacts typically occur abruptly and without any delay, whereas true activations occur with the standard hemodynamic lag of nearly 5 s and with the characteristic hemodynamic response profile, the artifacts were eliminated by cutting out the first two volumes of every trial using Matlab v6.1 (The MathWorks, Natick, MA).

We performed numerous steps to ensure that our data were not contaminated by head motion or other artifacts. First, we viewed cine-loop animation of each functional run before any preprocessing to ensure there was no visible head motion or scanner artifacts. We also evaluated head motion using the output from Brain Voyager's motion-correction algorithm. Once the spikes arising from hand movement had been removed from the data, head motion within and between runs never exceeded 1 mm in translation and/or 1° of rotation. Although even small movements can lead to artifacts if they are correlated with the paradigm (Field et al. 2000), we found no evidence of such artifacts in the statistical maps (e.g., no rims of activation and negligible activation in white matter and ventricles). We also compared t -values and cluster sizes for motion-corrected and -uncorrected data, with no notable differences. We expect that motion correction had little effect on the data because our subjects were well immobilized and highly experienced and because motion correction works best for data acquired in block designs, not event-related designs, where task-related motion, if any, unfolds much quicker than the hemodynamic response (Oakes et al. 2005). We decided to report nonmotion-corrected data because 1) there was no evidence that motion correction improved the data; and 2) some suggested that motion correction can actually reduce data quality (Freire and Mangin 2001), particularly if there are any mass motion artifacts that may be misinterpreted as motion (Culham 2006).

REGION OF INTEREST (ROI) APPROACH. We analyzed the data using two different approaches: 1) an ROI approach and 2) a voxelwise approach. The aim of the ROI approach was to directly test whether the dorsal-stream area AIP and the ventral-stream area LOC are differentially involved in real and pantomimed grasping. The aim of the voxelwise approach was to investigate what other brain areas are active when participants perform real and pantomimed hand movements.

For ROI analyses, AIP was identified by a contrast between grasping and reaching (see Binkofski et al. 1998; Culham et al. 2003; Frey et al. 2005). LOC localizer data were made available by colleagues who had performed a separate experiment on the same set of subjects (Large et al. 2005). Their data enabled us to identify LOC in each participant. Large et al. (2005) used three runs with visual presentation of intact forms: two-dimensional line drawings of objects (animals, tools, and letters) versus their scrambled counterparts. Twelve images were presented in each 12-s epoch, at 1-s intervals, and participants performed a one-back matching task (as a control for attention). The functional activation from both our session and theirs was aligned with a high-resolution anatomical scan for each participant. ROIs for AIP and LOC were defined in each individual using a threshold no more liberal than $P < 0.005$, uncorrected.

From each ROI at the single-subject level (i.e., left and right AIP and LOC in each individual), we extracted an event-related time course and the beta weights based on a general linear model (GLM) that included the predictors, one for each condition: *Grasping*, *Pantomimed Grasping*, *Reaching*, *Pantomimed Reaching*, and *Passive Viewing* (where present). Each predictor was derived from a rectangular wave function (peak = 2-s duration; trough = 16-s intertrial interval) convolved with a standard hemodynamic response function (HRF). The HRF was shifted in time to account for cutting of the two

artifact-susceptible volumes at the start of each trial and its fit was validated by comparisons with the event-related responses across all conditions. The extracted beta weights represent an estimate of the magnitude of activation for each condition, constrained by the shape of the expected HRF. Before analysis, the data were normalized to z -scores.

To summarize the overall pattern of results, we performed independent 2×2 repeated-measures ANOVAs on the beta weights from each ROI to identify main effects for task (grasping vs. reaching) and movement type (real vs. pantomimed) and determined whether they interact. Because we also had a priori hypotheses that AIP would show significant differences between real grasping and real reaching and LOC would show significant differences between pantomimed grasping and pantomimed reaching, in addition, we conducted paired-samples t -tests between those specific conditions. One-sample t -tests were also performed to determine whether the activation for each condition was greater than the average activation during the intertrial baseline.

VOXELWISE ANALYSES OF GROUP ACTIVATION USING A RANDOM-EFFECTS MODEL. To determine whether any interesting pattern of activation for pantomimed grasping as opposed to pantomimed reaching could be found elsewhere in the brain, we performed a voxelwise random-effects analysis using a GLM (described above) across the entire group of ten subjects. Statistical activation maps for the voxelwise analysis were set to reliable threshold levels and cluster volumes ($P < 0.005$, minimum cluster size = 5 mm^3). Monte Carlo simulations (performed with AlphaSim software, courtesy of Douglas Ward, Medical College of Wisconsin) verified that the regions of interest were unlikely to have arisen by chance, given the problem of multiple comparisons.

Once significant activation clusters had been identified, we characterized the overall pattern of effects within each cluster. The pattern was summarized by performing a series of GLM contrasts on the beta weights within each cluster (using the ROI-GLM function of Brain Voyager). Specifically, we performed contrasts between real grasping and real reaching and between pantomimed grasping and pantomimed reaching. We also evaluated whether there were significant main effects and interactions for task (grasping vs. reaching) and movement type (real vs. pantomimed actions).

RESULTS

Region of interest analysis

ANTERIOR INTRAPARIETAL (AIP) AREA. Using a contrast of grasping and reaching, we first identified area AIP by selecting the focus of activation located at or near the junction of the anterior intraparietal sulcus (IPS) and the inferior segment of the postcentral sulcus (PCS), as shown in Fig. 2A. In rare cases with more than one focus around the junction, passive viewing (when available) was used as an additional criterion for defining AIP because, in contrast to primary somatosensory cortex, the response in AIP is significantly higher than the baseline for simple visual presentation of the object (Cavina-Pratesi et al., unpublished observations). We were able to identify AIP in nine of ten participants, bilaterally. In the tenth participant AIP could also be identified bilaterally, but only with a more liberal threshold, $P < 0.01$, uncorrected. Although we decided to exclude this subject from further ROI analyses for AIP, the overall pattern of results was the same regardless of whether this subject's data were included.

