NeuroImage **17,** 1693–1704 (2002)
doi:10.1006/nimg.2002.1265

Selective Activation of a Parietofrontal Circuit during Implicitly Imagined Prehension

S. H. Johnson,*'† M. Rotte,† S. T. Grafton,* H. Hinrichs,† M. S. Gazzaniga,* and H-J. Heinze†

**Center for Cognitive Neuroscience, Dartmouth College, Hanover, New Hampshire 03755-3569; and †Clinic for Neurology II, Otto-von-Guericke University, Magdeburg, Germany*

Received January 28, 2002

It is generally held that motor imagery is the internal simulation of movements involving one's own body in the absence of overt execution. Consistent with this hypothesis, results from numerous functional neuroimaging studies indicate that motor imagery activates a large variety of motor-related brain regions. However, it is unclear precisely which of these areas are involved in motor imagery per se as opposed to other planning processes that do not involve movement simulation. In an attempt to resolve this issue, we employed event-related fMRI to separate activations related to hand preparation—a task component that does not demand imagining movements—from grip selection—a component previously shown to require the internal simulation of reaching movements. Our results show that in contrast to preparation of overt actions, preparation of either hand for covert movement simulation activates a large network of motor-related areas located primarily within the left cerebral and right cerebellar hemispheres. By contrast, imagined grip selection activates a distinct parietofrontal circuit that includes the bilateral dorsal premotor cortex, contralateral intraparietal sulcus, and right superior parietal lobule. Because these areas are highly consistent with the frontoparietal reach circuit identified in monkeys, we conclude that motor imagery involves action-specific motor representations computed in parietofrontal circuits.

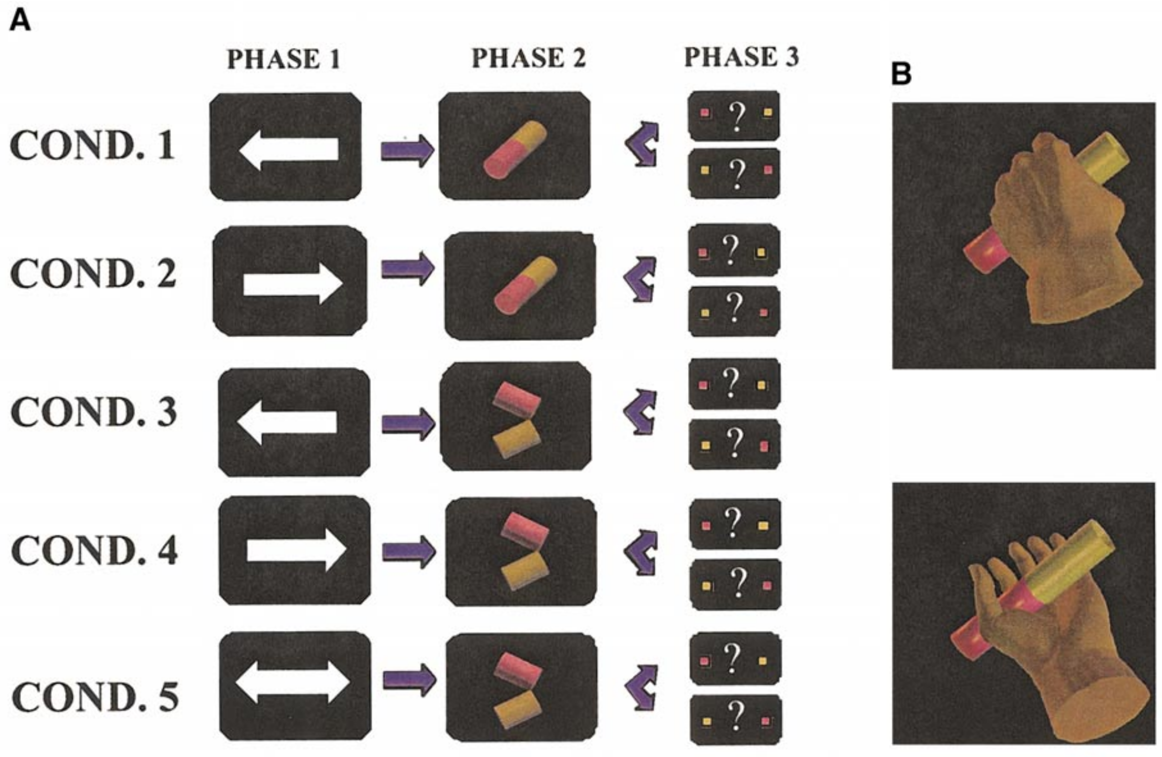
INTRODUCTION

The "imagery debate" of the last century was fueled by the question of whether representations underlying mental imagery phenomena are distinct from those involved in other cognitive processes that are not accompanied by quasi-perceptual experiences (e.g., language). Critical to this argument was the question of whether the experience of imagery involves perceptual structures despite the absence of perceptual stimulation. The advent of noninvasive neuroimaging techniques provided considerable support for this claim. For instance, visual imagery appears to involve higher level visual processing centers in the temporal lobes (Gulyas, 2001) and may also activate primary visual cortex (Klein *et al.*, 2000), while musical imagery activates regions of the temporal lobe involved in audition (Halpern, 2001; Shergill *et al.*, 2001). Furthermore, visual mental imagery of specific objects (e.g., faces) activates category-specific visual processing centers (Ishai *et al.*, 2000; O'Craven and Kanwisher, 2000). These results suggest a high degree of correspondence between representations involved in perceptual and imagery processing.

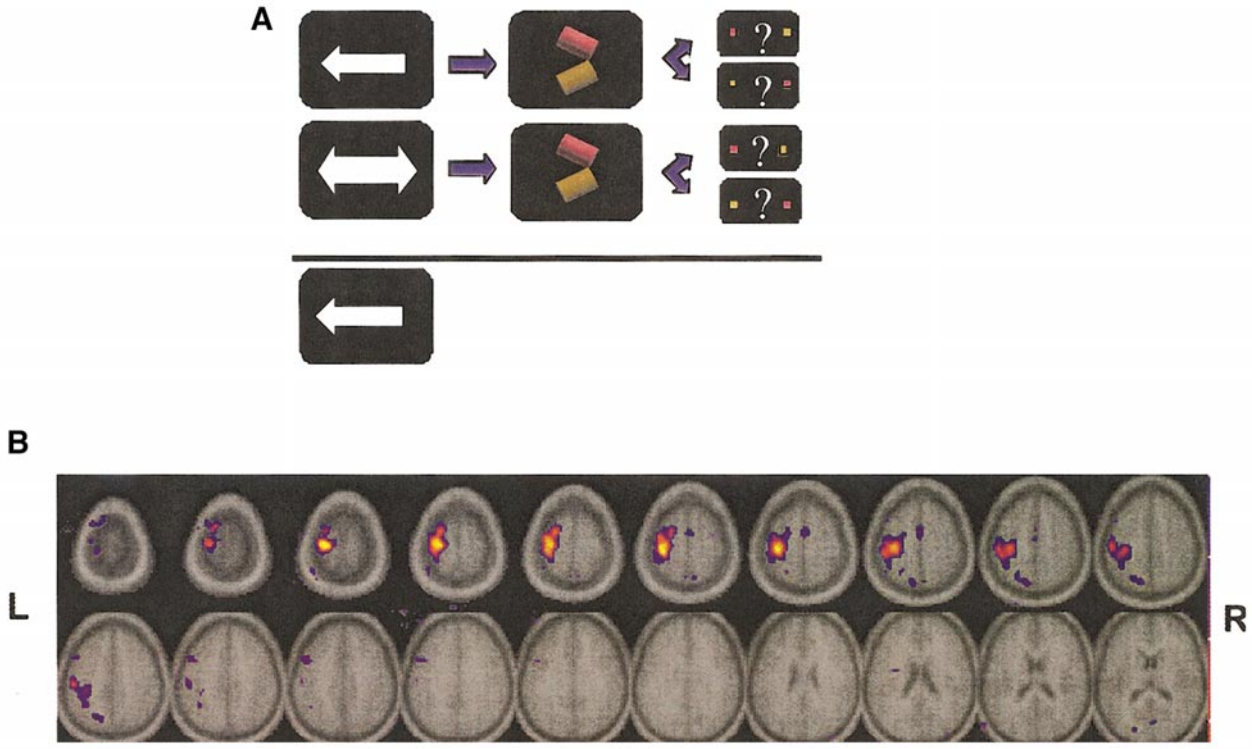
Results from over 2 decades of functional neuroimaging studies suggest an analogous relationship between motor representations and those involved in internally simulating movements of one's own body, or motor imagery. These studies indicate that motor imagery is associated with activation of a large number of motor-related areas in the brain, including supplementary (SMA) and/or premotor (PM) areas (e.g., Decety *et al.*, 1994; Gerardin *et al.*, 2000; Parsons *et al.*, 1995; Stephan *et al.*, 1995), cerebellum and basal ganglia (e.g., Decety *et al.*, 1988; Parsons *et al.*, 1995; Ryding *et al.*, 1993), posterior parietal cortex (e.g., Parsons *et al.*, 1995; Stephan *et al.*, 1995), and even primary motor cortex (Lotze *et al.*, 1999; Porro *et al.*, 1996; Richter *et al.*, 2000; Roth, 1996; Schnitzler *et al.*, 1997). The causal nature of these relationships is supported by evidence showing that lesions (Johnson, 2000a; Sirigu *et al.*, 1995, 1996) or transcranial magnetic stimulation (TMS; Fadiga *et al.*, 1999; Ganis, *et al.*, 2000) of certain brain areas involved in motor control can affect motor imagery.

