Visual features of an observed agent do not modulate human brain activity during action observation

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ABSTRACT

Recent neuroimaging evidence in macaques has shown that the neural system underlying the observation of hand actions performed by others (i.e., "action observation system") is modulated by whether the observed action is performed by a person in full view or an isolated hand (i.e., type of view manipulation). Although a human homologue of such circuit has been identified, whether in humans the neural processes involved in this capacity are modulated by the type of view remains unknown. Here we used functional magnetic resonance imaging (fMRI) to investigate whether the "action observation system", with specific reference to the ventral premotor cortex, responds differentially depending on type of view. We also tested this manipulation within regions of the human brain showing overlapping activity for both the observation and the execution of action ("mirror" regions). To this end, the same subjects were requested to observe grasping actions performed under the two types of view (observation conditions) or to perform a grasping action (execution condition). Results from whole-brain analyses indicate that overlapping activity for action observation and execution was evident in a broad network of areas including parietal, premotor and temporal cortices. Activity within such network was evident for both the observation of a person in full view or an isolated hand, but it was not modulated by the type of view. Similarly, results from region of interest (ROI) analyses, performed within the ventral premotor cortex, did confirm that this area responded in a similar fashion following the observation of either an isolated hand or an entire model acting. These findings offer novel insights on what the "action observation" and the "mirror" systems visually code and how the processing underlying such coding may vary across species. Further, they support the hypothesis that action goal is amongst the main determinants for the revelation of action observation activity, and to the existence of a broad system involved in the simulation of action.

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Introduction

Mirror neurons are a class of visuomotor neurons activated by both the execution and the passive observation of object-related actions. Cells having this property were found in macaques within the convexity behind the arcuate sulcus (area F5c) within the premotor cortex (Di Pellegrino et al., 1992; Gallese et al., 1996; Rizzolatti et al., 1996a), and in the complex PF/PFG (PF) within the rostral part of the convexity of the inferior parietal cortex (Gallese et al., 2002; Fogassi et al., 2005).

Following this discovery, many functional resonance imaging (fMRI) studies have been performed in order to uncover a similar system in humans (for review see Dinstein et al., 2008; Turella et al.,

2009). Amongst these studies the most convincing evidence of a "mirror-like" system in humans comes from a study by Gazzola et al. (2007a,b) and Gazzola and Keysers (2008) who tested both action execution and observation within the same individuals. In one day they asked participants to observe either a human model or an industrial robot performing a variety of actions and in a separate day to perform the actions. They found regions of overlap for action observation and execution in classic 'mirror' areas together with many areas which were not previously considered as mirror (Gazzola et al., 2007a,b, Gazzola and Keysers, 2008). Further, another interesting finding stemming from this work is that the mirror system is similarly activated by the sight of both the human and the robotic hand. This occurred despite the movement of the two agents exhibiting dramatically different kinematics. This was taken as the evidence that action goal rather than a tight kinematic match is amongst the main determinants for the revelation of mirror activity.

In this connection, recent findings from a fMRI study investigating the neural underpinnings of action observation in monkeys add a

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further level of complexity regarding the visual requirements necessary to activate the 'observation' component of the mirror system (Nelissen et al., 2005). Monkeys observed video clips showing a full view of a person grasping an object or an isolated hand grasping objects and static single frames or scrambled videos as controls. It was found that premotor area F5c (the area in which mirror neurons were first discovered) was active only when the monkey observed a human model presented in her entirety grasping an object, but it was not active when it observed a human hand detached from the body performing the task. In the other subregions of F5 (i.e., F5a, F5p) activation due to action observation was reported for both the model and the hand alone acting. These results seem to suggest that the type of view alerts different sectors of the premotor cortex and this occurs despite the fact that the goal for the two different agents, both biological in nature and presumably showing similar kinematics, remains the same. Therefore it might well be that visual features of agents are as important as action goal for modulating action observation activity, at least within the core "mirror" area F5c. We do not know whether manipulation concerned with the type of model would have produced similar results in other areas, with or without "mirror" properties, given that in this study the investigation was restricted to the ventral premotor cortex and nearby prefrontal regions by means of regions of interest (ROI) analyses (Nelissen et al., 2005).

Here we capitalize on the above mentioned findings to investigate for the first time whether in humans, as happens in monkeys, the action observation system or part of it is differentially activated depending on the type of view irrespective of action goal. This is a reasonable question to ask considering that a number of fMRI studies in humans have shown that action observation in humans evokes widespread frontal activation, including that of premotor area 6 and of prefrontal areas 44 and 45 which may modulate, as reported in monkeys (Nelissen et al., 2005) depending on the type of view (for review see Turella et al., 2009). Further, because 'mirror' activity in humans is detected across a number of areas which exceed those classically considered as 'mirror' (Gazzola et al., 2007a,b, Gazzola and Keysers, 2008), it may be relevant to test the possible differences related to the type of view at whole-brain level in terms of action observation and execution overlapping activity.

Therefore, here we asked the same individual to observe a grasping action performed either by a fully visible model or by a hand alone (action observation conditions) and to perform a visually-guided grasping action (action execution condition) while scanned. These data may allow us to identify overlapping areas for both the observation and the execution of hand actions and how such activity might be modulated by the type of model.

Materials and methods

Subjects

Seventeen paid right-handed volunteers (10 female, mean age 27.8 years, range 21–39) were recruited for the present study. They all had normal or corrected to normal vision and had no history of neurological problems. Informed consent was obtained from all subjects before the testing session in accordance with the declaration of Helsinki. One subject was discarded due to head motion exceeding 3 mm (voxel size).

Apparatus

We used a custom-built MRI-compatible apparatus consisting of two main parts (Fig. 1A). A lower part embedding a screen which served to present the video clips and an upper part consisting of a pneumatic piston containing a stick with a spherical stimulus attached to it. The stimulus could be lowered down within the scanner at a reachable distance using compressed air. The use of a pneumatic/mechanical apparatus allowed for a precise control of the timing of the sequence of events and to avoid the interaction of the subject with the experimenter. The apparatus was positioned over the subject's legs and the subject's head was tilted in the coil (30°) allowing both the screen and the stimulus (when lowered down) to be visually available by the subjects.