In most of the participants there was typically a single focus of activation at the junction of IPS and PCS in each hemisphere. The average Talairach coordinates of AIP (for details,

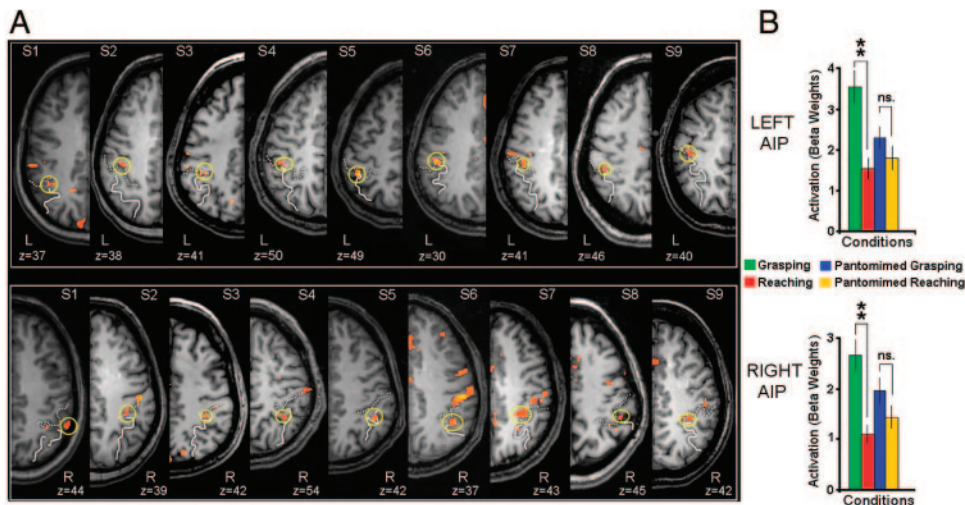


FIG. 2. Single subjects' activation maps and the average beta weights in the left and right anterior intraparietal (AIP) sulci. *A*: AIP, as localized in 9 of the 10 participants, was identified by contrasting brain activation for real grasping vs. real reaching. Left AIP (L, left) and right AIP (R, right) are shown in their most clear transverse slices for each of the 9 participants individually. In each participant, AIP (marked with yellow circle) was located at or near the junction of the anterior end of the intraparietal sulcus (plain line) and the inferior segment of the postcentral sulcus (dotted line). *B*: beta weights for the 4 visuomotor conditions clearly indicate that the activation for real grasping was higher than that for real reaching in both left and right AIP, but the activation for pantomimed grasping vs. pantomimed reaching was not and, instead, showed only a trend toward significance. Error bars depict SEs.

see Table 1) were in very good agreement with AIP coordinates from previous fMRI experiments (e.g., Binkofski et al. 1998, 1999; Culham et al. 2003; Frey et al. 2005). The average beta weights that were subsequently obtained from the active voxels identified as left and right AIP are shown in Fig. 2*B* and the relevant statistics are presented in Table 1.

Left AIP. We found that left AIP showed significantly higher activation for grasping, but only when participants performed real grasping (vs. real reaching). The area does not appear to be differentially activated during pantomimed grasping versus pantomimed reaching. In particular, a 2 (tasks) \times 2 (movement types) repeated-measures ANOVA revealed that there was a significant main effect of movement type (real vs. pantomimed) [$F(1,8) = 8.8, P < 0.05$], such that the activation for real movements was significantly higher than the activation for pantomimed movements. There was also a significant main effect of task (grasping vs. reaching) [$F(1,8) = 57, P < 0.001$], such that grasping, whether real or pantomimed, led to significantly higher activation than reaching, whether real or pantomimed. Finally, and most important, there was a significant interaction between task (grasping vs. reaching) and movement type (real vs. pantomimed) [$F(1,8) = 26, P < 0.01$]. Further post hoc comparisons (Bonferroni adjusted, $\alpha_{FW} < 0.05$) revealed that the only significant difference was in fact between the activation for real grasping as opposed to real reaching ($P < 0.001$), although there was a trend toward

significance for the contrast between pantomimed grasping and pantomimed reaching ($P > 0.08$). Because the area was defined by a contrast of grasping versus reaching, a significant difference between real grasping and real reaching would be expected. However, it is notable that the activation difference for grasping versus reaching was considerably larger for real movements than for pantomimed movements. These conclusions were further validated by the results of voxelwise contrasts (see following text).

Right AIP. Similarly to left AIP, we also found that right AIP showed significantly higher activation only for real grasping as opposed to real reaching. In other words, right AIP, like left AIP, does not appear to be differentially activated during pantomimed grasping versus pantomimed reaching. In particular, a 2 \times 2 repeated-measures ANOVA revealed that there was a significant main effect of task [$F(1,8) = 49, P < 0.001$], such that both kinds of grasping movements (real and pantomimed) led to significantly higher activation than that generated by both kinds of reaching movements (real and pantomimed). Importantly, again there was a significant interaction between task (grasping vs. reaching) and movement type (real vs. pantomimed) [$F(1,8) = 11.9, P < 0.01$]. Post hoc comparisons (Bonferroni adjusted, $\alpha_{FW} < 0.05$) revealed that the only significant difference was between the activation for real grasping as opposed to real reaching ($P < 0.001$). As with left AIP, there was also a trend toward significance when the difference

TABLE 1. *Region of interest analysis*

Region	Average Talairach Coordinates			2 \times 2 Repeated-Measures ANOVAs: Beta Weights		
	x	y	z	Task	Movement type	Interaction
				Grasping > Reaching	Real > Pantomimed	Task \times Movement type
Left AIP	-42	-36	42	$F(1,8) = 57$ $P < 0.001$	$F(1,8) = 8.8$ $P < 0.05$	$F(1,8) = 26$ $P < 0.01$
Right AIP	40	-39	43	$F(1,8) = 49$ $P < 0.001$	$F(1,8) = 5.0$ $P > 0.06$	$F(1,8) = 11.9$ $P < 0.01$
Left LO	-43	-65	-8	$F(1,9) = 0.5$ $P > 0.5$	$F(1,9) = 0.7$ $P > 0.4$	$F(1,9) = 0.2$ $P > 0.7$
Right LO	42	-69	-4	$F(1,9) = 0.4$ $P > 0.5$	$F(1,9) = 0.7$ $P > 0.4$	$F(1,9) = 0.04$ $P > 0.9$

The areas were identified with a localizer task: AIP, grasping vs. reaching; LOC, viewing intact images of objects vs. scrambled images. The average Talairach coordinates and statistics for the main effects of task and movement type, as well as their interaction, are reported.

