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The Different Neural Correlates of Action and Functional Knowledge in Semantic Memory: An fMRI Study

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Previous reports suggest that the internal organization of semantic memory is in terms of different "types of knowledge," including "sensory" (information about perceptual features), "action" (motor-based knowledge of object utilization), and "functional" (abstract properties, as function and context of use). Consistent with this view, a specific loss of action knowledge, with preserved functional knowledge, has been recently observed in patients with left frontoparietal lesions. The opposite pattern (impaired functional knowledge with preserved action knowledge) was reported in association with anterior inferotemporal lesions. In the present study, the cerebral representation of action and functional knowledge was investigated using event-related analysis of functional magnetic resonance imaging data. Fifteen subjects were presented with pictures showing pairs of manipulable objects and asked whether the objects within each pair were used with the same manipulation pattern ("action knowledge" condition) or in the same context ("functional knowledge" condition). Direct comparisons showed action knowledge, relative to functional knowledge, to activate a left frontoparietal network, comprising the intraparietal sulcus, the inferior parietal lobule, and the dorsal premotor cortex. The reverse comparison yielded activations in the retrosplenial and the lateral anterior inferotemporal cortex. These results confirm and extend previous neuropsychological data and support the hypothesis of the existence of different types of information processing in the internal organization of semantic memory.

Keywords: anterior inferotemporal cortex, conceptual knowledge, functional semantic features, inferior parietal lobule, manipulative semantic features

Introduction

How is semantic knowledge organized and how it is represented in the brain are central questions of cognitive neuroscience. The investigation of patients who, after a brain lesion, are affected by disorders of semantic memory, which selectively affect knowledge of living or nonliving items, has played a central role in this area of research. Although the existence of category-specific semantic impairment is relatively uncontroversial, the interpretation of the findings derived from the study of these patients remains a matter of discussion. A number of alternative hypotheses have been proposed, and the debate has been extensively reviewed in several recent publications (see, e.g., Laiacona et al. 2003; Thompson-Schill et al. 2003; Gainotti 2004, 2005). A basic distinction is between theories that propose that such category-specific impairments reflect the taxonomical, domain-specific organization of semantic memory (Caramazza and Shelton 1998) and "reductionist" interpretations, which interpret the semantic category effect as a by-product of other noncategorical aspects of conceptual representations. One of the most well-known approaches of the latter type is based on the idea that the internal organization of semantic memory is in terms of different "types of knowledge" (Warrington and Shallice 1984). These include "perceptual" (comprising information about perceptual features) and "functional" (including abstract and propositional properties, such as function, location, and context of use) knowledge. According to the original version of this model, category-specific deficits reflect the differential weighting of these types of knowledge in the semantic representations. Semantic knowledge of animals and other living things, which share a number of characteristics, relies more strongly on perceptual information, whereas knowledge of artifacts, which may share the same function despite remarkably different appearance, is primarily based on functional properties (Warrington and Shallice 1984). This "perceptual–functional" model was subsequently extended to account for a specific deficit at identifying smaller and manipulable items, such as kitchen tools, relative to larger non-manipulable man-made objects, such as vehicles. The revised model underlined the importance of the dominant channel of experience (perceptual or motor) associated with the acquisition, storage, and retrieval of the semantic representation of a given object (Warrington and McCarthy 1987).

As to the neural correlates of semantic knowledge, "feature-based models" are usually grounded in the proposal that object concepts may be represented in the brain as distributed networks of activity in the areas involved in the processing of perceptual or functional knowledge. Indeed, an extensive literature suggests that information about different object features (i.e., different "types of knowledge") may be stored in distinct regions of the cortex. In particular, different activations for the retrieval of functional versus perceptual knowledge (Cappa et al. 1998; Mummery et al. 1998; Thompson-Schill et al. 1999) and perceptual versus manipulative (Phillips et al. 2002) and for specific attributes (color, form, motion) (Chao et al. 1999) have been reported (see Martin and Chao 2001 and Thompson-Schill 2003, for a review).

Although the notion of perceptual features can be easily defined (see, e.g., Vinson et al. 2003), the definition of functional features has been used in a more loose way, to include widely different classes of information. Indeed, it is worth noting that the term functional does not refer exclusively to the knowledge of object's function but rather to those abstract propositional properties of concepts that do not belong to the perceptual or the motor domains (Martin and Chao 2001), for instance, the "context of use." An important distinction to be drawn, in particular, in the case of artifacts, is between functional and action knowledge. Although these 2 types of knowledge have been often treated as a unitary concept in the past, the distinction between them has been recently supported by neuropsychological evidence. In general, the use of an object and the way it is manipulated do not bear any relationship. The distinction between these two aspects is supported by the classical neuropsychological distinction between semantic deficits and apraxia. The latter has been associated with lesions in those frontoparietal structures, which are also responsible for visuomotor transformations from objects' visual properties into actions toward them, and in the retrieval of action knowledge (Haaland et al. 2000). By definition, apraxic subjects should show preserved object identification. On the other hand, there are several reports on record of patients who show a profound impairment of object knowledge but can nonetheless gesture appropriately for objects they fail to identify, in association with anterior, inferotemporal lesions (see, e.g., Sirigu et al. 1991; Buxbaum et al. 1997; Lauro-Grotto et al. 1997; Hodges et al. 1999; Magnie et al. 1999).

The distinction between "what for" knowledge and "how" knowledge was further specified by Buxbaum and Saffran (2002; see also Buxbaum et al. 2000). These authors studied 2 subpopulations of left hemisphere–lesioned patients and observed that apraxic patients with frontoparietal lesions had a specific loss of manipulation knowledge, which was associated with impaired general knowledge about tools and body parts but preserved functional knowledge. The opposite dissociation was observed in a nonapraxics patients, with lesions confined in the temporal lobe. Spatt et al. (2002) confirmed the presence of a severe impairment in mechanical problem solving in corticobasal degeneration, which, however, in some cases may be associated with defective conceptual knowledge, reflecting the overlap of this condition with frontotemporal dementia (Josephs et al. 2006). Moreover, Levy et al. (2004) reported a significant correlation between the extent of anterolateral temporal lesions and the severity of impaired semantic knowledge (including functional features). The site of the lesion in these patients is consistent with the results of a recent positron emission tomography (PET) study, aiming to investigate the cerebral regions recruited by the retrieval of knowledge regarding perceptual (structural and color) and functional aspects of familiar objects (Kellenbach et al. 2005). In fact, the left anterior middle/superior temporal regions and the temporal pole were activated only by the retrieval of functional knowledge, relative to both object structure and color.

The possible anatomical segregation of manipulative and functional knowledge has been already investigated in 2 imaging studies. The left posterior parietal cortex was reported to be more strongly activated by the retrieval of manipulative, compared with object's function, knowledge both by Kellenbach et al. (2003) and Boronat et al. (2005), using PET and epoch-based functional magnetic resonance imaging (*fMRI*), respectively. This region, together with its more occipital extension, is widely considered to be where the interface between perceptually related and action-related processes occur (Rizzolatti et al. 1997). The rostral portion of the inferior parietal lobule and the ventral premotor cortex in the left hemisphere were also activated in the same comparison in the former study. These studies, however, failed to detect cerebral regions specifically activated when retrieving functional knowledge.