Stimuli

Action observation

Four different types of video clips served as stimuli (4 s duration, AVI format, Xvid codec compression, resolution 360×240, 25 frames per second). As shown in Fig. 1B these video clips could represent: (i) a human model grasping an object; (ii) a static human model with the hand resting on the table in the proximity of the object; (iii) a human hand grasping an object; and (iv) a static human hand
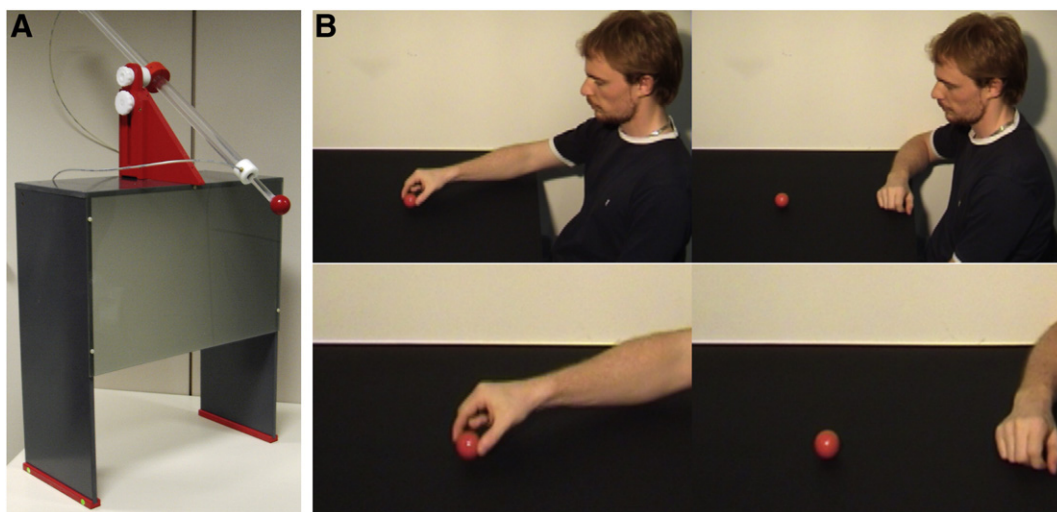

Fig. 1. Panel 'A' represents the apparatus used for the experiment. Panel 'B' represents a frame extracted from the videos for each experimental conditions characterizing the 'observation' component of the experiment. From top left to bottom right the following conditions are represented: "model grasping", "model static", "hand grasping" and "hand static".

resting on the table in the proximity of the object. The 'hand alone' video clips were created from the 'human model' video clips using Adobe Premiere (Adobe Systems, San Jose, CA, www.adobe.com). Specifically, this was done by editing the video in which the body of the human model was entirely visible. This ensured that exactly the same movement was presented for all 'action' conditions, therefore eliminating possible differences in kinematics which may confound data interpretation. Two different models (a female and a male) performed the action for a total of 30 videos for each condition. The video clips depicted either the model or the model's hand from the right side. Both the "model" and the "hand" videos were resized to 360×240 pixels in order to keep the same resolution. The resized videos were then compressed and their quality was the same in all conditions. All stimuli were presented by using the software Presentation (Neurobehavioral Systems, Albany, CA, www.neuro-bs.com) which ensured synchronization with the MR scanner. An LCD computer-controlled projector (NEC, resolution 1024×768, refresh rate 60 Hz) was employed to present the stimuli at the centre of the screen seated within the apparatus (every video subtended $11 \times 7.4°$ of visual angle).

Action execution

The stimulus was a firm red sphere (diameter: 40 mm) attached to the stick inside the piston of the pneumatic apparatus (see Fig. 1A). The sphere's surface was smooth at touch. The stimulus appearance was controlled by Presentation, via a parallel port, using a custom-built air pressured pump. The illumination produced by the projector and by the internal light of the scanner, enabled a clear view of the stimulus.

Tasks and procedures

Action observation

Subjects were asked to watch the videos carefully. Subjects were not asked to perform behavioural tasks within the scanner for the following reasons. First because we wanted to eliminate any possible confound due to the possible involvement of sharing/divided attentional processes (Chong et al., 2008). Second, because it has been recently suggested that the "action observation" system is mainly activated when no active inferential process is involved (Brass et al., 2007). Third, because we wanted to test a "pure" observation condition as tested in monkeys' studies (Rizzolatti et al., 2001). In between stimuli presentation subjects were requested to fixate a cross presented in the middle of the screen.

Action execution

Subjects were requested to fixate a black cross presented on the grey background of the screen embedded within the apparatus. Then they were requested to reach towards and grasp the stimulus with a precision grip (see Culham et al., 2003, for a similar procedure) or to fixate the stimulus. Specifically the sequence of events was the following: (i) subjects were requested to fixate the central cross (as for the observation part); (ii) the central cross disappeared; (iii) the stimulus was lowered down in the scanner and subjects were requested to fixate it. The time taken by the stimulus as to reach the pre-determined location was 1.5 s; (iv) subjects were requested to fixate the stimulus for 1.5 s until the beginning of the experimental conditions. The latter 3 s of the event sequence was defined as "preparation time". After "preparation time", subjects had 3 s either to perform the reach-to-grasp movement (if they hear a sound) or just to continue to fixate the ball (in case no sound was presented), afterwards the ball was removed from the subject's view. The task was performed by all subjects with the dominant (right) hand. Half subjects performed the execution task before the observation task, the other half performed the observation task before the execution task.

Experimental design

Action observation

We adopted a 2×2 factorial event-related design in which the main factors were "type of view" (two levels: model, hand alone) and "type of observed task" (two levels: grasping, static). The combination of the two factors led to four experimental conditions:

1. "Full-visible model grasping" condition in which subjects observed video clips depicting a human model grasping an object with a precision grip.
2. "Full-visible model static" condition in which subjects observed a human model with the hand resting on a table in the proximity of the stimulus.
3. "Hand alone grasping" condition, in which subjects observed a human hand grasping the stimulus with a precision grip.
4. "Hand alone static" condition in which subjects observed a human hand resting on a table in the proximity of the stimulus.