Nevertheless, a number of questions regarding the precise relationship between motor imagery and motor representations remain. First, to what extent are these effects associated with motor imagery as opposed to other premovement processes that do not involve internal movement simulations (e.g., motor preparation and/or attention)? Due to reliance on block designs, previous investigations have lacked the ability to make this important distinction. For instance, Stephan *et al.* (1995) attempted to separate effects related to motor imagery from those related to preparation for *overt* joystick movements. However, as with other investigations, they did not control for processes involved in preparation of *covert*, or mentally simulated, movements. Instead, it was implicitly assumed that preparing covert and overt actions involve the same processes, which may not be so.

1053-8119/02 $35.00



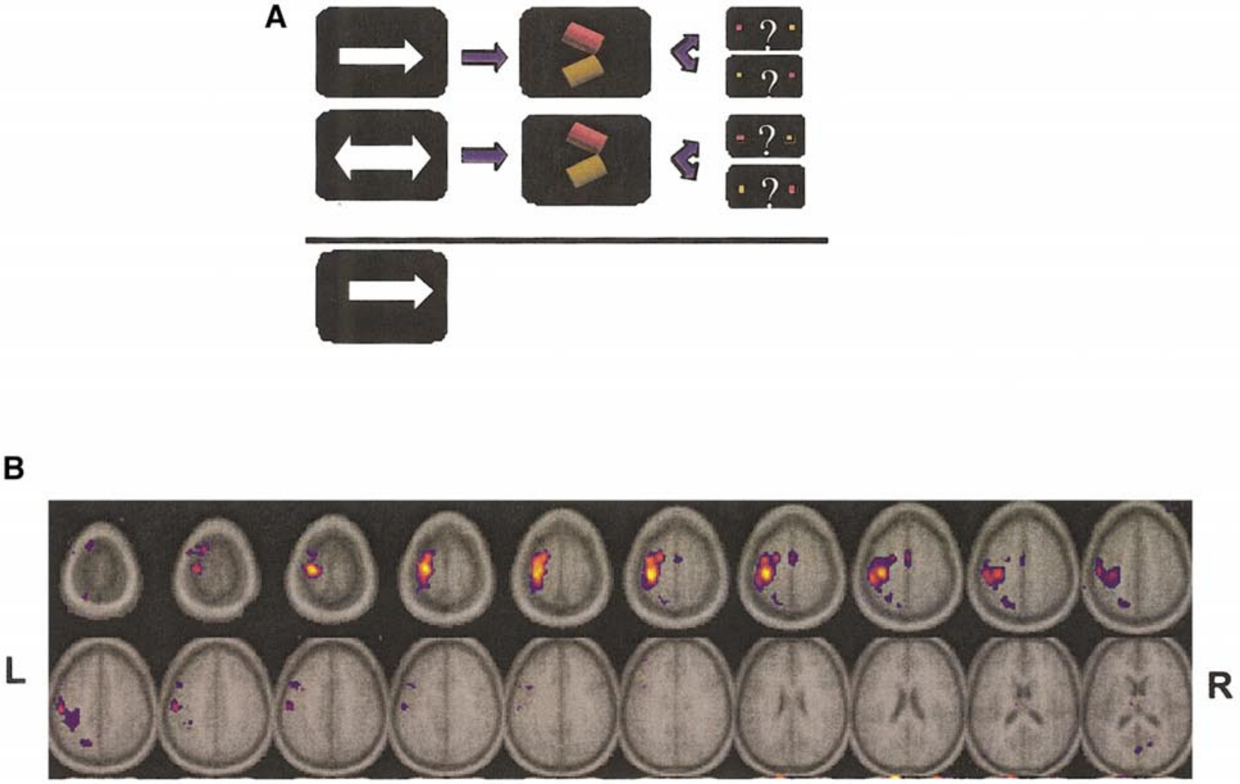
1



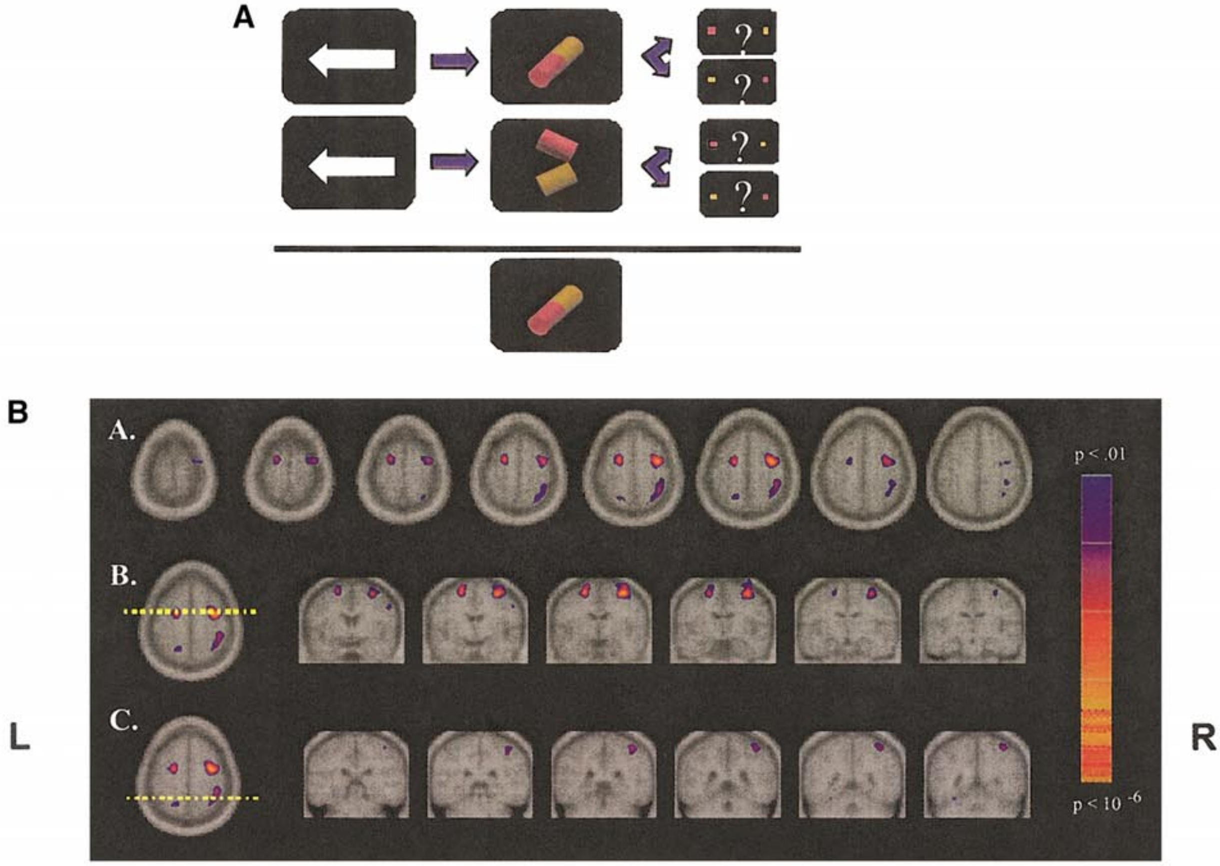
2

FIG. 1. Design of ER-fMRI experiment. (A) Vertical columns depict the four stimulus phases occurring in each trial of the experiment. The five conditions that resulted from collapsing across handle orientations and response cues are organized in the horizontal rows. (B) A left hand supinated, or underhand, power grip that places the thumb on the tan end of the handle and a left hand pronated, or overhand, power grip that places the thumb on the pink end of the dowel.