In the present study, the cerebral organization of action and functional semantic representations was investigated using event-related modeling of single trials. Based on the above reviewed neuropsychological evidence, we predicted stronger anterior lateral temporal activations for the retrieval of functional knowledge relative to action knowledge and stronger frontoparietal activations in the opposite comparison.

Materials and Methods

Participants

Fifteen right-handed healthy monolingual native speakers of Italian (8 females and 7 males; mean age = 24.6 years; age range = 22–28 years) with normal vision took part in the experiment. Handedness was verified by means of the Edinburgh Inventory (Oldfield 1971). None of them had a history of neurological or psychiatric disorders. Subjects gave informed written consent to the experimental procedure, which was approved by the local Ethics Committee.

Tasks and Experimental Procedure

A semantic-decision task was used, with 2 experimental conditions. Subjects were presented with photographs showing pairs of manipulable man-made objects and asked whether the 2 objects within each pair were used with the same manipulation pattern (i.e., tongs and potato squasher; vacuum cleaner and metal detector) or not ("action knowledge" condition, A), or in the same context, based on their function (i.e., tongs and screwdriver; vacuum cleaner and carpet beater) or not ("functional knowledge" condition, F) (see Table 1 and Fig. 1).

The study was composed by 8 scanning periods lasting 4 min 32 s each. A blocked design for the presentation of the stimulus pairs was used, with every period comprising one A and one F block condition, each including 12 trials overall (see Fig. 1). In each trial, a pair of object was presented. Every block started with a screen alerting the subject ("Ready!," 1000 ms), followed by a screen displaying the instructions (1500 ms), which were phrased as a question ("Same manipulation?" or "Same context of use?" for A and F tasks, respectively). All verbal instructions were presented in Italian. Instructions were followed by a screen displaying the first pair of objects, which was visible for a 4-s period during which subjects had to perform the task and prepare the answer, based on the instructions and the presented objects. These were followed by a white cross on black background, prompting subjects to answer (Yes/No). Subjects were asked to give a vocal response, which was recorded by means of a digital microphone lying outside the scanner room and connected via a plastic tube in proximity of the volunteers' mouth. A vocal, rather than a manual, response was used to reduce possible confoundings with the systems involved in the A task. The appearance of the white cross and the onset of the next trial were separated by a variable-length interval, allowing for implicit modeling of the baseline. In order to optimize statistical efficiency, interstimulus intervals between successive trials within a block were presented in different ("jittered") durations across trials (4.8, 7.2, and 10.1 s, in the proportion of 4:2:1) (Dale 1999). Any possible priming effect within subjects was prevented for by requiring them to name all the 48 stimuli prior to scanning. Stimulus pairs were viewed via a back-projection screen located in front of the scanner and a mirror placed on the head coil. Stimulus pairs were presented, and subjects' answers and experimental timing information were recorded, using the software Presentation 9.13 (http://www.neurobs.com).

Table 1
An example of the object pairs in the 2 tasks

Task	First object	Second object	Same context?	Same manipulation?
F	Poultry shears	Hand spiral beater	Yes	No
F	Poultry shears	Computer keyboard	No	No
A	Poultry shears	Tongs	No	Yes
A	Poultry shears	Stamp for postmark	No	No

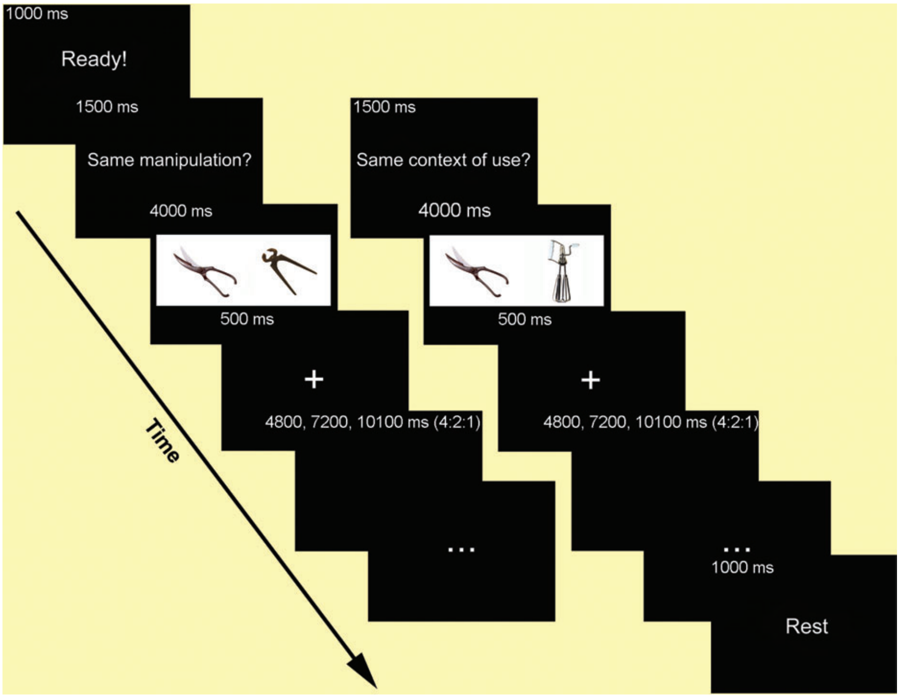

Figure 1. Experimental tasks. Schematic depiction of the sequence of events in a representative trial of A (on the left) and F (on the right) tasks. The numbers reported in the superior and left portion of each image represent the duration of the corresponding event and were not shown to the participants.

Stimuli

Forty-eight digitized color photographs of manipulable man-made objects on a white background served as stimuli. Both large and small objects were depicted as similar sizes. In the F blocks, the objects within a pair always differed in their manner of manipulation, and in the A blocks, they always differed in their context of use. The same set of photographs was used across the 2 tasks. Objects were paired so as that all the 48 stimuli were presented in each period. Therefore, none of the objects was presented more than once within each scanning period, and all were presented exactly 8 times. In both tasks, half the pairs within each block were made to cue a "yes" response, the other half to cue a "no" response. It was possible to create 4 A and 4 F blocks (see Appendix). Within the 4 A and F blocks, each object was always paired with a different object. Each of these blocks occurred twice. The left-right position of the objects within a pair was reversed at the second repetition of each block. The order of the 8 periods, and the order of all the trials within each block, were individually randomized for every subject. In order to avoid the temporal proximity of 2 blocks belonging to the same experimental condition, the order of the 2 blocks within a scanning period was always the same throughout the experiment (AF-AF for 9 subjects, FA-FA for the other 6 subjects).