For each condition, 30 video clips were presented in each of the two runs of the observation part. The subjects observed a total set of 240 videos (4 conditions × 30 videos × 2 runs). Stimuli were pseudo-randomly presented on a variable schedule. The inter-stimulus interval (ISI) being determined by a 'long exponential' probability distribution (Hagberg et al., 2001), with a mean ISI of 6 s and a range of 2.5–11.5 s.

Action execution

Here the design involved two experimental conditions:

1. "Reach-to-grasp", in which subjects reached towards and grasped the stimulus following the presentation of a sound (frequency = 800 Hz; duration = 200 ms).
2. "Object fixation", in which no sound was presented and subjects simply fixated the object for the entire trial duration.

Subjects performed 30 trials (15 trials × 2 runs) per condition. A minimum of 28 repetitions for each of the two conditions were collected for each subject. As suggested by Culham et al. (2003, 2006), we adopted various solutions to optimise the acquisition of the execution data. For instance, we adopted a slow event-related paradigm (Birn et al., 1999) to sample the functional imaging data to dissociate possible artefacts from head and arm movements (which occur in parallel with the action) from real activation (which are associated with the characteristic haemodynamic lag). In order to avoid artefacts due to movements within the scanner subjects were also explicitly instructed to minimise head's movement and their shoulder was restricted. To ensure that the starting position of the hand was always the same for all conditions subjects wore an MRI-compatible belt and positioned their hand in a fist posture on a specific part of it. Stimuli were pseudo-randomly presented on a fixed interval with an ISI between two conditions of 14.5 s.

Data acquisition

Whole-brain fMRI data were acquired on a 3T scanner (Siemens Magnetom Trio) equipped with a 12-channel head array RF coil. Functional images were obtained with a gradient echo-planar (EPI) T2*-weighted sequence in order to measure blood oxygenation level-dependent (BOLD) contrast throughout the whole brain (36 slices, 3 mm isotropic voxel size, 0.75 spacing, in-plane resolution of 64×64 voxels, FOV = 192×192 mm, flip angle = 90°, TR = 2500 ms, TE = 35 ms). The first 5 volumes of every run were discarded from the analysis due to initial instability in the signal of EPI images. Scans were acquired for each subject in four scanning runs, two runs (437 volumes each) for the observation part of the experiment and two runs (229 volumes each) for the execution part. In addition, high-resolution T1-weighted images (anatomical scans) were also acquired for each

participant (MP-RAGE, 160 slices, in-plane resolution 224×256, 1 mm isotropic voxels, TR = 2300 ms, TE = 3.03 ms, flip angle = 8°).

Data analysis

Functional MRI data were analysed using Statistical Parametric Mapping software (SPM5, Wellcome Department of Cognitive Neurology, London, www.fil.ion.ucl.ac.uk/spm/), implemented in Matlab 7.3 (Mathworks Inc., USA, www.mathworks.com). First, individual scans were realigned to the first functional volume of each series in order to correct for any head movement occurring within the run. Second, high quality T1 images were co-registered to the mean EPI image and segmented. The co-registered grey matter segment was normalised onto the grey matter template and the resulting normalisation parameters applied to all functional images (resampling the voxels at 2×2×2 mm). The original T1 image was also normalised to the MNI space using the same parameters, keeping the original resolution of 1×1×1 mm. Finally functional data were spatially smoothed using 8 mm FWHM (Full Width at Half Maximum) Gaussian kernel. A high-pass temporal filter (cut-off 128 s) was also applied to the time series.

Whole-brain analyses

Two whole-brain analyses, one for the observation and one for the execution part of the experiment were carried out by applying the General Linear Model (GLM) for analysis of fMRI time series implemented in SPM5 (Friston et al., 1995). Regressors were defined based on the timing of presentation for each of the conditions, and these functions were convolved with a canonical, synthetic HRF (haemodynamic response function) in order to produce the model. In addition, predictors of no interest were modelled to account for residual effects of the movements measured during the realignment procedure.

Action observation

Four conditions were extracted as events for each subject at first level and then entered in a second level within-subject ANOVA with two factors, "type of observed task" (grasping, static) and "type of view" (model, hand alone).

Action execution

The contrast of interest, reach-to-grasp against object fixation, was extracted for each subject at first level and then tested in a second-level analysis with one-sample *t*-test. In order to distinguish effects only related to the different tasks, "preparation time" was modelled as a regressor of no interest. Specifically it was defined as the time from the moment the stimulus started to be lowered down up to the time the different tasks begun. The tasks, "reach-to-grasp" and "object fixation", were modelled as regressors starting from the end of the preparation time regressor up to the time the stimulus started to re-enter within the piston. Both the task and the preparation time duration was 3 s. Errors were separately modelled as an "error" regressor of no interest within the first level design matrix.

The alpha level for these second-level analyses was set at *p* < 0.0001 uncorrected at voxel level and at *p* < 0.05 corrected at cluster level. Data were superimposed on the mean normalised anatomy of the group in order to have a better anatomical localization of the activated clusters.

Conjunction analysis

To define regions in which activation was elicited by both grasping observation and execution a conjunction for the main effect of 'type of observed task' (i.e., Model grasping + Hand alone grasping > Model static + Hand alone static) and the contrast between hand grasp

execution versus object fixation was performed. In order to find common voxels we created a binary image overlapping the SPM{t} maps for the two contrasts of interest reported above. The statistical threshold of the two maps was the same reported for the single contrasts, i.e. *p* < 0.0001 uncorrected at voxel level and at *p* < 0.05 corrected at cluster level. Thus, we logically inferred that both action observation and execution would trigger activity within cerebral areas in which both contrasts of interest reached statistical significance (Nichols et al., 2005; Friston et al., 2005).

Region of interest (ROI) analyses

In order to make our analyses more consistent with the analyses performed in the study which inspired the present research (Nelissen et al., 2005), we performed a ROI analysis confined to one region, i.e. the ventral premotor cortex. This area was chosen as to compare the most probable functional homologue region between our study and the Nelissen et al. (2005) investigation. Further, a recent meta-analysis on human fMRI data regarding action observation and execution supports our choice indicating that the area in the human brain consistently activated in both conditions is the left ventral premotor cortex (Chouinard and Paus, 2006). Because in humans it is more difficult than in monkeys to determine a precise localization for a ventral premotor ROI, we determined our ROI on the basis of functional properties. Specifically, our ROI was identified by means of the results obtained for the conjunction analysis. The ROI analysis was performed on the mean percent signal change (PSC) extracted using Marsbar SPM Toolbox (Brett et al., 2002) from all the voxels within the selected region. PSC data were analysed by means of an ANOVA similar to that performed for the whole-brain "observation" part. This analysis included two within-subjects factors, "type of observed task" (grasping, static) and "type of view" (model, hand alone).