FIG. 2. Left hand preparation. (A) The subtractive comparisons used to isolate areas involved in left hand preparation. (B) Areas at or above $T = 6.9$ ($P < 0.001$, uncorrected) from this comparison displayed on axial slices. In this and all subsequent figures, activations contain at least five contiguous voxels and are displayed on slices taken from the grand average of all subjects' normalized, T-1-weighted, anatomy.



3



4

FIG. 3. Right hand preparation. (A) The subtractive comparisons used to isolate areas involved in right hand preparation. (B) Areas at or above $T = 6.9$ ($P < 0.001$, uncorrected) from this comparison displayed on axial slices.

Second, does imagining specific actions selectively engage areas that are functionally specialized for planning and control of comparable overt movements? While numerous studies indicate that motor imagery activates a variety of motor structures, whether these activation patterns are specific to particular actions is considerably less clear. Analogous to findings of category-specific effects in visual imagery, evidence for "action-specific" effects in motor imagery would provide strong evidence for the claim that motor imagery and motor behavior share common representations.

These issues were addressed through use of an event-related fMRI paradigm designed to distinguish processes involved in hand preparation from those associated with mental simulation of reaching movements. As illustrated in Fig. 1A, each trial began with a 2-s precue: a left- or rightward pointing arrow, instructing subjects to prepare a grip selection judgment based either on the right or left hand, respectively. Because the orientation of the stimulus on which the judgment was to be based was as yet unspecified, we reasoned that no movement simulation would be involved with this component of the task. On the one hand, even though no overt hand movements will be forthcoming, preparing for a grip selection judgment might be expected to prime contralateral brain areas involved in representing the cued limb. On the other hand, preparation for motor simulation might engage areas in the dominant hemisphere associated with motor attention effects observed prior to overt execution. Specifically, Rushworth and colleagues have shown that left parietal cortex is selectively activated when subjects are required to attend to movements they are about to perform with either limb (Rushworth *et al.*, 2001a,b,c, 1997). In their experiments, the critical area involved in motor attention is located in the anterior, inferior parietal lobule (IPL, BA40) and within the anterior sector of the IPs. To the extent that preparing the hand for upcoming movement simulation involves these same mechanisms, comparable effects might be observed during the precue phase of the present experiment.

As illustrated in Fig. 1B, 2 s after the onset of the precue, subjects were shown a handle in one of 24 different, 3-D orientations and required to determine whether their thumb would be on the pink or tan end if they were to grasp the object with the chosen hand using the most comfortable power grip (i.e., under- or overhand). Previous behavioral studies demonstrated that this grip selection decision is accomplished by internally simulating a reaching movement based on the cued hand (Johnson, 1998, 2000a,b; Johnson *et al.*, 2001). Specifically, time required to select a grip increases as a function of the angular distance the subject's hand would traverse if moving from its present location into the selected posture via the shortest *biomechanically plausible* trajectory. Further, subjects exhibit a near perfect correspondence between grip preferences in imagery and those chosen on actual prehension versions of this task. In both imagery and prehension, grip preferences based on left and right hands are inversely related to one another, a reflection of the fact that the two limbs' biomechanical constraints are 180° out of phase (Johnson, 2000b). If subjects in the present study are basing their grip selection decisions on internally simulated movements, then this same pattern should be apparent in their grip preference data.

Because all stimuli in the present experiment had the same shape, and judgments were based on use of a power grip, the grip selection decision did not demand representing different hand configurations. Put differently, the opposition space of the fingers remained constant across changes in handle orientation, while the trajectory of the reach was accommodated through pronation or supination of the forearm (Johnson, 2000b). Therefore, to the extent that motor imagery is action-specific, we expected selective activation of areas previously associated with reaching during the grip selection phase of this task; specifically, dorsal premotor cortex (PMd) and the medial intraparietal area (MIP) with which it is connected (Caminiti *et al.*, 1996; Johnson *et al.*, 1996; Kalaska and Crammond, 1992; Wise *et al.*, 1997).

Finally, 2 s after presentation of the dowel, subjects were provided with response cues indicating which of two hand-held buttons represented the pink or tan response options on that particular trial (Fig. 1A). Because the time required to make a grip selection decision in this task averages less than 1 s (Johnson, 2000b), this manipulation forced subjects to wait until *after* having completed their movement simulations before planning and executing the appropriate button press response.

Further details of the paradigm can be found under Method below.

METHOD

Subjects

Eight healthy, right-handed adults participated in this experiment. All subjects were naïve to the hypotheses under investigation and provided informed consent in accordance with the Declaration of Helsinki.

Magnetic Resonance Imaging

Imaging was performed using a 1.5-T GE scanner with a standard birdcage head coil. First, a set of structural images were acquired. Namely, an anatomical high-resolution, T1-weighted three-dimensional, rf-spoiled, GRASS sequence se-

FIG. 4. Left hand grip selection. (A) The subtractive comparison used to isolate areas involved in grip selection judgments involving the left hand. (B) Areas activated at or above $T = 4.6$ ($P < 0.01$, uncorrected) for this contrast. Axial slices in row "A" show the areas significantly associated with left hand grip selection decisions. As illustrated by the yellow line on the accompanying coronal slice, axial slices in row "B" depict bilateral regions of the superior frontal gyrus or putative area PMd (standardized coordinates: −18, −6, 53; 34, −6, 53). Similarly, as illustrated by the yellow line on the accompanying coronal slice, axial slices in row "C" were chosen to depict the medial region of the intraparietal sulcus. Putative area MIP is located in the right hemisphere (standardized coordinates: 34, −46, 56) contralateral to the hand on which the grip selection decision is based.

ries (256 × 256 matrix, FOV 23, 60 slices, 2.8 mm thickness) in sagital orientation. A high-resolution, T1-weighted SE (512 × 256 matrix, FOV 20, 16 slices, 7 mm, with 1-mm gap) and a T1-weighted IR-prepared SE EPI (64 × 64 matrix, FOV 20, 16 slices, 7 mm, with 1-mm gap) were also acquired to provide anatomical background pictures before normalization.

Functional imaging was performed using an ultrafast echo planar gradient echo imaging sequence sensitive to blood oxygenation level-dependent (BOLD) contrast (TR, 2 s; TE, 40 ms; flip angle, 90°) with the 16 slices oriented along the anterior and posterior commissure (oblique axial; 7-mm thickness; 1-mm gap; in-plane resolution, 3.125 × 3.125 mm). Prior to each run, four images were acquired and discarded to allow for longitudinal magnetization to reach equilibrium.

Structural and functional data for each individual subject were transformed into a standardized, stereotaxic space (Talairach, 1988) using previously described procedures (Buckner, 1998a). This resulted in 39 axial slices of isotropic 3.125-mm^3 voxels.

Tasks

Each subject performed 10 functional runs presented in different random orders. Every run included 48 8-s randomized trials consisting of four consecutive 2-s phases (Fig. 1A): Phase 1 consisted of either a left- or rightward pointing arrow, (subtending approx. 2° × 2°), indicating which hand should be prepared for the upcoming grip selection decision, or a double-headed arrow that served as a perceptual control but provided no hand preparation information. In Phase 2, subjects were shown either a graspable handle (subtending approx. 2° × 8°)—appearing in 1 of 24 different 3-D orientations—or a broken, ungraspable handle (also subtending approx. 2° × 8°). The ungraspable handle served as a Phase 2 perceptual control. As illustrated in Fig. 1B, if a graspable handle appeared in Phase 2 subjects were to decide whether it would be preferable to grasp it using an underhand or overhand power grip and note whether this posture would place their thumb on the pink or tan end of the object. No actual reaching movements were made. Trials where double-headed arrows occurred in Phase 1 always contained broken dowels in Phase 2. In Phase 3, subjects were shown a question mark flanked by two colored squares indicating which response key (left or right) represented the pink or tan option on that particular trial. Subjects used the index or middle finger of the right hand to press the response key corresponding to the color of the end of the handle on which their thumb would have been located. If a broken, ungraspable dowel appeared in Phase 2, subjects were instructed to wait until the Phase 3 response cue and press the key corresponding to pink. Importantly, because the identity of Phase 3 response cues varied randomly across trials, all conditions, including those involving a broken dowel, involved solving an arbitrary mapping from color to response key (Fig. 1A). Finally, Phase 4 served as an intertrial interval during which subjects maintained fixation on a centrally presented point.