The consistency with which the pairings between objects were associated with the target (yes or no) response was tested across all stimulus sets by means of a behavioral study, in which 10 subjects (5 females and 5 males who would not take part at the functional study) underwent the same experimental procedure as that described. The results showed an average agreement of 0.97 (standard deviation [SD] = 0.02; range = 0.78–1) and 0.96 (SD = 0.02; range = 0.75–1) for the A and F tasks, respectively. In order to investigate the amount of time needed to produce the response, we carried out a second behavioral study, in which the experimental procedure was slightly modified. Ten subjects (5 females and 5 males) were asked to solve the same task as above, except that they were required to respond as soon as possible. The results showed a small and not statistically significant difference between the reaction time in the tasks F (mean = 1640 ms, SD = 343 ms) and A (mean = 1718 ms, SD = 257 ms) ($F(1,9) = 2.69$; $P > 0.05$). In addition, there was no significant effect of the order of task presentation ($F(7,63) = 1.654$; $P > 0.05$) or a significant interaction between the task and the presentation order ($F(7,63) = 0.506$; $P > 0.05$).

fMRI Data Acquisition

Anatomical T1-weighted and functional T2*-weighted MR images were acquired with a 3 Tesla Philips Intera scanner (Philips Medical Systems, Best, the Netherlands), using an 8-channel Sense head coil (sense reduction factor = 2). Functional images were acquired using a T2*-weighted gradient-echo, echo-planar (EPI) pulse sequence (30 interleaved slices parallel to the anterior commissure-posterior commissure line, covering the whole brain, time repetition [TR] = 2000 ms, time echo [TE] = 30 ms, flip angle = 85°, field of view = 240 × 240 mm, no gap, slice thickness = 4 mm, in-plane resolution 2 × 2 mm). Each scanning sequence comprised 136 sequential volumes. Immediately after the functional scanning, a high-resolution T1-weighted anatomical scan (3D, spoiled-gradient-recalled sequence, 124 slices, TR = 600 ms, TE = 20 ms, slice thickness = 1 mm, in-plane resolution 1 × 1 mm) was acquired for each subject.

Data Analysis

Image preprocessing and statistical analysis were performed using SPM2 (Wellcome Department of Cognitive Neurology; http://www.fil.ion.ucl.ac.uk/spm), implemented in Matlab v6.5 (Mathworks, Inc., Sherborn, MA). The first 5 volumes of each subject were discarded to allow for T1 equilibration effects. EPI images were realigned temporally to acquisition of the middle slice, spatially realigned and unwarped, spatially normalized (voxel size: 2 × 2 × 2 mm) to the Montreal Neurological Institute (MNI) brain template (Evans et al. 1993), spatially smoothed (full-width-half-maximum Gaussian kernel: 6 × 6 × 6 mm) and globally scaled to 100. The resulting time series across each voxel were then high-pass filtered to 1/128 Hz, and serial autocorrelations were modeled as an AR(1) process.

Statistical maps were generated using a random-effect model (Friston et al. 1999), implemented in a 2-level procedure.

At the first level, single-subject *fMRI* responses, synchronized with the acquisition of the middle slice, were modeled as delta "stick" functions by a design matrix comprising the onset of the stimulus pair for each trial of both tasks. An additional regressor per condition was included to model the effect of the type of response (yes or no). Regressors modeling events were convolved with a canonical hemodynamic response function (HRF), along with its temporal and dispersion derivatives, and parameter estimates for all regressors were obtained by maximum-likelihood estimation.

At the second level, random-effect group analyses across the 15 subjects were computed. Statistical parametric maps for the "simple main effects" were generated by an analysis of variance incorporating the HRF and its derivatives for each condition (corrected for nonsphericity using a restricted maximum-likelihood procedure [Friston et al. 2002]). The resulting statistical maps were then used to perform a "conjunction analysis," which tests for areas activated by both tasks, by means of inclusive masking. "Direct comparisons" between tasks were performed using paired *t*-tests on images of the contrasts of HRF parameter estimates, masked by the main effect of the task at $P < 0.001$. All the statistical maps were thresholded at $P < 0.05$, family-wise error corrected for multiple comparisons.

A "regions of interest (ROIs) analysis" was carried out using the Spm-toolbox Marsbar 0.40 (http://marsbar.sourceforge.net). First, we computed the percentage of blood oxygen level-dependent (BOLD) signal change during each task for the regions highlighted by the direct comparisons (see Fig. 2, top). Then, we focused on the involvement of the left occipitoparietal and inferior parietal cortices in the 2 experimental conditions, as these regions have consistently activated in related studies and are ones held to be critical for the perception-action interface. In order to investigate the differential contribution of different areas within this regions in the 2 tasks, the percentage of signal change was examined in 3 stripes of seven 6 mm radius spheres each, running in parallel from the occipital cortex to the rostral portion of the intraparietal sulcus along its fundus (ROIs 8-14) and the uppermost portions of its lateral (1-7) and medial (15-21) banks (see Fig. 3).

The location of the activation foci in terms of Brodmann areas was determined using the nomenclature given by Talairach and Tournoux