Localization

Anatomical details of significant signal changes were obtained by superimposing the SPM{t} maps on the mean anatomy image of the group. Results were also checked against structural images of each participant. As a general neuroanatomical reference we used the atlas by Mai et al. (2004). Further, the SPM Anatomy Toolbox (Eickhoff et al., 2005), based on three-dimensional probabilistic cytoarchitectonic maps, was used to determine probability of the peak activity voxels and of the clusters. For premotor, motor and somatosensory cortices we also ascertained the position of the cluster and the peak

Table 1
Brain areas showing differential activation for the main effect of type of observed task (Model grasping + Hand grasping) > (Model static + Hand static).

Maxima position	*t*	*Z*	Coordinates (*x, y, z*) mm		
Middle temporal gyrus	11.43	Inf	44	−66	0
Postcentral gyrus	9.89	7.58	−34	−42	58
Middle temporal gyrus	9.29	7.28	−40	−68	4
Cingulate cortex	8.87	7.06	−14	−24	40
Precentral gyrus	8.57	6.9	−28	−12	56
Superior temporal gyrus	8.07	6.62	66	−36	18
Precentral gyrus	6.68	5.75	−54	4	38
Superior occipital cortex	6.44	5.59	−24	−84	34
Superior occipital cortex	6.31	5.5	26	−80	34
Cingulate cortex	5.98	5.27	14	−22	44
Thalamus	5.71	5.08	−14	−22	8
Precentral gyrus	5.59	4.99	34	−6	56
Cerebellum: lobule VI	5.48	4.92	−12	−70	−20
Cerebellum: lobule VII	5.43	4.88	10	−74	−40
Cerebellum: lobule VI	5.00	4.56	32	−52	−26
Cerebellum: lobule VIII	4.88	4.46	22	−58	−50

Notes. Only regions surviving a voxel-level threshold of *p* < 0.0001 (uncorrected) and a cluster-level threshold of *p* < 0.05 (corrected) are reported. MNI coordinates of peaks of BOLD change.

with the data of the meta-analysis by Mayka et al. (2006). For cerebellar activation, the atlas by Schmahmann et al. (2000) was used to improve accuracy in localization.

Results

Whole-brain analyses

Action observation

Main effect of type of observed task. As shown in Table 1, the *t*-contrast testing "action observation" against "static control", (Model grasping + Hand alone grasping) > (Model static + Hand alone static), showed differential activation within the so-called "action-observation system" comprehending premotor, temporal and parietal cortices (Buccino et al., 2001; Pierno et al., 2006; Gazzola et al., 2007a,b; Gazzola and Keysers, 2008). Activation map related to action observation is overlaid on the mean image of the group (see Fig. 2A). Consistent with previous findings,

significant differential activation was evident bilaterally within both the dorsal (Grafton et al., 1996a; Decety et al., 1997; Buccino et al., 2001; Grèzes et al., 2003; Grosbras and Paus, 2006; Pierno et al., 2006; Shmuelof and Zohary, 2006; Filimon et al., 2007; Gazzola et al., 2007a,b; Gazzola and Keysers, 2008) and the ventral sectors of the premotor cortex (Grafton et al., 1996a; Rizzolatti et al., 1996b; Decety et al., 1997; Johnson-Frey et al., 2003; Grosbras and Paus, 2006; Shmuelof and Zohary, 2006; Gazzola et al., 2007a,b; Gazzola and Keysers, 2008). Further, two bilateral clusters were activated within the caudal cingulate motor area (Decety et al., 1997; Gazzola et al., 2007a,b; Gazzola and Keysers, 2008). For the parietal cortex bilateral activation was evident within the superior and the inferior parietal lobules and the intraparietal sulcus (Grafton et al., 1996a; Buccino et al., 2001; Shmuelof and Zohary, 2005, 2006; Grosbras and Paus, 2006; Pierno et al., 2006, 2008; Gazzola et al., 2007a,b; Gazzola and Keysers, 2008). Parietal activity within the left hemisphere also spread within the postcentral gyrus (Grosbras and Paus 2006; Gazzola et al., 2007a,b; Gazzola and Keysers, 2008; Pierno et al., 2008). Bilateral activation was also evident in the superior, the middle and the inferior temporal gyri
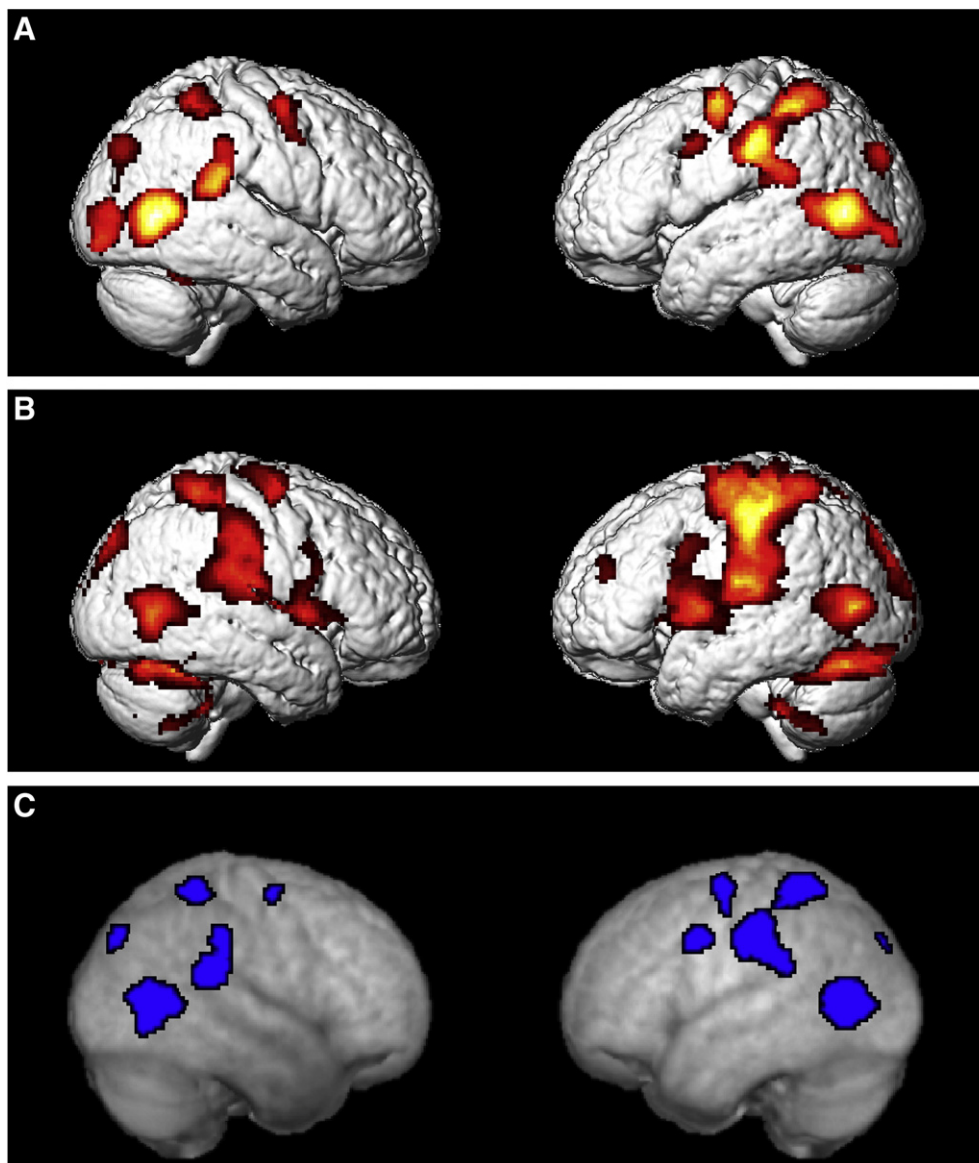