Given the inherent sequential relationship between hand preparation, grip selection, and response execution processes, the ordering of phases within trials was necessarily fixed. However, counterbalancing of the different trial types within each run—created by all possible combinations of Phase 1–3 events—was optimized using a previously described linear simulation tool (Buckner, 1998b). This strategy controls for possible overlap effects in the BOLD response by ensuring that equal numbers of each trial type both precede and follow all others.

Data Analysis

Data from individual runs of each subject were first normalized to correct for global between-run signal intensity changes and temporal drift. Normalized data were then sorted into five primary conditions by collapsing across the 24 different handle orientations (Phase 2) and the two different response cues (Phase 3, Fig. 1A). Within each condition, BOLD responses that occurred during 20-s epochs time-locked to the onset of the hand cues (Phase 1) on individual trials were selectively averaged. This resulted in epochs that captured mean effects related to all four stimulus events within each condition. To enable interindividual averaging, mean and variance images for each subject were finally transformed into standard stereotaxic space (Talairach, 1988).

In order to isolate effects specifically related to hand preparation or grip selection, respectively, we performed subtractive comparisons between average BOLD responses associated with specific trial types as detailed below. Statistical activation maps were constructed based on differences between trial types using a t statistic (Dale and Buckner, 1997). Clusters consisting of at least five voxels, separated by a minimum of 8 mm, and having t values greater than 4.6 ($P > .01$, uncorrected for multiple comparisons), were considered statistically significant.

Hand preparation. Figures 2A and 3A illustrate the subtractive comparisons used to isolate effects related to left or right hand preparation, respectively. Mean BOLD responses associated with trials on which subjects were shown a meaningless precue (double-headed arrow) followed by the broken handle were subtracted from average responses from trials where subjects were shown a left or right arrow precue and prepared to make a grip decision based on that hand, but then were shown a broken, ungraspable handle (i.e., Trial Type 3–5 for the left hand and Trial Type 4–5 for the right, Figs. 2A and 3A). As demands associated with stimulus perception and response execution are equivalent in each of the conditions being compared, resulting differences should be associated with brain areas involved in preparing either the left or right hand for movement simulation.

Grip selection. Figures 4A and 5A illustrate the subtractive comparisons used to isolate effects associated with the grip selection component of the task based on either the left or right hand, respectively. Average BOLD responses from trials on which subjects were precued to prepare either the left or right hand, but then were shown a broken, ungraspable handle were subtracted from mean responses on trials where they prepared either hand and then selected the most natural grip for engaging an unbroken dowel (i.e., Trial Type 1–3, for the left hand, and Trial Type 2–4, for the right, Figs.

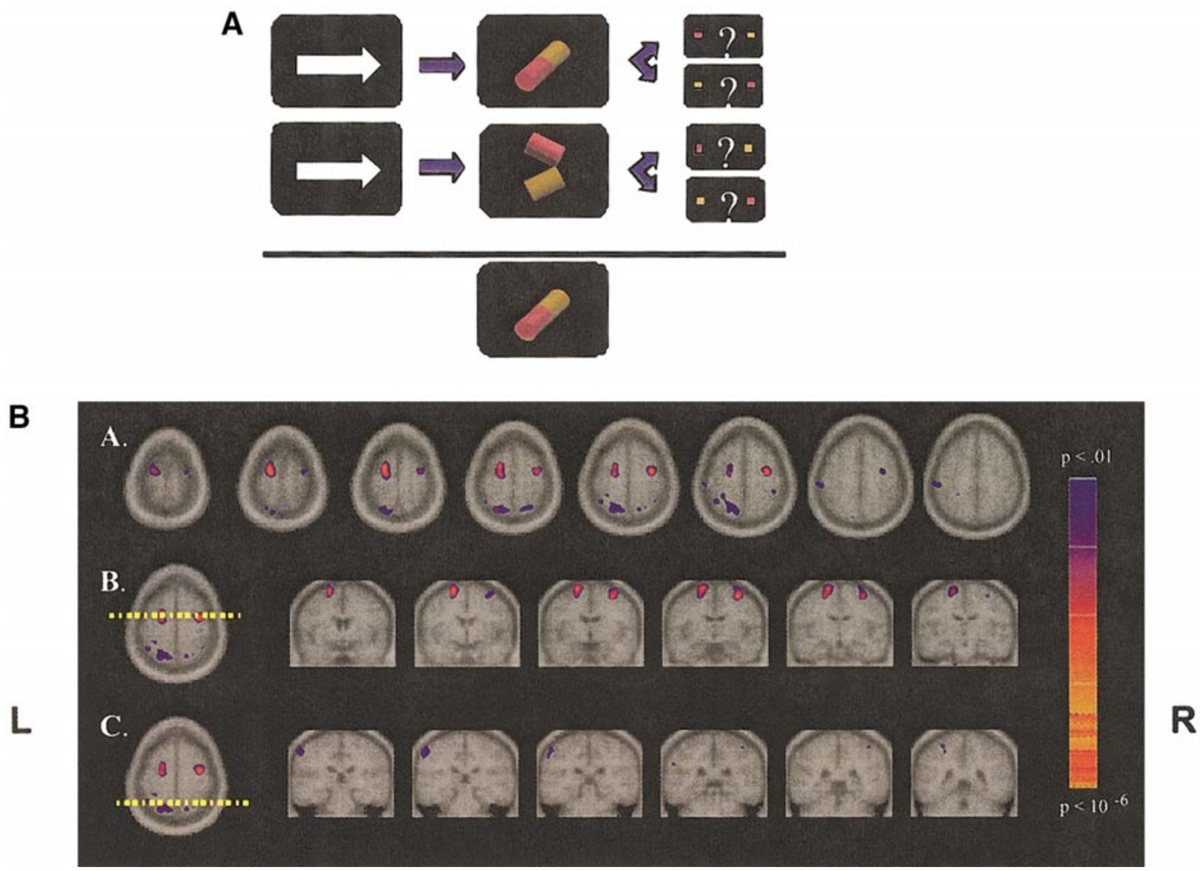


FIG. 5. Right hand grip selection. (A) The subtractive comparisons used to identify areas involved in grip selection judgments based on the right hand. (B) Areas activated at or above $T = 4.6$ ($P < 0.01$, uncorrected) for this contrast. Axial slices in row "A" show areas associated with right hand grip selection. As illustrated by the yellow line on the accompanying coronal slice, axial slices in row "B" depict bilateral regions of frontal superior gyrus or putative area PMd (standardized coordinates: −18, −3, 62; 31, −9, 56). Similarly, as illustrated by the yellow line on the accompanying coronal slice, axial slices in row "C" were chosen to depict the medial region of the intraparietal sulcus. Putative area MIP is located in the left hemisphere (standardized coordinates: −40, −49, 53) contralateral to the hand on which the grip selection decision is based.

4A and 5A). Because demands associated with stimulus perception, left vs right hand preparation, and response execution are equivalent under each of the conditions being compared, resulting differences should be associated with brain areas involved specifically in imagining how best to grasp the handle. Likewise, it is important to note that due to the randomization procedure, results of these subtractive comparisons are unbiased with respect to the identity of preceding phases.

RESULTS

Hand Preparation

Comparison of Figs. 2B and 3B reveals a striking symmetry between areas activated when preparing movement simulations on the basis of either the left or right hand, respectively. Similar to previous studies of motor attention (Rushworth *et al.*, 2001a,b,c, 1997), significant effects were predominantly localized to the left cerebral hemisphere during preparation (Tables 1 and 2). Significantly activated areas within the parietal cortex involved BA7 and primary somatosensory cortex (BA2), but—in contrast to motor attention—did not include BA40 or anterior IPs. The absence of these areas may be attributable to the fact that the present task involved preparing to mentally simulate movements, whereas motor attention paradigms involve preparation for overt execution. Sites in the left frontal cortex included the primary motor area (BA4), medial frontal gyrus (BA10), dorsal premotor (BA6), SMA, and cingulate motor area (CMA). In the right hemisphere, significant frontal activations were observed in the primary motor cortex (BA4), medial frontal gyrus (BA10), and CMA. Finally, several areas in the right cerebellum were also activated (Tables 1 and 2). Activations within medial and posterior IPs were observed only in the left hemisphere during preparation of the left hand.