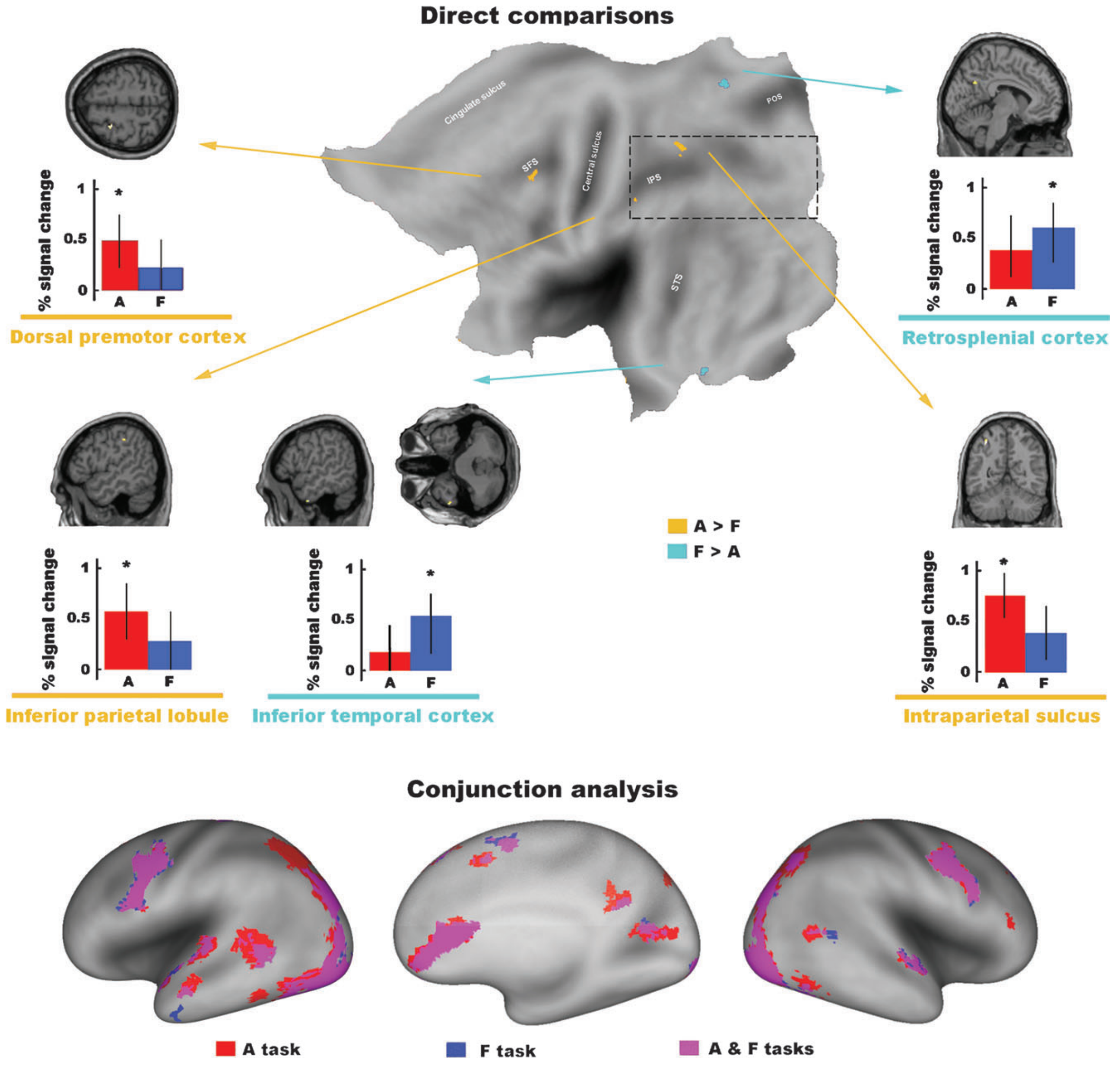

Figure 2. Top: direct comparisons. Activation foci for A versus F (orange) and F versus A (light blue) tasks ($P < 0.05$, family-wise error corrected for multiple comparisons) superimposed on the flattened cortical surface of the left hemisphere. Major sulcal landmarks are labeled. The colored arrows link each activated cluster with a section showing the same activation superimposed on the MNI template provided with SPM2. Under each section, histograms representing the BOLD signal change percentage in both tasks are shown (red, A task; blue, F task). For each effect, standard error bars are indicated. Asterisks above histogram bars show a statistically significant effect ($P < 0.05$). The dashed box on the flattened surface highlights the region investigated in the ROIs analysis described in Figure 3. Bottom: conjunction analysis. Activation foci for the A task (red), the F task (blue) and both tasks as shown by the results of the conjunction analysis (violet) ($P < 0.05$, family-wise error corrected for multiple comparisons). Activations were superimposed on inflated cortical surfaces of the 2 hemispheres. IPS, intraparietal sulcus; POS, parieto-occipital sulcus; SFS, superior frontal sulcus; STS, superior temporal sulcus.

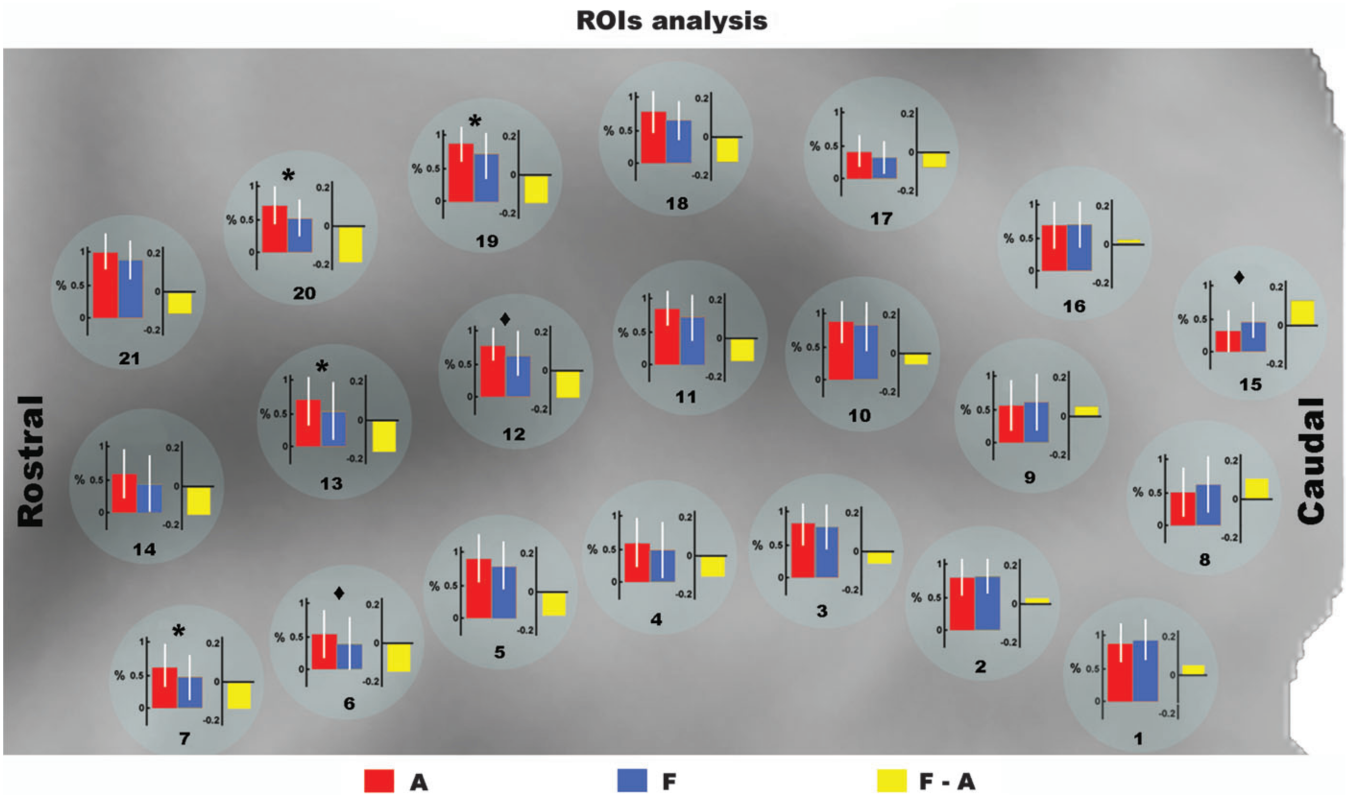

Figure 3. ROIs analysis. The results of the ROIs analysis on the left occipitoparietal and inferior parietal cortices (highlighted by the dashed box in the upper part of Fig. 2) are depicted. The percentage of BOLD signal change in A (red) and F (blue) tasks and the difference between F and A (F minus A: yellow) are shown within each sphere. For each effect, standard error bars are indicated. A single asterisk above histogram bars indicates a statistically significant difference between the 2 tasks (paired *t*-test, $P < 0.05$), whereas effects approaching statistical significance are signaled by ♦; (ROI6, $P = 0.063$; ROI12, $P = 0.055$; ROI 15, $P = 0.072$).

(1988) after correcting for differences between the MNI and Talairach coordinate systems by means of a nonlinear transformation (see http://imaging.mrc-cbu.cam.ac.uk/Imaging/MniTalairach). For visualization purposes, the activated foci were superimposed on inflated or flattened cortical surfaces of the 2 hemispheres using Caret 5.4 software (http://brainmap.wustl.edu/caret.html).

Results

Behavioral results during functional scanning showed no significant difference in the percentage of correct answers between the A (mean = 0.95, SD = 0.02) and the F (mean = 0.96, SD = 0.01) tasks ($F(1, 14) = 0.356$, $P > 0.05$). Moreover, there was no significant effect of the order of task presentation throughout the 8 scanning sequences ($F(7,98) = 0.898$; $P > 0.05$) or a significant interaction between the task and the presentation order ($F(7,98) = 0.400$; $P > 0.05$).