Fig. 2. Panel 'A' represents the regions activated for the main effect of 'type of observed task' overlaid on the group mean anatomy. Panel 'B' represents the regions activated when contrasting grasp execution and object observation overlaid on the group mean anatomy. In both panel 'A' and 'B', contrasts were thresholded at *p* < 0.0001 uncorrected at voxel level and at *p* < 0.05 at cluster level. Panel 'C' represents the binary image of overlapping areas. Regions colored in blue were activated both in grasping execution and observation. MriCron software was used to render the binary image obtained with the conjunction analysis on the mean anatomy of the group.

Table 2
Brain areas showing differential activation for the main effect of agent (Model grasping + Model static) > (Hand grasping + Hand static).

Maxima positions	t	Z	Coordinates (x, y, z) mm		
Occipital cortex	9.73	7.51	− 16	− 96	− 2
Middle temporal gyrus	5.15	4.67	52	− 74	0
Fusiform gyrus	5.18	4.69	40	− 52	− 20

Notes. Only regions surviving a voxel-level threshold of p < 0.0001 (uncorrected) and a cluster-level threshold of p < 0.05 (corrected) are reported. MNI coordinates of peaks of BOLD change.

(Decety et al., 1997; Buccino et al., 2001; Perani et al., 2001; Grèzes et al., 2003; Grosbras and Paus, 2006; Gazzola et al., 2007a,b; Gazzola and Keysers, 2008) and in two clusters within the superior occipital cortex (Grafton et al.,1996a; Grèzes et al., 1999; Perani et al., 2001). Activity was also evident in the thalamus (Gazzola et al., 2007a,b; Gazzola and Keysers, 2008). Finally, activation within the cerebellum was evident at the level of the VI, VII and VIII lobules (Grafton et al., 1996a; Grèzes et al., 1999; Grosbras and Paus, 2006; Gazzola et al., 2007a,b; Gazzola and Keysers, 2008). The reverse t-contrast considering "static control" versus "action observation", (Model static + Hand alone static) > (Model grasping + Hand alone grasping), did not show any significant activation.

Main effect of type of view. When contrasting activity related to the type of view, (Model grasping + Model static) > (Hand grasping + Hand static) differential activations were found within the occipital and the temporal cortices (see Table 2). The occipital activation, chiefly involving the primary visual cortex, was confined to the left hemisphere. Such lateralization may have happened because of the presence of the model on the right side of the visual field with respect to the subject. The fusiform and occipito-temporal activation resembles those previously obtained for body and face processing (for review see Peelen and Downing, 2007). Specifically the occipito-temporal activation strongly resembles, in terms of stereotaxic coordinates, the so-called extrastriate body area (EBA; Astafiev et al., 2004; Downing et al., 2001). The opposite contrast (Hand alone grasping + Hand alone static) > (Model grasping + Model static), shows a significant effect related to the presence of the hand only within the inferior temporal gyrus (see Table 3).

Interaction type of view by type of observed task. The two t-contrasts regarding the interaction between type of view and type of observed task did not reveal significant areas of activation. The tested t-contrasts were: (Model grasping − Model static) > (Hand alone grasping − Hand alone static) and (Hand alone grasping − Hand alone static) > (Model grasping − Model static).

Action execution

Activations related to grasping execution versus object fixation are shown Fig. 2B and Table 4. In general, the revealed pattern of activation was similar to that reported in previous grasping studies (for review see Castiello, 2005; Castiello and Begliomini, 2008). Specifically, activation was significant within the dorsal (Grafton et al., 1996b; Ehrsson et al., 2000, 2001; Grol et al., 2007; Begliomini et al., 2007a,b; Gazzola et al., 2007a,b; Gazzola and Keysers 2008; Kuhtz-Buschbeck et al., 2008; for review see Picard and Strick, 2001) and the ventral (Ehrsson et al., 2000, 2001; Grèzes et al., 2003; Grol et al.,

Table 3
Brain areas showing differential activation for the main effect of agent (Hand grasping + Hand static) > (Model grasping + Model static).