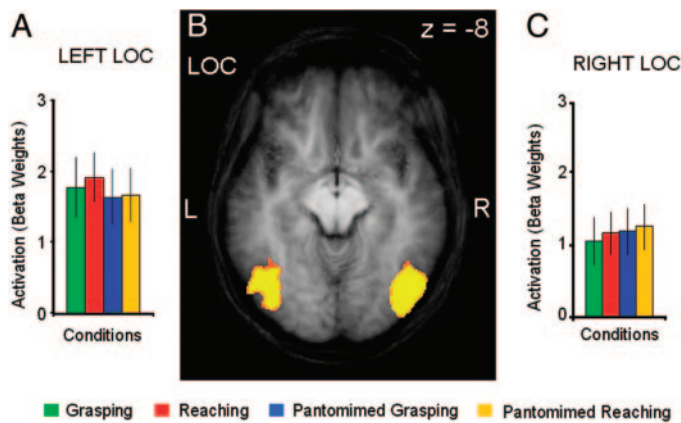


FIG. 3. Group activation maps of left and right lateral occipital cortex (LOC) (B) and their average activation in beta weights (A and C). LOC bilaterally is shown in the transverse slice of an average anatomical for all subjects. Clusters were defined separately in each individual by contrasting intact and scrambled images. Beta weights were subsequently derived separately from each individual's LOC and used for further analyses. As can be seen on the basis of the average beta weights, LOC did not show any differential activation across the 4 visuomotor tasks. Error bars depict SEs.

between activation for pantomimed grasping and pantomimed reaching was compared ($P > 0.07$). Finally, there was a trend toward a significant main effect of movement type [$F(1,8) = 5$, $P > 0.06$], such that the activation for real movements tended to be higher than the activation for pantomimed movements.

Further testing for left and right AIP. Additional testing revealed that in AIP bilaterally, in each of the four visuomotor conditions, as well as in the control passive-viewing condition, the activation was significantly greater than the baseline activity ($P < 0.001$ for real movements, $P < 0.01$ for pantomimed movements).

LATERAL OCCIPITAL CORTEX (LOC). To our surprise we found that LOC, as defined by a contrast between intact and scrambled images of objects from a separate experiment, did not show any differential activation across the four visuomotor tasks. A 2×2 repeated-measures ANOVA revealed that there was no significant effect of task, or movement type, and no significant interaction (for details, see Table 1 and Fig. 3).

A priori contrasts between grasping versus reaching as well as pantomimed grasping versus pantomimed reaching also did not reveal any significant effects [real grasping vs. real reaching: left LO $t(9) = -0.8$, $P > 0.5$; right LO $t(9) = -0.7$, $P > 0.5$; pantomimed grasping vs. pantomimed reaching: left LO $t(9) = -0.1$, $P > 0.9$; right LO $t(9) = -0.3$, $P > 0.8$].

Voxelwise analysis for group data

We carried out additional voxelwise random-effects analyses for three reasons: 1) to determine what other brain areas might be involved in real grasping, pantomimed grasping, and in pantomimed actions in general; 2) to determine whether, despite the absence of an effect of pantomiming across the whole LOC, there might be a subdivision of the complex that showed such an effect; and 3) to validate the effects in AIP that were reported at the single-subject level.

REAL GRASPING VERSUS REAL REACHING. Random-effects analysis using a contrast of real grasping versus real reaching revealed bilateral clusters of activation in the parietal cortex

(AIP), somatosensory cortex [S1, including the right superior postcentral gyrus (sPCG)], and the left and right thalamus, as well as unilateral activation in the left motor cortex (M1), the right anterior to mid IPS (amIPS), the left rostral superior temporal gyrus (rSTG), the right cerebellum, and in the right frontal cortex at the junction of the inferior frontal sulcus and precentral sulcus (IFS/PreCS). Talairach coordinates for the identified areas, their cluster sizes, and the relevant statistics for the contrasts are shown in Table 2.

In AIP, the obtained group results were indeed similar to those revealed by the single-subject analyses. Given the contrast used, both left and right AIP showed greater activation for grasping as opposed to reaching. Importantly, as measured by ROI-GLM contrasts, although in left AIP there was a significant main effect of task (grasping $>$ reaching, whether real or pantomimed, $t = 4.8$, $P < 0.001$), there was also a clear trend toward an interaction between task and movement type ($t = 1.8$, $P = 0.07$). The a priori contrasts we performed confirmed that left AIP shows greater activation for real grasping versus real reaching ($P < 0.001$), but pantomimed grasping was not significantly higher than pantomimed reaching ($P > 0.1$). In right AIP there was a main effect of task (grasping $>$ reaching, whether real or pantomimed, $t = 4.5$, $P < 0.001$; specifically, real grasping $>$ real reaching, $P < 0.001$; and pantomimed grasping $>$ pantomimed reaching, $P < 0.01$), but no interaction between task and movement type ($P > 0.3$).