Turning to the imaging results, the analysis of simple main effects showed comparable cerebral networks recruited in the 2 experimental conditions (see Fig. 2, bottom). Both tasks, in fact, activated bilaterally the same temporo-occipital, medial frontal and lateral frontal cerebral regions. Regions differentially activated by either task were observed as well: the left lateral anterior inferotemporal cortex was activated in the F task only, whereas the posterior parietal cortex was bilaterally activated in the A task only. No significant effect of the type of response (yes or no), or an interaction between the latter and the task, was observed. No activation was observed in the rostral portion of the inferior parietal lobule in any of the 2 tasks using a corrected statistical threshold. However, the fact that an activation in these region was predicted based on previous related findings (see Introduction) justified the use of an appropriate correction (small volume correction, SVC; Worsley et al. 1996). The procedure was applied to a 6 mm radius sphere centered on the coordinates which Grezes et al. (2003) derived by averaging the coordinates reported in 5 related studies ($x = -37$, $y = -40$, $z = 44$). The results showed that, with such a correction, a significant activation ($P < 0.05$) was observed in this region in the A, but not in the F, task.

The conjunction analysis showed the commonalities between tasks (see Fig. 2, bottom and Table 2). In the frontal lobe, common activations were observed in the precentral gyrus (Brodmann areas [BA] 6) and, in the medial wall, both in the pre-supplementary motor area (SMA) and in the proper-SMA (BA 6). In addition, the superior frontal gyrus (BA 8) was also activated, bilaterally, in both tasks. Common activations were also observed in the anterior cingulate gyrus (BA 24, 32), extending rostrally into the medial frontal gyrus (BA 10). In the temporal lobe, common activations were observed bilaterally in the posterior lateral temporal cortex and the superior temporal gyrus (BA 22) and in the anterior portion of the middle temporal gyrus (BA 21) on the left. In the occipital lobe, both tasks activated bilaterally a large occipitotemporal cluster, extending from the inferior and middle occipital gyri (BA 18, 19) through the inferior temporal and the fusiform gyrus (BA 37, 20). The precuneus (BA 31, 7) was activated as well. Finally the parieto-occipital junction, at the border between the superior occipital gyrus and the angular gyrus (BA 19), was also bilaterally activated.

Table 2

Spatial coordinates of the local maxima in the group analysis

H	Anatomical region	MNI			t-value
		x	y	z	
Conjunction analysis					
L	Inferior occipital gyrus	−24	−100	−10	24.98
R	Inferior occipital gyrus	14	−96	−6	17.48
L	Middle occipital gyrus	−30	−86	8	24.75
R	Middle occipital gyrus	34	−94	4	23.61
L	Fusiform gyrus	−32	−46	−28	35.65
R	Fusiform gyrus	34	−48	−28	35.19
L	Precuneus	−12	−62	18	29.74
R	Precuneus	12	−62	14	30.65
L	Posterior middle temporal gyrus	−52	−58	10	27.47
R	Posterior middle temporal gyrus	54	−54	12	19.98
L	Superior temporal sulcus	−54	−64	24	19.53
R	Superior temporal sulcus	54	−62	16	27.93
L	Superior temporal gyrus	−62	−24	10	29.06
R	Superior temporal gyrus	60	−26	6	21.57
L	Middle temporal gyrus	−56	−14	−24	19.30
L	Superior occipital gyrus	−30	−78	24	24.98
R	Superior occipital gyrus	28	−72	32	26.34
R	Superior parietal lobule	30	−66	52	23.61
L	Ventral premotor cortex	−58	−6	42	21.80
R	Ventral premotor cortex	56	−10	46	18.39
L	Opercular premotor cortex	−60	−6	8	21.99
R	Opercular premotor cortex	64	−2	10	28.84
L	Superior frontal gyrus	−18	38	46	22.02
R	Superior frontal gyrus	20	26	48	17.94
L/R	Pre-SMA	0	10	52	24.29
L/R	SMA-Proper	0	−4	58	36.33
L/R	Anterior cingulate gyrus	−2	26	14	33.15
R	Anterior cingulate gyrus	4	28	10	29.74
L	Anterior cingulate gyrus	−4	40	−2	24.75
L/R	Medial frontal gyrus	−2	50	−4	23.61
Direct comparisons					
A > F					
L	Intraparietal sulcus	−32	−56	54	9.80
L	Inferior parietal lobule	−50	−30	42	8.07
L	Dorsal premotor cortex	−26	4	58	9.77
F > A					
L	Lateral anterior inferotemporal cortex	−54	−2	−38	11.23
L	Retrosplenial cortex	−6	−60	30	9.70

Note: Stereotactic coordinates and t-values of the foci of maximum activation in the conjunction analysis and in the direct comparisons ($P < 0.05$, family-wise error corrected for multiple comparisons). Coordinates are expressed in MNI space adopted by SPM2 in terms of distance (in mm) from the anterior commissure. The foci were anatomically localized on the standard stereotactic brain atlas developed by Talairach and Tournoux (1988) after correcting for differences between the MNI and Talairach coordinate systems using a nonlinear transformation. H, hemisphere.

"Direct comparisons" highlighted the selective differences between the tasks: (see Fig. 2, top and Table 2). Compared with the F task, the A task activated the left caudal intraparietal sulcus (BA 7), the rostral portion of the inferior parietal lobule (BA 40), and the dorsal premotor cortex (BA 6). The reverse comparison revealed an activation in the lateral anterior portion of the inferior temporal gyrus (BA 20/21) as well as in the retrosplenial cortex (BA 7).

The general picture shown by the statistical maps of the main effects was confirmed by the results of the ROIs analysis on the percentage of signal change in the areas which were highlighted by the direct comparisons (see Fig. 2, top). In addition, the ROI analysis on the left occipitoparietal and inferior parietal cortices confirmed the differential involvement of these regions in the 2 tasks. For all the 3 stripes of ROIs, direct comparisons between average BOLD signal for the 2 tasks in each ROI largely confirmed the prediction. The only statistically significant differences (paired t-test, $P < 0.05$) between the 2 tasks were observed in the rostral ROIs (approximately in the same cerebral regions where significant differences were also highlighted in the statistical maps; see asterisks in Fig. 3). Nonetheless, a larger BOLD signal for the F, compared with A, task (as indicated by a positive difference between the respective average intensity values; see yellow columns in Fig. 3) was observed in the first 2 ROIs of each strip, located in occipital BA 18 and 19. In contrast, an increasingly larger BOLD signal for the A, compared with the F, task was observed in the more rostral ROIs, extending from occipitoparietal BA 19 through caudal (BA 7) to rostral (BA 40) inferior parietal regions. Such an increase was observed to grow constantly up to the last ROI of each strip, where the difference started to decrease. The statistical significance of this trend was assessed by means of a multiple regression on the difference between the signal intensity in the 2 tasks (A minus F), which showed a significant effect of the position of the ROI (1–7) ($t(18) = 2.82$; $P < 0.05$) and no significant effect of the stripe (1–3) ($t(18) = -0.29$; $P > 0.05$]).