In sum, preparing to mentally simulate an upcoming reaching movements on the basis of either hand was associated with widespread activation of motor-related areas throughout the left cerebral and right cerebellar hemispheres. Indeed, many of the same regions previously reported to be involved in motor imagery tasks were also active during this nonimagery phase of the task.

TABLE 1

Areas of Peak Activation in Hand Preparation, Expressed in Standardized Coordinates

Left hand preparation				
Functional area	Talaraich coordinates			−Log(*P*)
Left BA4 GPrC (precentral gyrus)	−34	−27	56	57.8
Left BA4 GPrC	−25	−21	65	55.0
Left BA9 GFs (superior frontal gyrus)	−34	56	−28	46.6
Left BA6 GFs	−21	−3	62	38.2
Left BA10 GFm (medial frontal gyrus)	−21	56	9	32.9
BA6 SMA	0	−6	56	25.5
Left BA7 SPL	−15	−65	43	22.4
Left BA44 GFi	−46	9	37	20.2
Left BA7 IPs	−21	−55	53	18.1
Left BA7 IPs	−34	−49	43	16.6
Left BA7 IPs	−37	−49	50	16.5
Right BA4 GPrC	31	−9	56	15.9
Left BA4 GPrC	−28	−6	21	15.8
Left BA2 GPOc (postcentral gyrus)	−43	−21	28	15.7
Left thalamus (nucleus dm)	−9	−21	12	15.2
Right cerebellum	43	−58	−25	12.3
Left putamen	−21	−3	6	12.0
Right cerebellum	18	−62	−40	11.8
Right cerebellum	28	−62	−15	11.8
Right BA10 GFm	34	50	0	10.5
Right cerebellum	9	−62	−12	9.8
Left BA31 CMA	−3	−55	37	9.8
Left BA6 GFm	−40	9	53	9.6
Left GP (globus pallidus)	−12	0	9	9.2
Left BA7 SPL	−6	−58	62	8.7
Left GC (cingulate gyrus)	−18	−49	37	8.6
Right CMA (cingulate motor area)	9	−30	28	8.2
CMA	0	16	46	8.0

Note. To attain statistical significance ($P < .01$, $T = 4.6$), clusters must include at least five voxels and peaks must be separated by 8 mm.

Grip Selection

As expected if subjects are using internally simulated reaching, grip preferences (i.e., over- vs underhand) for each handle orientation were virtually identical to what was observed previously during actual prehension ($R = .99$, $P < .00001$; Johnson, 2000b). Consistent with observations of reach planning in monkeys, these imagined reaches were associated with highly selective activations within dorsal premotor cortex (BA6) and within the medial IPs. Tables 3 and 4 summarize areas activated during left and right hand grip selection, respectively. Figure 4B shows that grip selection based on the left hand was associated with bilateral activation of putative PMd. As shown in Fig. 5B, these same regions were also activated during grip selection based on the right hand. Under both conditions unilateral activations within the medial IPs were observed contralateral to the hand on which grip decisions were based (Figs. 4B and 5B). These locations are probable homologues of monkey MIP, an area containing cells that represent the intention to move the arm in a specific direction (Andersen *et al.*, 1997) and whose responses are most pronounced when forthcoming arm move-

TABLE 2

Areas of Peak Activation in Hand Preparation, Expressed in Standardized Coordinates

Right hand preparation				
Functional area	Talaraich coordinates			−Log(*P*)
Left BA4 GPrC	−34	−24	56	65.5
Left BA4 GPrC	−25	−21	65	51.8
Left PMd BA6 GFs	−21	−6	62	45.7
Left BA4 GPrC	−34	−9	59	41.4
Left BA2 GPOc	−43	−33	53	37.2
Left BA10 GFm	−21	53	−9	30.2
Left BA6 SMA	0	−6	53	29.7
Left BA7 SPL	−34	−40	43	26.0
Left BA7 SPL	−15	−65	43	25.4
Left BA7 SPL	−21	−55	53	21.3
Left thalamus (nucleus dm)	−6	−18	12	16.7
Left BA10 GFm	−40	6	31	15.7
Left BA10 GFm	−46	9	37	15.3
Right cerebellum	37	−58	−21	13.2
Right cerebellum	28	−65	−43	12.6
Left putamen	−21	−3	6	12.4
Left cerebellum	−18	−74	−9	12.4
Right BA7 SPL	18	−62	−37	12.0
Left BA4	−31	−6	21	11.7
Right cerebellum	9	−62	−15	10.7
Left BA6 SMA	−40	6	53	10.3
Left BA7 SPL	−34	−62	53	9.9
Right BA2	59	−21	25	9.5
Left putamen	−15	−33	6	9.4
SMA	0	13	46	9.1
Left BA31	3	−37	34	8.9
Left BA6 GFm	25	0	46	8.7
Right BA4 GPrC	31	−9	53	8.7
Left cerebellum	−9	−52	−18	8.3
Left cerebellum	−6	−71	−9	7.8

Note. To attain statistical significance ($P < .01$, $T = 4.6$), clusters must include at least five voxels and peaks must be separated by 8 mm.

TABLE 3

Areas of Peak Activation in Grip Selection Based on the Left Hand, Expressed in Standardized Coordinates

Left hand grip selection				
Functional area	Talaraich coordinates			−Log(*P*)
Left PMd Area 6 medial frontal gyrus	−18	−6	53	13.71
Right PMd Area 6 precentral gyrus	34	−6	53	13.28
Right PMd Area 6 precentral gyrus	28	−3	53	13.27
Right 40 inferior parietal lobule putative MIP	34	−46	56	9.83
Right intraoccipital sulcus	34	−77	−9	9.31
Right Area 40 inferior parietal lobule	37	−37	53	9.13
Right Area 7 superior parietal lobule	25	−58	59	8.77

Note. To attain statistical significance ($P < .01$, $T = 4.61$), clusters must include at least five voxels and peaks must be separated by 8 mm.

TABLE 4

Areas of Peak Activation in Grip Selection Based on the Right Hand, Expressed in Standardized Coordinates

Right hand grip selection				
Functional area	Talaraich coordinates			−Log(P)
Left Area 6 precentral gyrus	−18	−3	62	12.51
Right Area 6 precentral gyrus	31	−9	56	11.19
Left Area 6 precentral sulcus	−21	−12	56	9.65
Left lingual area 18	−21	−77	−3	7.42
Left lateral cerebellum	−34	−62	−15	7.36
Right Area 3 posterior bank central sulcus	37	19	40	7.14
Right calcarine sulcus area 18	18	−87	−3	6.88
Left Area 40 inferior parietal lobule putative MIP	−40	−49	53	6.32
Right Area 7 superior parietal lobule	21	−58	59	6.26
Left postcentral gyrus area 2	−59	−24	46	5.58
Left Area 7 superior parietal lobule	−21	−52	53	5.58
Right inferior occipital gyrus	25	−83	−6	5.36
Left precuneus	−12	−58	53	5.12

Note. To attain statistical significance ($P < .01$, $T = 4.61$), clusters must include at least five voxels and peaks must be separated by 8 mm.

ments will involve the contralateral hand (Colby and Duhamel, 1991). Grip decisions based on either hand also activated a circumscribed region of the right SPL (Figs. 4B and 5B). As mentioned earlier, monkey SPL represents higher level proprioceptive and visual information and projects directly to area PMd. Likewise, previous neuroimaging studies of humans have associated SPL with the representation of hand and arm movements (Deiber *et al.*, 1991; Grafton *et al.*, 1996; Iacoboni *et al.*, 1999).

DISCUSSION

The purposes of this study were twofold: First, we sought to distinguish effects associated with motor imagery from those linked to other motor planning processes that do not involve internal movement simulations. Consistent with earlier studies of preparation for overt action (Deiber *et al.*, 1996; Toni *et al.*, 1999), our results show that preparing to imagine an as yet unspecified hand movement—a task component that does not involve movement simulation—activated a widely distributed network of frontal (BA4, BA6, BA10, SMA, CMA), parietal (BA2, BA7), and subcortical (BG, cerebellum, thalamus) areas, most of which have been claimed to participate in motor imagery. By contrast, imagined grip selection—a task component that involves movement simulation—was associated with focal activation in a small subset of parietal and premotor sites. The present findings therefore suggest that many of the areas previously attributed to motor simulation may instead be involved in nonimagery processes such as preparing to *imagine* movements on the basis of a specific effector.

Second, we sought to determine whether motor imagery selectively activates action-specific motor representations. Consistent with this hypothesis, we found that areas selectively activated during imagined grip selection were consistent with a putative homologue of the monkey parietofrontal reach circuit. Taken together, these two findings suggest that when other premovement processes are properly controlled, motor imagery selectively activates those areas involved in controlling comparable actions.