Left M1, left rSTS, left and right S1, left and right thalamus, and the right frontal cortex (IFS/PreCS) all showed a significant main effect of task (grasping $>$ reaching, whether real or pantomimed) and a significant interaction between task and movement type. With the exception of left S1, the source of the interaction was such that the activation for real grasping was higher than that for real reaching, but pantomimed grasping was not higher than pantomimed reaching. For left S1 the source of interaction was different—here the activation for real grasping was significantly higher than that for pantomimed grasping, but the activation for real reaching as compared with pantomimed reaching was not. The three remaining areas—right amIPS, the right cerebellum, and right sPCG—also showed a main effect of task (grasping $>$ reaching, whether real or pantomimed), but no significant main effect of movement type and no significant interaction (for details, see Table 2).

PANTOMIMED GRASPING VERSUS PANTOMIMED REACHING. Random-effects analysis using a contrast of pantomimed grasping versus pantomimed reaching revealed activation mainly in the right hemisphere. In particular, this contrast revealed activation in several areas in the right posterior parietal cortex (PPC), that is, in the right superior parietal lobe (SPL), the supramarginal gyrus (SMG), and two clusters in mid IPS, one more anterior (amIPS) and one more posterior (pmIPS). We also found additional clusters of activation in the right supplementary motor area (SMA complex), at the temporoparietal junction (TPJ), near the right lateral superior parietooccipital sulcus (lsPO), in the right superior occipital gyrus (sOG), and in the right insula. Three more clusters were found in the left hemisphere: in the left thalamus, the left supramarginal gyrus (SMG), and the left cerebellum. Consistent with the ROI analyses, no significant activation was observed in or near AIP, as defined by the contrast of real grasping versus real reaching. No activation was found anywhere within the expected vicinity

TABLE 2. Areas significantly active for real grasping vs. real reaching, pantomimed grasping vs. pantomimed reaching, and pantomimed actions vs. real actions

Region	Talairach Coordinates			Volume, mm ³	Significance of Contrasts: <i>P</i> Values				
	x	y	z		G > R	PG > PR	GM > RM	PA > RA	T × MT
<i>A. Grasping–Reaching: t(9) = 3.6, P < 0.005</i>									
Left AIP	−47	−34	37	38	0.001	0.100	0.001	0.600	0.070
Left MI	−36	−30	60	87	0.001	0.400	0.001	0.300	0.010
Left rSTG	−66	−26	11	37	0.001	0.400	0.010	0.400	0.001
Left S1	−45	−26	42	77	0.001	0.001	0.001	0.001*	0.010
Left thalamus	−13	−16	7	528	0.001	0.090	0.001	0.500	0.050
Right AIP	43	−37	42	103	0.001	0.010	0.001	0.400	0.300
Right amIPS	34	−43	46	61	0.001	0.010	0.001	0.500	0.200
Right cerebellum	15	−47	−17	93	0.001	0.001	0.001	0.060	0.600
Right IFS/PreCS	54	9	34	22	0.001	0.400	0.010	0.300	0.050
Right S1	40	−20	43	61	0.001	0.080	0.001	0.200	0.010
Right sPCG	33	−33	51	59	0.001	0.050	0.001	0.300	0.100
Right thalamus	9	−16	8	85	0.001	0.600	0.010	0.800	0.050
<i>B. Pantomimed Grasping–Pantomimed Reaching: t(9) = 3.6, P < 0.005</i>									
Right amIPS	33	−45	45	154	0.001	0.010	0.001	0.700	0.600
Right insula	27	0	17	98	0.300	0.010	0.010	0.200	0.300
Right lsPO	21	−72	30	53	0.600	0.050	0.070	0.300	0.200
Right pmIPS	33	−55	47	33	0.700	0.010	0.050	0.080	0.050
Right SMA complex	5	−1	52	183	0.010	0.010	0.001	0.090	0.900
Right SMG	42	−47	42	134	0.010	0.001	0.001	0.900	0.400
Right sOG	21	−83	27	39	0.010**	0.010	0.900	0.700	0.001
Right SPL	23	−48	52	56	0.800	0.001	0.050	0.050*	0.050
Right TPJ	48	−35	23	49	0.010	0.001	0.001	1.000	0.500
Left cerebellum	−15	−45	−16	94	0.200	0.001	0.001	0.500	0.100
Left SMG	−50	−48	40	15	0.050	0.010	0.001	0.400	0.800
Left thalamus	−16	−20	7	32	0.001	0.010	0.001	0.300	0.600
<i>C. Pantomimed Movement–Real Movement: t(9) = 3.6, P < 0.005</i>									
Right ITS	51	−37	−14	6	0.500	0.080	0.080	0.010	0.500
Right MTG/STS	39	−61	12	17	0.900	0.600	0.800	0.001	0.700

For each area identified with a given contrast at $t = 3.6$, $P < 0.005$, Talairach coordinates, volume (in mm³), and statistical significance (P values) for region of interest GLM contrasts are reported. G, grasp; R, reach; PG, pantomimed grasping; PR, pantomimed reaching; GM, grasping movement (whether real or pantomimed); RM, reaching movement (whether real or pantomimed); PA, pantomimed actions; RA, real actions; T × MT, task × movement type interaction. *RA > PA, **G < R.

of LOC, reaffirming the findings from the ROI analysis and confirming that no subdivisions within LOC showed differential activation during pantomimed grasping versus pantomimed reaching. Talairach coordinates for the areas identified with this contrast, their cluster sizes, and the relevant statistics for the contrasts are also presented in Table 2.

Notably, the contrast between pantomimed grasping versus pantomimed reaching revealed a number of clusters in the right PPC. Although these areas were posterior to those found earlier with a contrast of real grasping versus real reaching, as can be seen in Fig. 4, sometimes there was clearly some degree of overlap (e.g., amIPS).

Closer inspection of the PPC areas identified by contrasting pantomimed grasping and pantomimed reaching showed that the overall pattern of activation within adjacent clusters could be different; thus each cluster is presented separately. In the right amIPS and right SMG there was a significantly greater activation when participants performed both real and pantomimed grasping compared with when participants simply reached toward the target, whether with real or pantomimed movement. In contrast, right pmIPS and right SPL also showed a significant interaction between task and movement type, such that only pantomimed grasping was higher than pantomimed reaching, but real grasping was not higher than real reaching.