Discussion

The imaging results indicated that, although the patterns of activation in the 2 tasks largely overlap, some cerebral regions are preferentially activated by each experimental condition (i.e., dependently of the specific type of knowledge retrieved). We first discuss the differential activations and then consider those that were commonly activated in the 2 tasks.

Neural System Related to Action Knowledge

Direct comparisons highlighted a left frontoparietal cerebral network, which was more strongly activated by manipulation than functional judgments, including the caudal intraparietal sulcus (BA 7), the rostral portion of the inferior parietal lobule (BA 40), and the dorsal premotor cortex (BA 6) (see Fig. 2, top). All these regions are part of the neural circuits responsible for object-related action organization and control.

The posterior parietal cortex is known to play a critical role in the sensorimotor transformations underlying action organization and objects' use. The likely involvement of this region in a direct "pragmatic" route from vision to object-directed action has been initially fueled by neuropsychological double dissociations between object use and semantic knowledge of objects (Goodale et al. 1991; Hodges et al. 1999). This view has been confirmed by recent neurophysiological data, indicating that this region consists of a mosaic of areas, each receiving specific sensory information and transforming it into information appropriate for action organization (see Rizzolatti and Luppino 2001 for a review).

The location of the 2 foci resulting from the A > F comparison is consistent with this view. The most posterior of the foci was located in the caudal portion of the intraparietal sulcus, a region that has typically been associated with observation of object-related actions in previous studies (Buccino et al. 2001, 2004a, 2004b) and explained in terms of higher order visual functions, possibly reflecting the first stages of the extraction of object affordances (Buccino et al. 2004a, 2004b). The second activated parietal focus was located in the rostral portion of the inferior parietal lobule, a region involved in computing the sensorimotor transformations necessary for grasping and manipulating objects and most likely corresponding to primate anterior intra-parietal areas. Based both on neurophysiological (Taira et al. 1990; Sakata and Taira 1994; Sakata et al. 1995) and inactivation (Gallese et al. 1994) data, it has been suggested that this area provides multiple descriptions of a three-2dimensional object, thus facilitating several different possibilities for grasping it (Gallese et al. 1997). A region with analogous properties has been described in the human brain, in the anterior part of the lateral bank of the intraparietal sulcus, approximately at the same location as that reported here (Decety et al. 1994; Bonda et al. 1996; Grafton et al. 1996a, 1996b; Binkofski et al. 1998, 1999; Krams et al. 1998; Moll et al. 2000; Perani et al. 2001; Grefkes et al. 2002; Grezes and Decety 2002; Johnson-Frey et al. 2005).

To summarize, the available evidence is in agreement with the proposed interplay between perception and action in the left occipitoparietal and posterior parietal cortices (Rizzolatti et al. 1997, 2001b). Such a view suggests that different portions of a perception-to-action system should be preferentially involved in the 2 tasks, the rostral, inferior parietal, portion being more strongly activated by manipulation, compared with functional judgments, with its caudal, occipitoparietal part being more strictly associated with the more visually demanding processing required by the F task. This hypothesis was confirmed by the results of the ROIs analysis on the percentage of BOLD signal change in these regions in the 2 tasks (see Materials and Methods and Fig. 3), which showed a statistically significant shift in the percentage of BOLD signal change from F to A task when moving from caudal to rostral ROIs. This confirms the existence of a perceptual-to-motor gradient in the activity of the left occipitoparietal and posterior parietal cortex and provides further support for the hypothesis that the cerebral regions resulting from the A > F comparison are part of a graded process, involved in the visuomotor analysis of objects' properties for their use.

A third focus selective for the A task was located in the left dorsal premotor cortex. This region is known to be involved in movement selection. Lesions in premotor cortex disrupt the selection of responses to visual cues both in monkeys (Halsband and Passingham 1985; Petrides 1987) and in patients (Halsband and Freund 1990). By using transcranic magnetic stimulation, Schluter et al. (1998) demonstrated that stimulation over the dorsal premotor cortex (mainly in the left hemisphere) can temporarily interfere with the selection of movements that are instructed by visual cues. The involvement of the dorsal premotor cortex in movement selection was further supported by the imaging data provided by Johnson et al. (2002), Grezes et al. (2003), and Choi et al. (2001).

Neural System Related to Functional Knowledge

In the complementary comparison, which failed to yield any significant results in previous studies, 2 regions were more strongly activated by functional than by manipulation judgments (see Fig. 2, top). The first is in the retrosplenial cortex. This is consistent with the results reported by Bar and Aminoff (2003), who found that observing objects with a characteristic context of use (e.g., roulette), by comparison with those that lack such a context (e.g., mobile phone), activates the parahippocampal cortex (PHC) and the retrosplenial cortex. In addition, they observed that only the latter structure is activated independently of the presence or absence of the object's typical background (e.g., a casino) and by both spatial (e.g., a kitchen) and nonspatial (e.g., a birthday) contexts. They argued that both these structures are involved in the analysis of context but with a different level of abstraction: whereas the PHC is more strictly associated with the analysis of visual properties that define a specific place, the retrosplenial cortex holds the abstract representations of an object's contextual associations, whose retrieval is essential in the current task. This might explain why only the latter was found active in the present study: subjects were presented with objects "floating" in isolation on a white background, and both objects characterized by spatial (e.g., a kitchen) and by nonspatial context (e.g., sport) might be presented within a given trial. Based on the data provided by Bar and Aminoff (2003), both these factors were likely to facilitate the activation of the retrosplenial, compared with the parahippocampal, cortex.

The second region that resulted from the F > A comparison is in the lateral anterior inferotemporal cortex. This is in excellent agreement with previous neuropsychological data showing a loss of functional knowledge, with preserved action knowledge, after a damage to this region in certain patients with semantic dementia (Buxbaum et al. 1997; Lauro-Grotto et al. 1997; Hodges et al. 1999) and herpes simplex encephalitis (Sirigu et al. 1991). Semantic dementia is typically characterized by progressive atrophy involving the anterolateral temporal cortex, particularly in the left hemisphere (Mummery et al. 2000), and herpes simplex encephalitis involves nearby areas. This fits with the suggestion of Damasio (1989, 1990) that the anterior temporal lobe is a higher order convergence zone, which integrates simple semantic features (and which would therefore include functional features) into a single object representation (see also Devlin et al. 2002 and Noppeney and Price 2002). Supporting evidence comes from neurophysiological studies on monkeys (Meunier et al. 1993; Buckley et al. 1997; Murray and Bussey 1999), imaging data in humans (Damasio et al. 1996; Gauthier et al. 1997), and lesion simulations on connectionist models by Bussey and Saksida (2002). The involvement of the anterior, inferior temporal cortex in the present study may thus be explained in terms of retrieval and integration of multiple semantic features, which are processed in different and specific cerebral regions (the retrosplenial cortex, in the case of the typical context of use).