Hand Preparation

Earlier investigations demonstrated that preparing to move is associated with activation of numerous cortical areas contralateral to the involved effector (Deiber *et al.*, 1996; Toni *et al.*, 1999, 2001). We observed that preparing to simulate an as yet unspecified action on the basis of either limb induced activations primarily within the motor-dominant, left, cerebral hemisphere. This suggests that preparing overt vs covert simulated movements may involve different processes. There are at least two possible reasons for this cerebral asymmetry. The most obvious possibility is that the left, motor-dominant, hemisphere may play a key role in preparing for movement simulations involving either hand. In right-handed individuals, it is well known that the left cerebral hemisphere is dominant not only for fine motor control, but also for several aspects of motor planning, including movement sequencing (Kimura and Archibald, 1974), representation of skilled actions (Leipmann, 1900) and, most recently, motor attention. As reviewed earlier, Rushworth and colleagues have shown that left parietal cortex is selectively activated when subjects are required to attend to movements they are about to perform with either limb (Rushworth *et al.*, 2001a,b,c, 1997). In their experiments, the critical area involved in “motor attention” is located in the inferior parietal lobule (BA40) and within the anterior sector of the IPs. In the present study, more posterior areas within the left IPs were only observed during left hand preparation, and neither left nor right hand preparation involved BA40. These important differences may reflect the fact that in our study, subjects were preparing to imagine rather than execute movements. In contrast to the motor attention experiments, during the precue phase, subjects in our study were not aware of the specific movements to be imagined during the upcoming grip selection phase of the each trial. It is also possible that preparing a limb, as opposed to preparing to perform a specific action, may contribute to the more widespread left hemisphere activity we observed. This hypothesis is consistent with left BA40 participating in the storage of motor programs for specific actions (Haaland *et al.*, 2000; Johnson *et al.*, 2002). A final possibility is that left-lateralized motor preparation effects may partly reflect the fact that subjects will ultimately be required to press one of two response buttons using the contralateral right hand. Experiments designed to disentangle these possibilities are currently under way.

Grip Selection

Electrophysiological studies of monkeys have demonstrated the existence of a functionally specialized, parietofrontal system for the planning and control of reaching movements that includes areas PMd and MIP (Johnson *et al.*, 1996; Kalaska and Crammond, 1992). By carefully isolating grip from hand preparation, we isolated a putative homologue of this reach system in humans. Regardless of the hand involved, grip selection was associated with bilateral activation in PMd. Individual PMd neurons are involved in integrating proprioceptive input regarding characteristics of the limb to be used with visual information specifying a target object's location to construct plans for specific reaching actions (Hoshi and Tanji, 2000). Area PMd receives direct visual (Caminiti *et al.*, 1996; Johnson *et al.*, 1993) and higher level proprioceptive (Lacquaniti *et al.*, 1995) input from the superior parietal lobule (SPL) and is reciprocally connected with a medial region of the intraparietal sulcus (area MIP) that contains cells responsive to the intention to move the arm along a specific trajectory in space (Andersen *et al.*, 1997; Crammond and Kalaska, 1989; Matelli *et al.*, 1998). Both SPL and a putative homologue of MIP were activated during grip selection. The area proposed here as homologous to monkey MIP is virtually identical to a location previously shown to be involved in the modification of unfolding reaching plans on the basis of sensory feedback (Desmurget *et al.*, 1999; Desmurget and Grafton, 2000).

This work builds on earlier PET studies indicating a homologous reach system in humans (Grafton *et al.*, 1996; Kertzman *et al.*, 1997; Lacquaniti *et al.*, 1997). The present findings demonstrate that this system is also selectively activated when implicitly simulating reaching movements. We interpret these effects as strong support for the hypothesis that motor imagery involves action-specific motor representations. Considered in the context of earlier psychophysical studies of grip selection, these findings also suggest an alternative model of motor imagery.

Parietofrontal Circuits and Motor Simulation

The common wisdom is that motor imagery is the simulation of an *existing* motor plan while execution is inhibited (e.g., Jeannerod, 1994). Alternatively, Johnson argued that movement simulation may actually be involved in the refinement and selection of the premovement plan (2000b). Results of a number of studies indicate that motor simulation is used to solve the problem of movement selection in tasks, such as the one used in the present experiment, where a relatively small number of response alternatives exist (e.g., over- vs underhand; Johnson, 1998, 2000a, 2000b; Johnson *et al.*, 2001). Specifically, these studies indicate that: (1) Time required to make a grip selection decision is predicted by the angular distance between the involved effectors' physical location and what would be the end state of the simulated reach, following the shortest *biomechanically plausible* trajectory; (2) movement simulations appear to be extremely rapid, on the order of 1000°/s; (3) prior to selecting a grip, both reach alternatives appear to be simulated (see also Parsons, 1994); (4) selected responses are those rated as being less biomechanically awkward in actual prehension; and (5) times to select a grip are substantially inflated when both response options have similar awkwardness ratings. Johnson proposed the Prospective Action Model (PAM) to account for these findings. The distinctive feature of this model is that analog simulations are used to evaluate response options *in advance* of movement selection. Results of these simulations are then used to select the most biomechanically efficient alternative. The present neuroimaging results can be interpreted within the PAM framework.

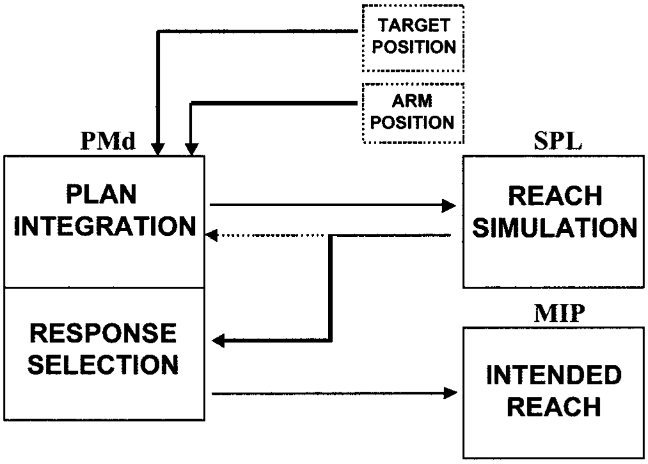


FIG. 6. A simplifying model of reach simulation. As detailed in text, the present grip selection results can be interpreted within a theoretical framework in which internal movement simulations are used to refine and select premovement plans for reaching.

The question of whether premotor and parietal circuits act as functional loops for representing imagined movements has been raised previously (Gerardin *et al.*, 2000). Our grip selection data indicate that this is indeed the case for implicitly simulated reaching movements. Considered within the context of earlier psychophysical results, the present findings suggest specific neural mechanisms for various components of PAM. As depicted in Fig. 6, input to the model consists of the spatial properties of the target object and precued limb (dashed boxes). Note that areas involved in representing this perceptual information are not apparent in the grip selection results because the control condition involves both limb preparation and stimulus processing (Figs. 4A and 5A). On the basis of electrophysiological work (Hoshi and Tanji, 2000; Shen and Alexander, 1997), we suggest that this perceptual information is integrated within area PMd to form an initial premovement plan for reaching that represents one of the two possible alternatives (over- or underhand). This initial reach plan is then projected from PMd through reafferent pathways to SPL, where it is actively simulated. The hypothesized role of SPL in movement simulation is consistent with previous functional imaging results implicating this area in mental rotation (Haxby *et al.*, 1991; Richter *et al.*, 1997, 2000; Tagaris *et al.*, 1996), implicit motor imagery (Parsons *et al.*, 1995), and the representation of finger, hand, and arm movements (Deiber *et al.*, 1991; Grafton *et al.*, 1992; Iacoboni *et al.*, 1999). Whether an entire movement is simulated at once is an open question. One possibility is that the movement is simulated stepwise as a series of submovements. This could be achieved iteratively by having results of a partial simulation project back onto PMd (dashed arrow), where they could be used to update and revise the motor plan on the basis of predicted sensory consequences. In turn, the updated plan for the next submovement could be projected back onto SPL for further simulation, and so on. Alternatively, it is also possible that the entire plan is simulated in its entirety. In either case, both response options (over- and underhand reaches in this case) are simulated before a grip is selected. According to PAM, results of these simulations are estimates of the biomechanical costs, or awkwardness, of each response option. In keeping with the well-established role of PMd in movement selection (Deiber *et al.*, 1991; Grafton *et al.*, 1998; Passingham, 1993), we suggest that a comparator within this region weighs simulation results and selects the least costly response option. If rated awkwardness values of the two reach options are highly dissimilar, then the least costly option is selected immediately. If awkwardness ratings of the two options are similar additional processing is necessary prior to selection, resulting in inflated response times. Finally, the plan for the selected response is projected to MIP (or the parietal reach region, Andersen *et al.*, 1997), where neurons are known to represent the intention to reach in a particular manner for a target (Andersen *et al.*, 1997; Batista and Andersen, 2001; Snyder *et al.*, 2000).