Maxima position	t	Z	Coordinates (x, y, z) mm		
Inferior temporal gyrus	5.48	4.91	− 52	− 56	− 12

Notes. Only regions surviving a voxel-level threshold of p < 0.0001 (uncorrected) and a cluster-level threshold of p < 0.05 (corrected) are reported. MNI coordinates of peaks of BOLD change.

Table 4
Brain areas showing differential activity when contrasting grasping execution and object fixation.

Region	t	Z	Coordinates (x, y, z) mm		
Postcentral gyrus	24.72	7.39	− 42	− 22	56
Middle temporal gyrus	18.37	6.80	− 42	− 74	6
Superior frontal gyrus	13.84	6.19	28	− 6	66
Middle frontal gyrus	6.21	4.31	− 34	42	26

Notes. Only regions surviving a voxel-level threshold of p < 0.0001 (uncorrected) and a cluster-level threshold of p < 0.05 (corrected) are reported. MNI coordinates of peaks of BOLD change.

2007; Gazzola et al., 2007a,b; Gazzola and Keysers, 2008) sectors of the premotor cortex. Activation was also evident bilaterally in the inferior frontal gyrus (Ehrsson et al., 2000, 2001; Gazzola et al., 2007a,b; Gazzola and Keysers, 2008) and the insula (Ehrsson et al., 2000; Gazzola et al., 2007a,b; Gazzola and Keysers, 2008; Kuhtz-Buschbeck et al., 2008). For the parietal cortex significant differential activation comprehended the postcentral gyrus, the superior and the inferior parietal lobule together with the intraparietal sulcus (Ehrsson et al., 2000, 2001; Chapman et al., 2002; Culham et al., 2003; Grèzes et al., 2003; Frey et al., 2005; Grol et al., 2007; Begliomini et al., 2007a,b; Gazzola et al., 2007a,b; Gazzola and Keysers, 2008; Kuhtz-Buschbeck et al., 2001, 2008; for review see also Culham et al., 2006 and Tunik et al., 2007). Other activations closely associated with actual execution included SMA and caudal cingulate motor area (Ehrsson et al., 2000, 2001; Gazzola et al., 2007a,b; Gazzola and Keysers, 2008; Kuhtz-Buschbeck et al., 2008; for review see Picard and Strick, 1996) together with the inferior and the middle temporal (Oreja-Guevara et al., 2004; Gazzola et al., 2007a,b; Gazzola and Keysers, 2008) and the superior occipital cortices (Grol et al., 2007). An involvement of subcortical structures was also detected at the level of the basal ganglia (Ehrsson et al., 2000), the cerebellum (Grafton et al., 1996b; Begliomini et al., 2007a,b; Kuhtz-Buschbeck et al., 2008; Gazzola et al., 2007a,b; Gazzola and Keysers, 2008) and the thalamus (Ehrsson et al., 2000; Gazzola et al., 2007a,b; Gazzola and Keysers, 2008). Whereas all the above mentioned brain loci were characterized by a bilateral pattern of activity there was an evident left lateralization of activity within the postcentral gyrus and precentral sulcus resembling somatomotor activation within regions related to the movement of the thumb, the index finger, the arm and the elbow (Lotze et al., 2000).

Conjunction analysis

As shown in Fig. 2C, various regions showed overlapping activation related to both the execution and the observation of grasping actions. These regions were the left ventral premotor cortex together with bilateral activation within the dorsal premotor cortex, caudal cingulate motor area, the middle temporal gyrus and the parietal cortex. Subcortical regions included the left thalamus and the cerebellum bilaterally. These results confirm the pattern of overlaps for action execution and observation previously reported by Gazzola et al. (2007a,b) and Gazzola and Keysers (2008). Further, with particular reference to the left ventral premotor cortex our coordinates are strikingly similar to those obtained by Chouinard and Paus (2006). These authors performed a meta-analysis by considering activation-likelihood-estimation maps produced from neuroimaging

Table 5
Data regarding the ventral premotor ROI data.

Center of mass (x, y, z coordinates)	− 55	5	37
Range for x coordinates	− 52		− 60
Range for y coordinates	10		− 2
Range for z coordinates	42		32

studies that measured changes in cerebral activity during the execution of object-related hand movements with those during the observation of object-related hand movements (see Table 5 for the data concerned with the ventral premotor ROI).

Testing further the type of model manipulation

We reasoned post-hoc that the rather stringent threshold adopted for testing the interaction of interest (Model grasping − Model static) > (Hand alone grasping − Hand alone static) at whole-brain analysis level might have masked more subtle effects. Therefore, we tested this interaction by using less conservative thresholds. We estimated the whole-brain model using an explicit masking procedure. This was done to limit the analysis within the voxels found to be active within all possibly "mirror" areas identified by means of the conjunction analysis (see above). Then we applied rather liberal thresholds at voxel level ($p < 0.001$ uncorrected, $p < 0.005$ uncorrected, $p < 0.01$ uncorrected) and no threshold on the minimum number of activated voxels was considered. The results indicated that the interaction of interest was not significant for the considered areas at each of the tested thresholds.

ROI analyses

An ANOVA, conducted on the PSC for the entire region of overlap within the ventral premotor cortex, yielded only to a significant main effect of "type of observed task" ($F_{1,15} = 89.4$, $p < 0.001$, see Fig. 3A for a plot of the data and Fig. 3B for a localization of the ROI). Both the main effect of model and the interaction between the two factors were not significant ($F_{1,15} = 1.36$, $p = 0.263$ and $F_{1,15} = 0.07$, $p = 0.800$ respectively). On the basis of these results we reasoned that testing the mean effect of an entire ROI (comprehending 99 resampled voxels with a resolution of $2 \times 2 \times 2$ mm) might not be representative of the real effects occurring in this region. More subtle effects could be present in subareas of the ventral premotor ROI. Indeed, when performing a ROI analysis a strong assumption is made, that is that all the voxels have a homogeneous pattern of activation. Normally this is not tested, but taken as true. Therefore, to remove this possible confound we performed another analysis to test the presence or lack of effect in all the voxels within our ventral premotor ROI. We extracted every single voxel within the ROI. Each voxel was considered as an independent ROI. Then 99 separate ANOVAs on the PSC for each sub-ROI were conducted. Because of the exploratory nature of this analysis, we used no correction for the number of tested regions. None of the 99 voxels showed a significant interaction between the two considered factors ($p > 0.05$ uncorrected). But, all voxels showed a main effect of type of "observed task" (grasping versus static, $p < 0.001$

uncorrected). This indicates that the results obtained for the original ROI analysis were not biased by restricting the analysis only to the mean timecourse of the entire region.