It has been suggested that featural integration may be particularly important in the representation of stimuli in the "living" domain, which are associated with more featural overlap between category members than, say, tools (Devlin et al. 1998; Tyler et al. 2000; McRae and Cree 2002) and consequently may rely more heavily on anterior inferotemporal activity (Devlin et al. 2002). However, the processing of "living" stimuli is typically associated with activity of the more medial portions of the anterior temporal cortex (see Devlin et al. 2002). Instead, consistent with previous clinical reports (see Gainotti 2000; Mummery et al. 2000), its lateral portion was specifically activated by the retrieval of functional knowledge in the present study. This discrepancy suggests a functional specialization within this cerebral region. The medial portion of the anterior and inferior temporal cortex may be involved in the integration of perceptual features, whereas its lateral portion may be more engaged by the integration of abstract features, including those related to functional knowledge.

Common Activations

Both tasks activated bilaterally a cluster of areas extending from the inferior and middle occipital gyri (BA 18, 19) to the fusiform gyrus (BA 37, 20), corresponding to the so-called "lateral occipital complex." This region is known to play an important role in both explicit (see Grill-Spector et al. 2001 for a review) and implicit (Pins et al. 2004) object recognition.

In the temporal lobe, the region at the border between the posterior part of the middle and the superior temporal gyrus has been extensively shown to be involved in processing objects, and actions on them, in a variety of experimental tasks in previous studies (Cappa et al. 1998; Mummery et al. 1998; Moore and Price 1999; Perani et al. 1999; Devlin et al. 2002; Phillips et al. 2002; Grezes et al. 2003; Creem-Regehr and Lee 2005; Johnson-Frey et al. 2005; see Lewis 2006 for a review), and its damage has been associated with a selective loss of knowledge about tools by Tranel et al. (1997). Based on its proximity to the MT/V5 complex, this region has been associated with processing of different features of moving stimuli (Chao et al. 1999) and in particular of nonbiological tool motion (Beauchamp et al. 2002, 2003; Kable et al. 2005). The same region as that described here was found by Ruby and Decety (2001) to be activated during mental simulation of object use, suggesting an automatic activation of implicit motion imagery by visual presentation of objects in the present study. This also fits with the activation of the medial precuneus, which has been previously involved in imagery (Fletcher et al. 1995, 1996), also in the motor domain (Bonda et al. 1995; Parsons et al. 1995; Gerardin et al. 2000; Ruby and Decety 2001; Hanakawa et al. 2003). A second temporal focus of activation was observed in the anterior portion of the left middle temporal gyrus, which, according to previous reports, is associated both with the acquisition (Maguire and Frith 2004) and the retrieval of different kinds of semantic information (Vandenberghe et al. 1996; Phillips et al. 2002).

In the precentral gyrus, the dorsal-most activation foci were located close to the hand/arm premotor cortex field, previously associated with manipulation of complex objects (Binkofski et al. 1999) and mental simulation of hand actions across different tasks (Decety et al. 1994; Parsons et al. 1995; Stephan et al. 1995; Grafton et al. 1996b; Krams et al. 1998; Ruby and Decety 2001; Grezes and Decety 2002). Activation extended caudally to the ventral premotor cortex, which has consistently been associated with perceptual and semantic tool–related tasks (Martin et al. 1996; Perani et al. 1999; Chao and Martin 2000; Devlin et al. 2002; Kellenbach et al. 2003; Fridman et al. 2006; see Lewis 2006 for a review). Noteworthily, both the dorsal and the caudal sectors of the cluster here described were found to be active also during passive object viewing by Grafton et al. (1997) and Grezes and Decety (2002) and interpreted in terms of implicit activation of motor representations by their visual presentation. This can also explain the activation in the SMA (from the rostral-most portion of the SMA-proper to the pre-SMA), which were found to be active during simple observation of objects by Grafton et al. (1997) and Grezes and Decety (2002).

A similar interpretation may be proposed for the activations in the anterior cingulate cortex (BA 24, 32), extending into the orbital portion of the medial frontal gyrus (BA 10), whose involvement has been previously interpreted in terms of inhibition of the observed actions by Decety et al. (1997) and whose damage is typically associated with the so-called "utilization behavior" (Lhermitte 1983; Lhermitte et al. 1986; Shallice et al. 1989). Instead, the activation of the dorsal portion of this medial cluster, which is located in the supracallosal portion of the anterior cingulate cortex (BA 24/32), is likely to reflect the overall change in cognitive demands over time in carrying out the tasks. Stuss et al. (2005), in fact, have recently suggested this portion of the medial frontal cortex to be critical for 3 putative components of the so-called Supervisory System of Norman and Shallice (1986): energizing (activation and energization of the neural systems required to make the decision), inhibition of wrong responses, and monitoring the level of activity of these schemata (see also Luria 1973; Drewe 1975; Plum and Posner 1980; Leimkuhler and Mesulam 1985; Alexander 2001).

However, the interpretation of the results of a conjunction analysis is not always straightforward. The involvement of the same cerebral areas in 2, or more, experimental conditions suffers from different possible interpretations. The first is the one that is most often adopted in papers, namely, that all of the contrasting theoretical processes that are being assessed separately in one of the conditions require the observed, commonly activated regions. The second arises from the so-called "switch costs," that is, from carrying out an overall task that requires a switch in each period between 2 blocks and in each of which a different task is carried out on the same set of stimuli. Wylie and Allport (2000) used color/word Stroop and contrasted word naming with naming its color in successive alternating blocks. They found that although one of the tasks is being carried out, the other one continues to remain primed and so interferes with the first. Thus, a weaker activation related to 1 of the 2 tasks in our study may merely reflect the fact that the influence of a task in one block persists in a weaker form in the next block. Thus, in these cases observed common activations may not have been such if the study had been run on separate groups of subjects. A third possibility is that the existence of commonly activated regions and regions activated in A but not in F task derives from the lower sensitivity of the latter, compared with the former, say because of lower general attentional demands. Because, however, the 2 tasks activate occipital regions to roughly the same amount, it seems that this possibility can be discounted. Further studies are required to distinguish among these 3 possibilities.

Differences with Respect to Previous Related Studies

The involvement of the anterior inferotemporal cortex in the retrieval of functional knowledge was largely predicted based on previous neuropsychological findings. Yet, both Kellenbach et al. (2003) and Boronat et al. (2005) have failed to detect it. How to account for this discrepancy? The former study was based on a different task. Subjects were shown the picture of an object and asked whether it was used with a specific movement (e.g., with a circular motion, manipulative task) or to a specific goal (e.g., to alter the shape of another object, functional task). Hence, subjects were required to respond yes or no to a manipulative/functional feature that was already available to them, rather than to actively retrieve it. However, the anterior inferotemporal cortex has been associated with the active retrieval and linkage of semantic features, which are processed in other cortical regions (Noppeney and Price 2002). The fact that specific activations for manipulative judgments were still observed is likely to reflect the prominent role of action knowledge in the semantic representation of tools.

Instead, Boronat et al. used an identical task. However, an important difference can be found in the way single trials were statistically modeled. Whereas we analyzed single events within blocks, whole epochs were modeled by Boronat et al. Yet, based on the reaction times they report, it is likely that in each trial, subjects were engaged in the retrieval component of the task for less than half of the overall period during which activity was measured. In this kind of task, an event-related analysis, in which the hemodynamic responses to stimulus-induced neuronal transients are modeled without assuming constant within-block activity (Mechelli et al. 2003, p. 806), may capture changes in cerebral activity that cannot be accounted for by an epoch-based model.