CONCLUSIONS

In sum, our results support the hypothesis that motor imagery selectively involves parietofrontal circuits that represent comparable overt actions. These findings illustrate the importance of distinguishing between effects related to premovement processes that do and do not involve motor simulation when attempting to localize representations involved in motor imagery. Further, these findings also raise the possibility that nonimagery components may contribute to the diversity of cortical and subcortical areas that have been implicated in motor imagery by previous functional neuroimaging studies. The action-specific nature of the present findings suggests that, under carefully controlled conditions, motor simulation may indeed be a valuable and precise tool for probing the functional architecture of the human motor system.

ACKNOWLEDGMENTS

This work was supported by NIH Grant MH002022-01 and a grant from the James S. McDonnell Foundation. Thanks to Marty Woldorf, Max Hopf, and anonymous reviewers for helpful comments on earlier versions of the manuscript.

REFERENCES

Andersen, R. A., Snyder, L. H., Bradley, D. C., and Xing, J. 1997. Multimodal representation of space in the posterior parietal cortex and its use in planning movements. *Annu. Rev. Neurosci.* **20:** 303–330.

Batista, A. P., and Andersen, R. A. 2001. The parietal reach region codes the next planned movement in a sequential reach task. *J. Neurophysiol.* **85**(2): 539–544.

Buckner, R. L., Goodman, J., Burock, M., Rotte, M., Koutstaal, W., Schacter, D. Rosen, B., and Dale, A. M. 1998a. Functional-anatomic correlates of object priming in humans revealed by rapid presentation event-related fMRI. *Neuron* **20:** 285.

Buckner, R. L., and Koutstaal, W., *et al.* 1998b. Functional-anatomic study of episodic retrieval. II. Selective averaging of event-related fMRI trials to test the retrieval success hypothesis. *Neuroimage* **7**(3): 163–175.

Caminiti, R., Ferraina, S., and Johnson, P. B. 1996. The sources of visual information to the primate frontal lobe: A novel role for the superior parietal lobule. *Cereb. Cortex* **6**(3): 319–328.

Colby, C. L., and Duhamel, J. R. 1991. Heterogeneity of extrastriate visual areas and multiple parietal areas in the macaque monkey. *Neuropsychologia* **29**(6): 517–537.

Crammond, D. J., and Kalaska, J. F. 1989. Neuronal activity in primate parietal cortex area 5 varies with intended movement direction during an instructed-delay period. *Exp. Brain Res.* **76**(2): 458–462.

Dale, A. M., and Buckner, R. L. 1997. Selective averaging of rapidly presented individual trials using fMRI. *Human Brain Mapp.* **5**(5): 329–340.

Decety, J., Perani, D., Jeannerod, M., Bettinardi, V., Tadary, B., Woods, R., Mazziotta, J. C., and Fazio, F. 1994. Mapping motor representations with positron emission tomography. *Nature* **371**(6498): 600–602.

Decety, J., Philippon, B., and Ingvar, D. H. 1988. rCBF landscapes during motor performance and motor ideation of a graphic gesture. *Eur. Arch. Psychiatry Neurol. Sci.* **238**(1): 33–38.

Deiber, M. P., Ibanez, V., Sadato, N., and Hallett, M. 1996. Cerebral structures participating in motor preparation in humans: A positron emission tomography study. *J. Neurophysiol.* **75**(1): 233–247.

Deiber, M. P., Passingham, R. E., Colebatch, J. G., Friston, K. J., Nixon, P. D., and Frackowiak, R. S. 1991. Cortical areas and the selection of movement: A study with positron emission tomography. *Exp. Brain Res.* **84**(2): 393–402.

Desmurget, M., Epstein, C. M., Turner, R. S., Prablanc, C., Alexander, G. E., and Grafton, S. T. 1999. Role of the posterior parietal cortex in updating reaching movements to a visual target. *Nat. Neurosci.* **2**(6): 563–567.

Desmurget, M., and Grafton, S. 2000. Forward modeling allows feedback control for fast reaching movements. *Trends Cogn. Sci.* **4**(11): 423–431.

Fadiga, L., Buccino, G., Craighero, L., Fogassi, L., Gallese, V., and Pavesi, G. 1999. Corticospinal excitability is specifically modulated by motor imagery: A magnetic stimulation study. *Neuropsychologia* **37**(2): 147–158.

Ganis, G., Keenan, J. P., Kosslyn, S. M., and Pascual-Leone, A. 2000. Transcranial magnetic stimulation of primary motor cortex affects mental rotation. *Cereb. Cortex.* **10**(2): 175–180.

Gerardin, E., Sirigu, A., Lehericy, S., Poline, J. B., Gaymard, B., Marsault, C., Agid, Y., and Le Bihan, D. 2000. Partially overlapping neural networks for real and imagined hand movements. *Cereb. Cortex.* **10**(11): 1093–1104.

Grafton, S. T., Fagg, A. H., and Arbib, M. A. 1998. Dorsal premotor cortex and conditional movement selection: A PET functional mapping study. *J. Neurophysiol* **79**(2): 1092–1097.

Grafton, S. T., Fagg, A. H., Woods, R. P., and Arbib, M. A. 1996. Functional anatomy of pointing and grasping in humans. *Cereb. Cortex* **6**(2): 226–237.

Grafton, S. T., Mazziotta, J. C., Woods, R. P., and Phelps, M. E. 1992. Human functional anatomy of visually guided finger movements. *Brain* **115**(Pt.2): 565–587.

Gulyas, B. 2001. Neural networks for internal reading and visual imagery of reading: A PET study. *Brain Res. Bull.* **54**(3): 319–328.

Haaland, K. Y., Harrington, D. L., and Knight, R. T. 2000. Neural representations of skilled movement. *Brain* **123**(Pt 11): 2306–2313.

Halpern, A. R. 2001. Cerebral substrates of musical imagery. *Ann. N. Y. Acad. Sci.* **930:** 179–192.

Haxby, J. V., Grady, C. L., Horwitz, B., Ungerleider, L. G., Mishkin, M., Carson, R. E., Herscovitch, P., Schapiro, M. B., and Rapoport, S. I. 1991. Dissociation of object and spatial visual processing pathways in human extrastriate cortex. *Proc. Natl. Acad. Sci. USA* **88**(5): 1621–1625.

Hoshi, E., and Tanji, J. 2000. Integration of target and body-part information in the premotor cortex when planning action. *Nature* **408**(6811): 466–470.

Iacoboni, M., Woods, R. P., Brass, M., Bekkering, H., Mazziotta, J. C., and Rizzolatti, G. 1999. Cortical mechanisms of human imitation. *Science* **286**(5449): 2526–2528.

Ishai, A., Ungerleider, L. G., and Haxby, J. V. 2000. Distributed neural systems for the generation of visual images. *Neuron* **28**(3): 979–990.

Jeannerod, M. 1994. The representing brain: Neural correlates of motor intention and imagery. *Brain Behav. Sci.* **17:** 187–245.

Johnson, P. B., Ferraina, S., Bianchi, L., and Caminiti, R. 1996. Cortical networks for visual reaching: Physiological and anatomical organization of frontal and parietal lobe arm regions. *Cereb. Cortex* **6**(2): 102–119.

Johnson, P. B., Ferraina, S., and Caminiti, R. 1993. Cortical networks for visual reaching. *Exp. Brain Res.* **97**(2): 361–365.

Johnson, S. H. 1998. Cerebral organization of motor imagery: Contralateral control of grip selection in mentally represented prehension. *Psychol. Sci.* **9:** 219–222.

Johnson, S. H. 2000a. Imagining the impossible: Intact motor representations in hemiplegics. *Neuroreport* **11**(4): 729–732.

Johnson, S. H. 2000b. Thinking ahead: The case for motor imagery in prospective judgments of prehension. *Cognition* **74:** 33–70.