Interestingly, outside the parietal cortex in the right SMA complex, as well as in right TPJ, the activation pattern was similar to that found in amIPS and SMG, such that there was again a significantly greater activation for grasping (whether real or pantomimed) compared with reaching, irrespective of movement type (for details, see Fig. 5).

Interestingly, the right insula was the only area that showed a clear pattern in which the activation seemed to be highest in pantomimed grasping compared with the other three actions. Further post hoc contrasts, however, revealed that the difference between pantomimed grasping and real grasping just missed the significance level ($P = 0.05$ with one-tailed test). For two other areas identified with this contrast, the activation patterns were less straightforward to interpret. Right sOG showed a significant interaction between task and movement type, such that pantomimed grasping led to significantly higher activation than pantomimed reaching, but real grasping showed significantly lower activation than reaching. A closer inspection of the time course revealed, however, that this effect was primarily driven by a much less stable baseline than that observed in the other areas. Surprisingly, although the cluster in lsPO was properly revealed by this contrast—pantomimed grasping was higher than pantomimed reaching—there were neither significant main effects (i.e., task or movement type)

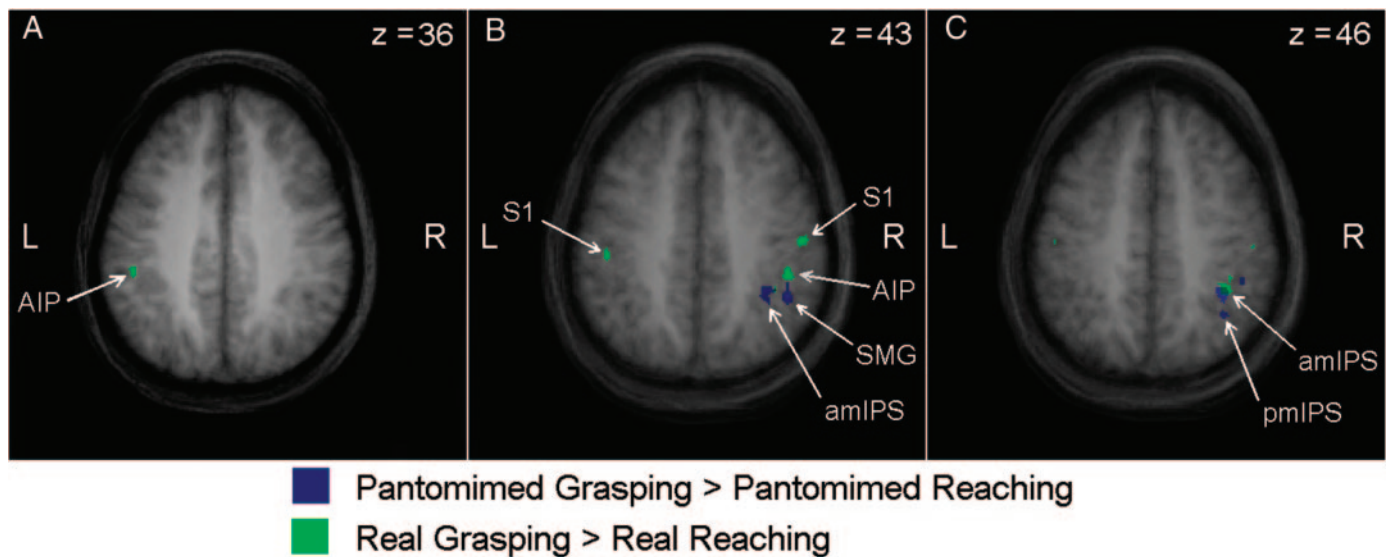


FIG. 4. Comparison of pantomimed grasping vs. pantomimed reaching (shown in blue) and real grasping vs. real reaching (shown in green). Activations for the 2 contrasts are rendered on 3 axial slices of an average anatomical for all subjects. Although pantomimed and real grasping are mediated by different neural systems (as shown in *A* and *B*), the 2 systems partially overlap in the right hemisphere. This is evident in *C* for the 2 activation clusters in amIPS (identified with the 2 different contrasts). amIPS, anterior to mid intraparietal sulcus; pmIPS, posterior to mid intraparietal sulcus; S1, primary somatosensory cortex; M1, primary motor cortex; AIP, anterior intraparietal sulcus; SMG, supramarginal gyrus.

nor a significant interaction in the ROI-GLM analyses (for further details, see Table 2).

PANTOMIMED ACTIONS VERSUS REAL ACTIONS. The voxelwise random effects comparison of pantomimed actions versus real actions revealed activation only in the temporal lobe of the right hemisphere. In fact, there were only two foci of activation. The most pronounced cluster of activation was located caudally in the middle temporal gyrus (MTG), but extending to the superior temporal sulcus (STS). In addition, there was a much smaller cluster in inferior temporal sulcus (ITS). Given the contrast used to identify these areas, both of them showed greater response only when participants performed pantomimed movements, as opposed to real movements, irrespective of whether the movements involved grasping or reaching [main effect of movement type, (MTG/STS) $t = 4.5$, $P < 0.001$, and (ITS) $t = 2.7$, $P < 0.01$; for further details, see Table 2 and Fig. 6].

DISCUSSION

In the current study we found compelling evidence that real and pantomimed grasping movements are in fact mediated by different though partially overlapping neural systems. Consistent with prior studies, bilateral AIP was activated more during real grasping than during pantomimed grasping. However, no differences were observed in LOC. Instead, we found that pantomimed grasping invokes activation mainly in several areas in the right posterior parietal lobe, as well as in some other areas in the right hemisphere. In addition, pantomimed actions in general recruited areas in the temporal lobe, again lateralized to the right side.