Discussion

The aim of the present study was to investigate whether in humans different areas belonging either to the action observation or to a potential "mirror" system were differentially activated depending on the type of view. As outlined below, our results demonstrate a broad network of areas involved in both action observation and execution. We did find evidence that such network was activated both by a hand or a model acting, and that there was no modulation due to the visual properties of the agent performing the observed task. Further, we found that a hand alone acting was sufficient to trigger activity within the human "mirror" ventral premotor cortex.

Modulation of activity due to the type of acting model

A recent fMRI study in monkeys has defined subregions within area F5 and the adjacent prefrontal cortex responding to different properties of observed actions (Nelissen et al., 2005). Specifically area F5c responded only when the monkey observed a fully visible human model, but not when a hand alone was presented, whereas in other subregions of F5 (i.e., F5a, F5p) activation due to action observation was similar for both a fully visible model and a hand alone grasping an object (Nelissen et al., 2005). Here we wanted to test whether a similar subdivision also applies to humans. This was done at both 'observation' and 'mirror' level by means of whole-brain and ROI analyses respectively.

In terms of whole-brain analysis, the significance of the main effect 'observed task' for a number of areas – previously reported to be active in both humans and monkeys following the observation of grasping actions (e.g., Buccino et al., 2001; Pierno et al., 2006, 2008; Gazzola et al., 2007a,b; Gazzola and Keysers, 2008; Nelissen et al., 2005; Raos et al., 2007; Evangeliou et al., 2008) – demonstrates that both types of view triggered a similar level of differential activation when compared with static stimuli. Furthermore, the ROI analyses demonstrate that these conclusions are also valid at a "mirror" level, particularly for what concerns ventral premotor cortex.

How can these findings be explained? A possibility is that the 'action observation' and the 'mirror' systems chiefly represent actions in terms of goals independently by contextual information (Ferrari et al., 2005; Gazzola et al., 2007a,b). Compelling evidence that this is what may happen comes from neuroimaging and neurophysiological studies. In first instance, two studies by Gazzola et al. (2007a,b) are particularly relevant. For one, observation of actions characterized by
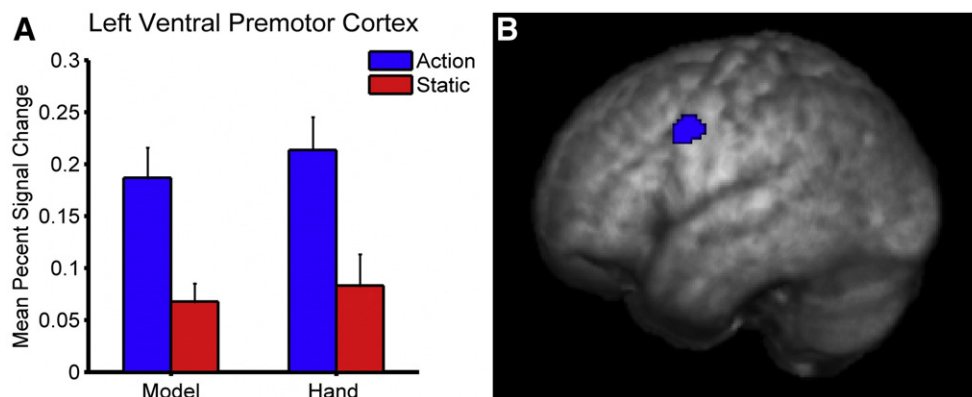

Fig. 3. Panel 'A' depicts the mean percent signal change occurring for the four experimental conditions in the region of overlap within ventral premotor cortex extracted from all the voxels using Marsbar Toolbox. Panel 'B' depicts the localization of the premotor ventral ROI (as extracted from the conjunction analysis) rendered on the mean anatomy of the group using MriCron software.

strikingly different kinematics (robotic versus human) similarly activated the action observation system and mirror areas (Gazzola et al., 2007a). For another, two aplasic subjects, born without arms or hands, were scanned while they watched hand actions. Results indicated that the BOLD signal of aplasic individuals within the putative action observation system augmented as much as in control subjects when they watched hand actions (Gazzola et al., 2007b). Specifically, the activations for the aplasic individuals fall in areas involved in foot and mouth action execution, whereas they fall in areas concerned with hand action execution for controls, suggesting a remapping of the goal of grasping whatever effector the observer would use to achieve this goal.

In second instance, Ferrari et al. (2005) demonstrated the existence of tool-responding mirror neurons in macaque ventral premotor cortex. These neurons respond to the sight of an action made with a tool, but only when the monkeys had a long previous experience of seeing how that tool was used (i.e., the action goal). Importantly, although the monkeys were not able to use the tools, the same neurons responded when the monkeys performed a grasping action on the same object with the mouth and/or with the hand.

Altogether these studies seem to support the idea that what is represented in the premotor cortex is not bounded to the physical appearance of the agent, but it is a rather abstract representation centered on the goal of the action, independently of what is acting, a human, a robot, or even a tool.