Johnson, S. H., Corballis, P. M., and Gazzaniga, M. S. 2001. Within grasp but out of reach: evidence for a double dissociation between imagined hand and arm movements in the left cerebral hemisphere. *Neuropsychologia* **39**(1): 36–50.

Johnson, S. H., Newland-Norlund, R., and Grafton, S. T. 2002. *Beyond the Dorsal Stream: A Distributed Left Hemisphere System for the Representation of Skilled Action*. Paper presented at the 9th Annual Meeting of the Cognitive Neuroscience Society, San Francisco, CA.

Kalaska, J. F., and Crammond, D. J. 1992. Cerebral cortical mechanisms of reaching movements. *Science* **255**(5051): 1517–1523.

Kertzman, C., Schwarz, U., Zeffiro, T. A., and Hallett, M. 1997. The role of posterior parietal cortex in visually guided reaching movements in humans. *Exp. Brain Res.* **114**(1): 170–183.

Kimura, D., and Archibald, Y. 1974. Motor functions of the left hemisphere. *Brain* **97**(2): 337–350.

Klein, I., Paradis, A. L., Poline, J. B., Kosslyn, S. M., and Le Bihan, D. 2000. Transient activity in the human calcarine cortex during visual-mental imagery: An event-related fMRI study. *J. Cogn. Neurosci.* **12**(Suppl. 2): 15–23.

Lacquaniti, F., Guigon, E., Bianchi, L., Ferraina, S., and Caminiti, R. 1995. Representing spatial information for limb movement: Role of area 5 in the monkey. *Cereb. Cortex* **5**(5): 391–409.

Lacquaniti, F., Perani, D., Guigon, E., Bettinardi, V., Carrozzo, M., Grassi, F., Rossetti, Y., and Fazio, F. 1997. Visuomotor transformations for reaching to memorized targets: A PET study. *Neuroimage* **5**(2): 129–146.

Leipmann, H. 1900. Das Krankheitshild der Apraxie (motorischen/Asymbolie). *Monatschrift Psychiatry Neurol.* **8:** 15–44, 102–132, 182–197.

Lotze, M., Montoya, P., Erb, M., Hulsmann, E., Flor, H., Klose, U., Birbaumer, N., and Grodd, W. 1999. Activation of cortical and cerebellar motor areas during executed and imagined hand movements: An fMRI study. *J. Cogn. Neurosci.* **11**(5): 491–501.

Matelli, M., Govoni, P., Galletti, C., Kutz, D. F., and Luppino, G. 1998. Superior area 6 afferents from the superior parietal lobule in the macaque monkey. *J. Comp. Neurol.* **402**(3): 327–352.

O'Craven, K. M., and Kanwisher, N. 2000. Mental imagery of faces and places activates corresponding stiimulus-specific brain regions. *J. Cogn. Neurosci.* **12**(6): 1013–1023.

Parsons, L. M. 1994. Temporal and kinematic properties of motor behavior reflected in mentally simulated action. *J. Exp. Psychol. Hum. Percept. Perform.* **20**(4): 709–730.

Parsons, L. M., Fox, P. T., Downs, J. H., Glass, T., Hirsch, T. B., Martin, C. C., Jerabek, P. A., and Lancaster, J. L. 1995. Use of implicit motor imagery for visual shape discrimination as revealed by PET. *Nature* **375**(6526): 54–58.

Passingham, R. E. 1993. *The Frontal Lobes and Voluntary Action*. Oxford Univ. Press, Oxford.

Porro, C. A., Francescato, M. P., Cettolo, V., Diamond, M. E., Baraldi, P., Zuiani, C., Bazzocchi, M., and di Prampero, P. E. 1996. Primary motor and sensory cortex activation during motor performance and motor imagery: a functional magnetic resonance imaging study. *J. Neurosci.* **16**(23): 7688–7698.

Richter, W., Ugurbil, K., Georgopoulos, A., and Kim, S. G. 1997. Time-resolved fMRI of mental rotation. *Neuroreport* **8**(17): 3697–3702.

Richter, W., Somorjai, R., Summers, R., Jarmasz, M., Menon, R. S., Gati, J. S., Georgopoulos, A. P., Tegeler, C., Ugurbil, K., and Kim, S. G. 2000. Motor area activity during mental rotation studied by time-resolved single-trial fMRI. *J. Cogn. Neurosci.* **12**(2): 310–320.

Roth, M., Decety, J., Raybaudi, M., Massarelli, R., Delon-Martin, C., Segebarth, C., Morand, S., Gemignani, A., Décorps, M., and Jeannerod, M. 1996. Possible involvement of primary motor cortex in mentally simulated movement. A functional magnetic resonance imaging study. *Neuroreport* **7:** 1280–1284.

Rushworth, M. F., Ellison, A., and Walsh, V. 2001a. Complementary localization and lateralization of orienting and motor attention. *Nat. Neurosci.* **4**(6): 656–661.

Rushworth, M. F., Krams, M., and Passingham, R. E. 2001b. The attentional role of the left parietal cortex: The distinct lateralization and localization of motor attention in the human brain. *J. Cogn. Neurosci.* **13**(5): 698–710.

Rushworth, M. F., Nixon, P. D., Renowden, S., Wade, D. T., and Passingham, R. E. 1997. The left parietal cortex and motor attention. *Neuropsychologia* **35**(9): 1261–1273.

Rushworth, M. F., Paus, T., and Sipila, P. K. 2001c. Attention systems and the organization of the human parietal cortex. *J. Neurosci.* **21**(14): 5262–5271.

Ryding, E., Decety, J., Sjoholm, H., Stenberg, G., and Ingvar, D. H. 1993. Motor imagery activates the cerebellum regionally. A SPECT rCBF study with 99mTc-HMPAO. *Brain Res. Cogn. Brain. Res.* **1**(2): 94–99.

Schnitzler, A., Salenius, S., Salmelin, R., Jousmaki, V., and Hari, R. 1997. Involvement of primary motor cortex in motor imagery: A neuromagnetic study. *Neuroimage* **6**(3): 201–208.

Shen, L., and Alexander, G. E. 1997. Preferential representation of instructed target location versus limb trajectory in dorsal premotor area. *J. Neurophysiol.* **77**(3): 1195–1212.

Shergill, S. S., Bullmore, E. T., Brammer, M. J., Williams, S. C., Murray, R. M., and McGuire, P. K. 2001. A functional study of auditory verbal imagery. *Psychol. Med.* **31**(2): 241–253.

Sirigu, A., Cohen, L., Duhamel, J. R., Pillon, B., Dubois, B., Agid, Y., and Pierrot-Deseilligny, C. 1995. Congruent unilateral impairments for real and imagined hand movements. *Neuroreport* **6**(7): 997–1001.

Sirigu, A., Duhamel, J. R., Cohen, L., Pillon, B., Dubois, B., and Agid, Y. 1996. The mental representation of hand movements after parietal cortex damage. *Science* **273**(5281): 1564–1568.

Snyder, L. H., Batista, A. P., and Andersen, R. A. 2000. Intention-related activity in the posterior parietal cortex: A review. *Vision Res.* **40**(10–12): 1433–1441.

Stephan, K. M., Fink, G. R., Passingham, R. E., Silbersweig, D., Ceballos-Baumann, A. O., Frith, C. D., and Frackowiak, R. S. 1995. Functional anatomy of the mental representation of upper extremity movements in healthy subjects. *J. Neurophysiol.* **73**(1): 373–386.

Richter, W., Somorjai, R., Summers, R., Jarmasz, M., Menon, R. S., Gati, J. S., Georgopoulos, A. P., Tegeler, C., Ugurbil, K., and Kim, S. G. 2000. Motor area activity during mental rotation studied by time-resolved single-trial fMRI. *J. Cogn. Neurosci.* **12**(2): 310–320.

Talairach, J. T., P. 1988. *Co-planar Stereotaxic Atlas of the Human Brain*. Thieme, New York.

Toni, I., Schluter, N. D., Josephs, O., Friston, K., and Passingham, R. E. 1999. Signal-, set- and movement-related activity in the human brain: an event-related fMRI study. *Cereb. Cortex* **9**(1): 35–49.

Toni, I., Thoenissen, D., and Zilles, K. 2001. Movement preparation and motor intention. *Neuroimage* **14**(1 Pt. 2): S110–117.

Wise, S. P., Boussaoud, D., Johnson, P. B., and Caminiti, R. 1997. Premotor and parietal cortex: Corticocortical connectivity and combinatorial computations. *Annu. Rev. Neurosci.* **20:** 25–42.