Areas with greater involvement in real grasping (vs. real reaching) than in pantomimed grasping (vs. pantomimed reaching)

Using a contrast of real grasping versus real reaching in an ROI and voxelwise approach, we aimed to identify areas in the

brain that are implicated in computing the information about object features for target-directed grasping. We found that within AIP, the difference between grasping and reaching is considerably stronger for real actions than for pantomimed actions. We also identified a host of other areas, including left M1, S1, the thalamus, the right cerebellum, and the right IPS, which were previously implicated in visuomotor, motor, and somatosensory processing (Binkofski et al. 1998, 1999; Culham et al. 2003; Frey et al. 2005; Handy et al. 2006; James et al. 2003; Tunik et al. 2005; Cavina-Pratesi et al., unpublished observations).

Our finding—that AIP is much more strongly active during real grasping than during pantomimed grasping—fits growing evidence that AIP predominantly represents the goal of a purposeful action. For example, since the seminal investigations of posterior parietal cortex by Mountcastle et al. (1975), it was established that some neurons in IPS are active only if the hand is moved toward the target object, but not during random movements of the hand. Fogassi et al. (2005) recently demonstrated that, in inferior parietal lobe, neurons coding for grasping movements can be influenced by the end goal of the action (bringing the object to the mouth vs. placing the object in a container). Moreover, in humans, Hamilton and Grafton (2006) demonstrated that anterior IPS encodes the goal of grasping rather than specifics such as the trajectory of hand movement. Our results further suggest that object acquisition may be critical to AIP activation and that pretend actions toward empty space do not suffice to drive AIP to its fullest (but cf. Shikata et al. 2003; Simon et al. 2002).

Of course, AIP does not contribute to real grasping movements in isolation. It joins forces with a host of other areas, such as left M1, S1, and the thalamus bilaterally, the right cerebellum, and the right anterior to mid IPS. Many of these areas were reported in previous studies of real grasping from our lab (Culham et al. 2003; Cavina-Pratesi et al., unpublished observations). Moreover, we found increased activation in

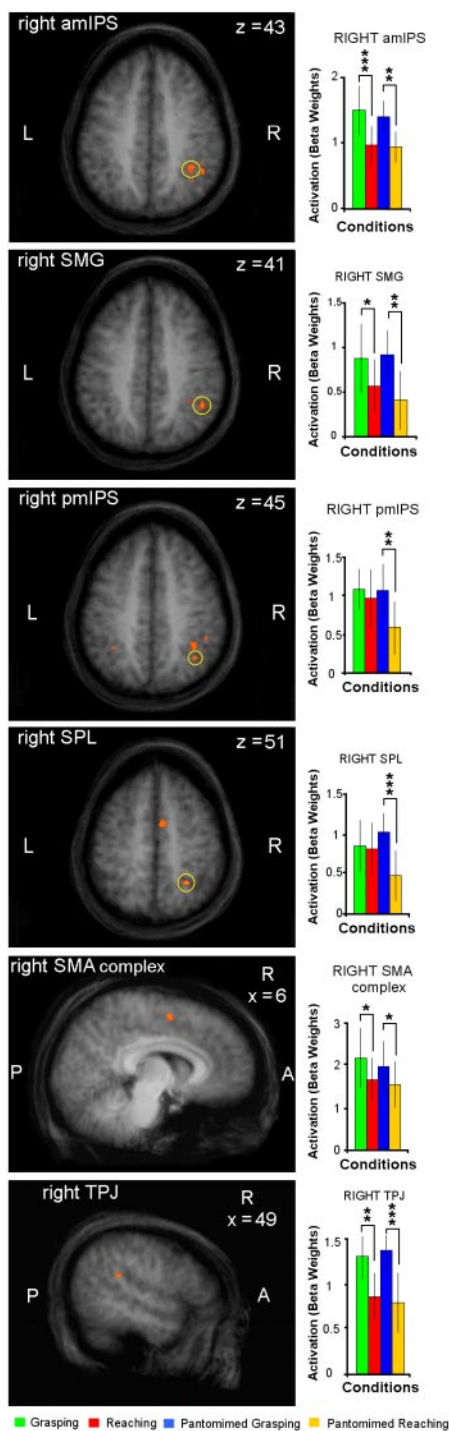


FIG. 5. Activation for pantomimed grasping (vs. pantomimed reaching) within the right hemisphere. Activation maps produced by a contrast of pantomimed grasping vs. pantomimed reaching are shown on axial or parasagittal slices through the group-averaged anatomical, along with the average beta weights extracted from each area. All 6 areas shown were activated only in the right hemisphere: amIPS, SMG, pmIPS, SPL, SMA complex (supplementary and presupplementary motor area), and TPJ (temporoparietal junction). All 6 areas showed a main effect of task (grasping > reaching, whether real or pantomimed). However, pmIPS and SPL also had a significant “task \times movement type interaction” in which greater activation was observed for pantomimed grasping than for pantomimed reaching, although no significant differences were observed between real grasping and real reaching. Error bars depict SEs.

right IFS/PreCS (close to pars opercularis) and in left STG, areas that were previously implicated in representing imagined actions, some aspects of the goal of action during observation of depicted hand–object interactions, as well as semantic information on manipulable objects, respectively (Grafton et al. 1996; Johnson-Frey et al. 2003, 2005). These areas, like AIP, respond more to real grasping than to pantomimed grasping. In some cases, such as M1 and S1, this may be attributable to differential control or stimulation of the fingers.