Our findings confirm and extend this notion by broadening the several dimensions within which action goals affect the response of the action observation system and how such dimensions may vary across species. Indeed on the basis of monkeys fMRI findings using a similar paradigm to ours (Nelissen et al., 2005) differences in action observation activity depending on type of view were expected, at least within premotor and other prefrontal areas. However, in our study the type of view had little impact at the level of action observation. We suspect that this might be ascribed to the fact that the processing of particular stimulus properties, which in principle should occur in homologue areas, might not be common to both species (Sereno and Tootell, 2005; Orban et al., 2004; Nakahara et al., 2007). In this perspective the conclusion would be that in humans the observation of a grasping hand alone (and an object) is sufficient to trigger significant differential activity (Morin and Grèzes, 2008). Alternatively the lack of effects might be due to two methodological factors. The first stems from the difficulty in defining homologue areas between monkey and human even using the same approach (i.e., architecture, connections or function). The second refers to the nature of the presented stimuli. To elaborate, in the study by Nelissen et al. (2005) the presented stimuli greatly differ in terms of salience. For instance, the grasping hand for the 'hand alone grasping' stimuli was much more visible than the grasping hand for the 'model grasping' stimuli. Therefore it might not be a matter of having elicited different type of representations within the premotor cortices. Rather, of having triggered a differential level of activity for the 'acting person' stimulus in F5c. This is because it was more difficult to decode the aspect of the context which was more salient for the animal, that is the grasping hand. It might be reasonable to hypothesize that if the grasping hand was not easy to contextualize, then the presentation of such stimuli may have produced significant BOLD signal increase with respect to when the grasping hand was easily coded ('hand alone grasping' condition). In this respect we took great care in preparing the stimuli for the present study, maintaining the proportions and kinematics for our stimuli similar. Importantly the videoclips for the hand alone condition were extracted from the videoclips in which the model was in full view. Therefore it is such consistency which might have allowed to reveal similar activations within the premotor cortex for the two types of stimuli. Such contention is supported, at least in humans, by a recent review examining activations in the premotor cortex during passive observation of actions (Morin and Grèzes, 2008). The suggestion here is that it is the specificity of used stimuli which

determines activity within specific areas of the prefrontal cortices. A challenge for future fMRI studies in monkeys will be to tease apart the contribution of the type of stimuli can have on activity within the action observation system.

Another aspect concerned with the stimuli used in the present experiment is that differences were detected in areas that are selective for the coding of body and/or hand movements depending on the type of view. When contrasting activity stemming from the viewing of the fully visible model with activity stemming from the observation of the hand alone, significant differential activity was found within an area of the occipito-temporal cortex which, as previously demonstrated, shows body-specific and body-with-face response, the so-called EBA (Downing et al., 2001), and in a sector of the fusiform gyrus which correspond to the fusiform body area (FBA) alone or in conjunction with the fusiform face area (FFA). Two areas which, as previously demonstrated, tend to overlap (Peelen and Downing, 2005; Peelen et al., 2006; Schwarzlose et al., 2005; Kanwisher et al., 1997). Conversely, the opposite contrast led to differential activation within the inferior temporal cortex which, as previously demonstrated, shows specific hand processing (McCarthy et al., 1999; Puce et al., 1999). Therefore, the two stimuli were able to trigger differential activation depending on their visual properties.

Overlapping activity for action observation and execution

The results obtained in the present study for the conjunction analysis revealed the existence of various regions of overlap in which activations related to both observation and execution of grasping actions were independently significant. The fact that areas showing possible 'mirror' type of activity exceed those considered as being part of the core 'mirror' system supports recent neuroimaging studies in both humans and monkeys (Gazzola et al., 2007a,b; Gazzola and Keysers, 2008; Raos et al., 2007; Evangeliou et al., 2008). In 'human' terms, Gazzola et al. (2007a,b; Gazzola and Keysers, 2008) reported a pattern of activation within a symmetric network involving temporal, parietal, and frontal areas similar to ours. In 'monkey' terms, two studies (Raos et al., 2007; Evangeliou et al., 2008), by using the quantitative ^{14}C-deoxyglucose method to map the activity pattern throughout the cortex of macaques, have found overlapping activity for the generation and the perception of hand actions within posterior parietal, somatosensory, motor and premotor cortices. Importantly, these latter results confirmed previous 'human' neuroimaging studies revealing activations for action execution and observation within the primary motor and somatosensory cortices (Hari et al., 1998; Avikainen et al., 2002; Gazzola et al., 2007a,b; Gazzola and Keysers, 2008; Pierno et al., 2008), the dorsal (Grafton et al., 1996a; Decety et al., 1997; Buccino et al., 2001; Gazzola et al., 2007a,b; Gazzola and Keysers, 2008) and ventral (Grafton et al., 1996a,b; Rizzolatti et al., 1996b; Decety et al., 1997; Gazzola et al., 2007a,b; Gazzola and Keysers, 2008; Pierno et al., 2008) premotor cortical areas together with medial cortical and the cingulated areas (Grafton et al., 1996a,b; Decety et al., 1997; Gazzola et al., 2007a,b; Gazzola and Keysers, 2008).

Altogether these and the present findings suggest that the resonant system responding to both action perception and action generation encompasses much more of the cortex than the mirror neuron concept would lead one to believe, suggesting the existence of a broader process possibly entailing mental simulation of action (Goldman and Sebanz, 2005; Raos et al., 2007; Gazzola et al., 2007a,b; Gazzola and Keysers, 2008; Evangeliou et al., 2008).

Conclusions

We set out to investigate an aspect concerned with "action observation" and "mirror" type of activity which so far has been untested in humans. That is, the possibility that different areas could

be differentially activated depending on the type of view. Our main findings might be explained along two main themes. A 'network' theme encompassing the notion that in humans overlapping activity between grasping activation and execution spreads across a number of areas which exceeds those classically thought to be part of the 'mirror' system (e.g., Raos et al., 2007; Gazzola et al., 2007a,b; Gazzola and Keysers, 2008; Evangeliou et al., 2008). Importantly, at the level of "mirror" regions, we have demonstrated that activity within this network is triggered by both a model or a hand alone acting, and that is not modulated by the type of view. In this respect, the present results highlight that it is the goal of an action which might be important as to determine action observation activation. A 'ROI' theme, which complements the 'network' theme, encompassing the notion that, in contrast to monkeys, the 'human' "mirror" premotor cortex is activated in a very similar way, irrespective of whether the agent's entire body, or only the grasping hand, is seen. These results are a novel addition to the growing body of literature pointing towards the plasticity of the human 'mirror' system in terms of what it visually codes (Bangert et al., 2006; Calvo-Merino et al., 2005; Gazzola et al., 2007b) and to possible differences across species in the type of properties characterizing premotor representations. This aspect is particularly important because most of the human studies on the mirror neuron system have been conducted with movies zooming into the hand-part of the stimulus. If, as monkeys' fMRI suggested (Nelissen et al., 2005), this was to cancel out key mirror areas, much of the human literature would have been challenged. The present data, however, show convincingly that this is not the case, at least in humans, and therefore enhance the validity of a large number of studies, providing important evidence for this flourishing field of the literature.

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