Thus, we reanalyzed our data set using an "epoch-like" approach, modeling mini-epochs of 2500 ms (convolving the stimulus function with the canonical HRF only). Although longer than the amount of time actually needed by the subjects to respond, the length of this period is shorter than the epochs analyzed by Boronat et al. Thus, any negative result found in the former case should be valid for the latter as well. Direct comparisons between tasks showed that no cerebral region was more strongly activated by functional, compared with manipulative, knowledge at the same corrected statistical threshold as both in our primary analysis and in Boronat et al. The activation of the inferotemporal focus reported in the primary analysis was observed only at an uncorrected threshold of $P < 0.001$. The opposite comparison revealed an activation in the caudal portion of the left intraparietal sulcus ($x = -34$, $y = -60$, $z = 54$), in the region they also reported ($x = 40$, $y = -63$, $z = 40$). Overall, this strongly suggests that the different statistical analysis to be the most likely reason for the discrepancy between findings of Boronat et al. and our findings.

Conclusions

In conclusion, both tasks activated a set of areas that are involved in the structural analysis and recognition of objects, tool-related action processing, and mental simulation of their use. The observed pattern of activation is coherent with previous studies, indicating 2 distinct regions to be consistently and automatically activated in studies employing tools as stimuli: the posterior temporal cortex and ventrolateral premotor cortex, likely reflecting the automatic engagement of cerebral structures associated with their use. This is consistent with previous reports, suggesting that simple perception of objects affords action toward them (Grezes and Decety 2002; Johnson-Frey et al. 2005). In addition, the observation of cerebral regions that were preferentially activated in either task confirms and extends previous neuropsychological evidence, supporting the hypothesis of different types of information processing in the internal organization of semantic memory. The involvement of the frontoparietal circuits responsible for object-related actions in the retrieval of action knowledge supports the strict link between action and cognition, and the contribution of cortical motor system to cognitive tasks that do not involve motor responses, already suggested in other domains (Rizzolatti et al. 2001b). Further, functional knowledge is at least not entirely dependent on the activity of these neural circuits but rather engages anterior temporal areas related to object-specific conceptual knowledge.

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Appendix

Tables A1–A4.

Table A1

Task	Response	Number	First object	Second object
F	True	1	Steering wheel	Battery clamps
F	True	2	Hockey stick	Hand grippers
F	True	3	Bellows	Gas lighter
F	True	4	Stretcher	Sphygmomanometer
F	True	5	Hoover	Carpet beater
F	True	6	Spiral beater	Poultry shears
F	False	7	Rotovator	Telephone keyboard
F	False	8	Nail polish	Doorknob
F	False	9	Metal detector	Shopping trolley
F	False	10	Push-botton calculator	Potato masher
F	False	11	Parrot pliers	Broom
F	False	12	Door handle	Pump horn
A	True	13	Screwdriver	Pencil sharpener with pencil
A	True	14	Meat pounder	Stamp for postmark
A	True	15	Nutcrackers	Pliers
A	True	16	Accordion	Pectoral expander
A	True	17	Piano keyboard	Computer keyboard
A	True	18	Colander	Mesh strainer
A	False	19	Tongs	Fly swatter
A	False	20	Stapler	Light bulb
A	False	21	Lever for water tubes	Correcting fluid
A	False	22	Pruning shears	Two-handled chopper
A	False	23	Machine gun	Fly reel
A	False	24	Garden roller	Electric drill

Table A2

Task	Response	Number	First object	Second object
F	True	1	Computer keyboard	Push-botton calculator
F	True	2	Electric drill	Screwdriver
F	True	3	Parrot pliers	Lever for water tubes
F	True	4	Potato masher	Meat pounder
F	True	5	Piano keyboard	Accordion
F	True	6	Doorknob	Door handle
F	False	7	Fly reel	Garden roller
F	False	8	Mesh strainer	Telephone keyboard
F	False	9	Pencil sharpener with pencil	Colander
F	False	10	Nutcrackers	Nail polish
F	False	11	Gas lighter	Correcting fluid
F	False	12	Broom	Rotovator
A	True	13	Hand grippers	Battery clamps
A	True	14	Tongs	Poultry shears
A	True	15	Carpet beater	Fly swatter
A	True	16	Two-handled chopper	Steering wheel
A	True	17	Hoover	Metal detector
A	True	18	Bellows	Pruning shears
A	False	19	Pump horn	Stapler
A	False	20	Light bulb	Sphygmomanometer
A	False	21	Pliers	Stamp for postmark
A	False	22	Hockey stick	Spiral beater
A	False	23	Stretcher	Pectoral expander
A	False	24	Shopping trolley	Machine gun

Table A3

Task	Response	Number	First object	Second object
F	True	1	Two-handled chopper	Nutcrackers
F	True	2	Pruning shears	Pliers
F	True	3	Mesh strainer	Metal detector
F	True	4	Steering wheel	Pump horn
F	True	5	Colander	Potato masher
F	True	6	Screwdriver	Tongs
F	False	7	Carpet beater	Accordion
F	False	8	Correcting fluid	Pectoral expander
F	False	9	Hoover	Lever for water tubes
F	False	10	Sphygmomanometer	Nail polish
F	False	11	Pencil sharpener with pencil	Battery clamps
F	False	12	Piano keyboard	Shopping trolley
A	True	13	Door handle	Light bulb
A	True	14	Gas lighter	Stapler
A	True	15	Telephone keyboard	Push-botton calculator
A	True	16	Fly reel	Spiral beater
A	True	17	Rotovator	Stretcher
A	true	18	Hockey stick	Broom
A	False	19	Meat pounder	Doorknob
A	False	20	Hand grippers	Fly swatter
A	False	21	Stamp for postmark	Poultry shears
A	False	22	Electric drill	Compute keyboard
A	False	23	Parrot pliers	Machine gun
A	False	24	Bellows	Garden roller

Table A4

Task	Response	Number	First object	Second object
F	True	1	Rotovator	Pruning shears
F	True	2	Stapler	Pencil sharpener with pencil
F	True	3	Broom	Fly swatter
F	True	4	Pectoral expander	Hockey stick
F	True	5	Two-handled chopper	Meat pounder
F	True	6	Spiral beater	Nutcrackers
F	False	7	Hoover	Piano keyboard
F	False	8	Carpet beater	Push-botton calculator
F	False	9	Metal detector	Colander
F	False	10	Poultry shears	Computer keyboard
F	False	11	Telephone keyboard	Tongs
F	False	12	Door handle	Battery clamps
A	True	13	Correcting fluid	Nail polish
A	True	14	Doorknob	Lever for water tubes
A	True	15	Pump horn	Sphygmomanometer
A	True	16	Shopping trolley	Garden roller
A	True	17	Parrot pliers	Potato masher
A	True	18	Electric drill	Machine gun
A	False	19	Gas lighter	Screwdriver
A	False	20	Stamp for postmark	Hand grippers
A	False	21	Pliers	Light bulb
A	False	22	Steering wheel	Bellows
A	False	23	Accordion	Stretcher
A	False	24	Fly reel	Mesh strainer

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