No effects of pantomiming or grasping in LOC

Comparable levels of activation in LOC were observed across all our visuomotor conditions in both ROI and voxel-wise analyses. Based on previous studies (Culham et al. 2003; Cavina-Pratesi et al., unpublished observations), we had expected that LOC would be equally active during real grasping and real reaching. However, on the basis of behavioral and neuroimaging experiments with patient D.F. (Goodale et al. 1994; James et al. 2003), we had expected greater activation in LOC during pantomimed grasping than during pantomimed reaching because spatially displaced pantomimed grasping may depend more on the perceptual representation of the object. This was not the case. Because the objects were shown briefly in all conditions, the visual perception of object might have been enough to elicit equal LOC activity irrespective of the action task performed. It is also possible that LOC would be more differentially activated by pantomimed grasping if common objects and/or tools were used. Perhaps with more realistic objects and different tasks and contrasts we would also have seen activation in a few more object-selective areas of the ventral stream. With our visuomotor tasks performed in the context of simple rectangular blocks, however, we were able to demonstrate only that other areas, particularly in the right posterior parietal cortex, may be critical to the performance of pantomimed grasping.

Areas involved in grasping (vs. reaching) for both real and pantomimed movements

Using a contrast of pantomimed grasping versus pantomimed reaching, we identified a few areas in which activation was higher for grasping tasks across both real and pantomimed actions. These included two parietal areas, amIPS and SMG, as well as several other regions. Unlike amIPS, the right SMG was previously linked not only to grasping but also to object discrimination (Cavina-Pratesi et al., unpublished observations). Thus it is likely that right SMG plays a general role in the processing of object contours regardless of the end goal of that processing. In contrast, in the right IPS, grasp-related activation—that typically extends further posterior than in the left—may be less goal dependent in that it responds to pretend as well as real grasping. Importantly, studies that use pantomimed grasping as a localizer (e.g., Shikata et al. 2003; Simon et al. 2002) may in fact be selecting amIPS rather than AIP-proper, particularly in group analyses with spatial smoothing where the distinction would be lost.

The involvement of the right SMA complex in pantomimed grasping is not surprising because SMA and pre-SMA were previously shown to play a role in the preparation and sequencing of voluntary movements and sensorimotor associations,

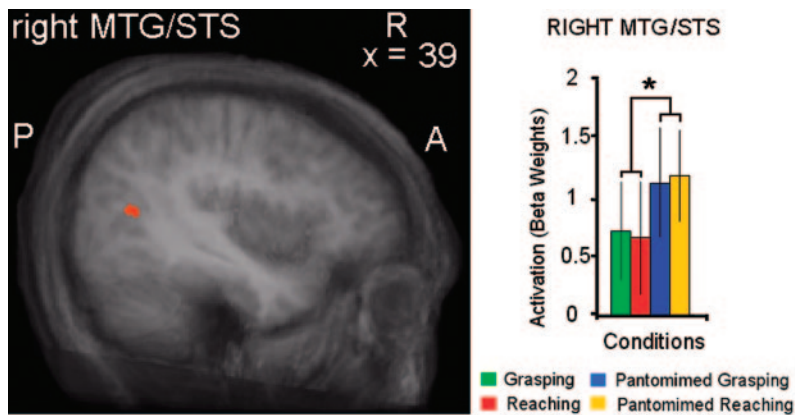


FIG. 6. Activation for pantomimed movements compared with real movements. Activation produced by a contrast of pantomimed actions (both pantomimed grasping and pantomimed reaching) vs. real actions (both real grasping and real reaching) is shown on a parasagittal slice through the group-averaged anatomical, along with the beta weights from the focus. Cluster is located caudally in the middle temporal gyrus, but extends to the superior temporal sulcus (MTG/STS). Given the contrast used to identify the region, it is not surprising that there was a main effect of movement type such that the activation for pantomimed actions was significantly higher than that for real actions. Error bars depict SEs.

respectively (for a review see Picard and Strick 2001), grasping (Ehrsson et al. 2000; Kuhtz-Buschbeck et al. 2001), and tasks that are not well rehearsed (cf. Paz et al. 2005).

Using a contrast of pantomimed grasping versus pantomimed reaching, we also found activation near the right temporoparietal junction. TPJ was previously linked to the voluntary processes of orienting and reorienting attention toward visual target locations (Corbetta et al. 2000). In fact, TPJ is thought to enable the parietofrontal attention system to control a variety of different actions in response to the same stimulus (Astafiev et al. 2006). Perhaps TPJ was activated by both real and pantomimed grasping because grasping requires attentional selection of one set of finger positions among multiple possibilities.

Areas activated during pantomimed grasping (vs. pantomimed reaching) but not real grasping (vs. real reaching)

Several brain areas, identified with a contrast of pantomimed grasping versus pantomimed reaching, demonstrated a significant interaction between task (grasping/reaching) and movement type (real/pantomimed), such that there was a significant difference between pantomimed grasping versus pantomimed reaching but not between real grasping versus real reaching. Although such a pattern could suggest that these areas are the real neural substrate of pantomimed grasping, a closer inspection of the data suggests otherwise.

Notably, the right insula showed a pattern in which, at first glance, the activation seemed to be highest in pantomimed grasping compared with the other three actions. Activation in the insula was previously observed in our lab (James et al. 2003) during both reaching and grasping with the right hand versus intertrial interval. However, this area was also linked to object representation and even action observation (e.g., Chao and Martin 2000). It is tempting to speculate, then, that the right insula may play an important role in perception and awareness of the hand and/or finger position with respect to the target object. The observed pattern of activation also suggests that this may be particularly important during pretend grasping.

Other areas—right pmIPS, right SPL and left lsPO—showed comparable activation for pantomimed grasping, real grasping, and real reaching, all of which were higher than pantomimed reaching. SPL and posterior parts of IPS have been often linked with the control of reaching movements but, most interestingly, the lsPO area is in the vicinity of a focus of activation found in

studies of pointing and reaching (Connolly et al. 2003; Pellijeff et al. 2006; Prado et al. 2005). One possible explanation of the effect observed here is that pantomimed reaching was more stereotyped and less object dependent than the other three types of movements and, as a result, associated with less activation in and/or near reach-related areas (such as lsPO).

Areas more activated during pantomimed actions than real actions

Interestingly, with a contrast of pantomimed actions versus real actions we found activation in an area superior to right LOC. Based on its coordinates, the area overlapped with both the right medial temporal gyrus (MTG) and superior temporal sulcus (STS). Activation in this general vicinity was previously reported in studies of the perception of body movements (for a review see Allison et al. 2000). Importantly, such activation was also observed in studies of hand actions (Astafiev et al. 2004). It may be that, in our study, activation in right MTG/STS reflects the fact that participants focus more on their own arm movements when pantomiming actions to an unnatural location. It is also possible that having subjects respond to the side of the goal object may recruit right MTG/STS mechanisms for the requisite spatial transformations and/or reprogramming of movement kinematics.

Comparisons of pantomimed grasping versus pantomimed gestures

Prior studies of pantomimed actions mostly reported left hemisphere activation; yet, here we found predominantly right hemisphere activation for pantomimed grasping. The majority of recent reports on pantomimed actions used either pretend (or imagined) tool use or gestures (involving the so-called praxis system) and found activation in the left hemisphere, that is, the intraparietal cortex, dorsolateral frontal cortex, and/or ventral premotor cortex (e.g., Frey et al. 2005; Moll et al. 2000; Ohgami et al. 2004; Rumiati et al. 2004). These results are consistent with the findings that patients with left hemisphere damage can experience apraxia, a deficit in skilled, purposeful movements. However, in these praxis tasks, such as pretend tool use, participants must rely on the memory of skilled actions that are appropriate for a given functional object. Such memory and/or the sensorimotor transformations of object affordances to skilled actions were previously shown to depend on the left parietal cortex (Rumiati et al. 2004). In contrast, our

pantomimed grasping task was performed shortly after the presentation of a meaningless rectangular block and thus did not require either long-term memory or object-based associations. Moreover, less familiar or meaningless movements were linked closer to the right hemisphere processing (e.g., in the right parietooccipital junction; Rumiati et al. 2005) and the ability to solve and perform multistep sequences of action, as opposed to simple object directed action, was shown to be sensitive to the damage of the right hemisphere (Hartmann et al. 2005). Indeed, the pantomimed tasks in our experiment are not that natural in everyday life and are thus less familiar. Their performance, no doubt, requires additional spatial transformations and/or reprogramming of movement kinematics. This probably explains why pantomimed grasping (and to a certain degree, pantomimed reaching) would depend on the right-hemisphere processing.

Interestingly, early studies of apraxia found that patients with left hemisphere damage performed better when the actual object was present (Liepmann 1905, 1920; cited in Rapcsak et al. 1993), suggesting that the left hemisphere may be relatively better at automatic, skilled, and more symbolic actions, whereas the right hemisphere may be relatively better at actions requiring explicit and more deliberate processing of the visual target (see also Rapcsak et al. 1993). In other words, pantomiming based on the presence of a real object may invoke different mechanisms than pantomiming based on associations invoked by an imagined object.

In sum, studies of praxis often involve real or imagined actions toward tools; and tool-related activation is invariably heavily left lateralized. In contrast, the objects presented to our participants were simple geometric shapes with no learned functional associations and the required action was not object directed; thus we would not have predicted left lateralization.

Intriguingly, recent evidence (Gonzalez et al. 2006a,b) also led to a proposal that within the dorsal stream, only the left hemisphere is specialized for the control of skilled and natural actions. When the movements are unnatural (as with the left hand or an awkward right-hand grasp) and require greater cognitive control, other mechanisms are invoked, i.e., the ventral stream. Our results suggest that in one type of unnatural movement—pantomimed grasping—it may be the right dorsal stream that is recruited rather than the ventral stream.

Why does D.F. have problems with pantomimed grasping?

Given the extent of the right temporal lesion in D.F. (James et al. 2003), it is quite possible that her damage either partially includes MTG/STS or that it disconnects that area (or ITS) from other parts of the network involved in pantomimed actions. If this is so, this could account to some extent for D.F.'s impaired pantomimed grasping. It is also possible that the information about object shape processed in LOC is needed for pantomimed grasping, but that the extraction of this information does not lead to an increased BOLD signal, as measured by fMRI. This could occur if LOC activation were at ceiling, though we believe this is unlikely with an event-related action task that would not be expected to tap LOC to its fullest. Alternatively, it could occur if LOC is necessary to provide general information about object features to another area, but the extraction of grasp-relevant information occurs in the other area (e.g., AIP) rather than LOC or does not require additional

blood oxygenation. This latter explanation is consistent with recent results by Singhal et al. (2005), who demonstrated that LOC was activated for actions after a delay, but was not differentially activated for delayed grasping and delayed reaching. Those results, along with the case of D.F., suggest that information from LOC is necessary for artificial grasping tasks, but the extraction of grasp-specific information does not differentially recruit the area.

In summary, we have found that one of the key areas involved in grasping, AIP, is activated more by real grasping (vs. real reaching) than pantomimed grasping (vs. pantomimed reaching), consistent with growing evidence that AIP represents the goal of an action. Pantomimed grasping does not appear to be related to increased activity in LOC, as we predicted; rather, it appears that numerous areas within a visuomotor circuit in the right hemisphere are involved in pantomimed grasping (vs. pantomimed reaching) to a degree similar to that of real grasping (vs. real reaching). These results, along with others from our group (Gonzalez et al. 2006a), may lead to a reconceptualization of the two-streams theory (Goodale and Milner 1992). That is, although highly skilled and automatic actions indeed recruit more the left dorsal stream (for reviews see Goodale and Milner 2004; Milner and Goodale 1995), unpracticed and deliberate actions may recruit mainly the right dorsal stream and rely more on conscious perceptual processes. A right MTG/STS area, superior to LOC, was activated more during pantomimed actions compared with real actions, and the right insula was the only area activated more by pantomimed grasping than by the other action conditions. Both areas are thought to play a role in perception and awareness of the body, which may have been more important in pantomimed actions. All in all, the outcome of our study clearly shows that fMRI can be used not only to map simple brain functions but also to test and modify prior theories about interactions between multiple brain areas.

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