The Human Premotor Cortex Is 'Mirror' Only for Biological Actions

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Summary

Previous work has shown that both human adults and children attend to grasping actions performed by another person but not necessarily to those made by a mechanical device [1–3]. According to recent neurophysiological data, the monkey premotor cortex contains "mirror" neurons that discharge both when the monkey performs specific manual grasping actions and when it observes another individual performing the same or similar actions [4–7]. However, when a human model uses tools to perform grasping actions, the mirror neurons are not activated [4–6]. A similar "mirror" system has been described in humans [8–15], but whether or not it is also tuned specifically to biological actions has never been tested. Here we show that when subjects observed manual grasping actions performed by a human model a significant neural response was elicited in the left premotor cortex. This activation was not evident for the observation of grasping actions performed by a robot model commanded by an experimenter. This result indicates for the first time that in humans the mirror system is biologically tuned. This system appears to be the neural substrate for biological preference during action coding.

Results and Discussion

In this experiment we used a factorial design to directly measure how neural responses associated with the observation of a manual grasping action are modulated by the biological or nonbiological nature of the model performing that action. Healthy volunteer subjects observed grasping actions targeted at a cylindrical object (height = 5 cm; base diameter = 3.5 cm) performed either by a human or a robot model commanded by a human experimenter while regional brain activation was measured with H_2O positron emission tomography (PET). Control conditions in which participants observed a static human or a static robot model together with the

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to-be-grasped object were also included (see Experimental Procedures).

Our prediction arises from previous neuroimaging studies showing that the observation of grasping movements activates the left premotor cortex [9–14]. We expect the left premotor cortex to be activated during observation of a human, but not a robot, hand grasping the target. If this were the case, it would parallel the finding of a lack of mirror neuron activation in monkeys observing actions performed by a human model with tools. This is because, as for the "tools" condition in monkey studies where there is a visible agent using the tool, our robot condition implies the presence of an agent activating the robot arm.

We performed a hypothesis-driven analysis by looking at voxels within left premotor cortex with significant activation between conditions (see Experimental Procedures). As predicted, we observed activation of the left premotor cortex in the region of the ventral premotor cortex during observation of manual grasping actions performed by the human versus observation of the static human ($P = 0.001$; Table 1); we did not see this activation for the grasping robot contrasted with the static robot (Table 1). The results for the human condition signify that when an individual observes an action made by another individual, a specific sector of the premotor cortex is activated. This would confirm that the premotor cortex is the neural substrate for a matching mechanism mapping the observed action on the observer's motor representation. The lack of premotor activation for the robot condition signifies that observation of an action performed by a nonbiological effector does not activate the mechanisms for mapping the observed action onto the observer's motor representation. These results were further corroborated by the significant interaction between the type of model (human, robot) and the type of observation (moving, static). The difference between observing grasping and static conditions was greater for the human than for the robot model. The regional cerebral blood flow (rCBF) response of the left premotor cortex showed a significant activation when subjects observed the grasping action performed by a human model (maximal voxel $x = -48$, $y = 20$, $z = 36$, $Z = 4.04$, $P < 0.0001$ uncorrected; Figure 1 and Table 1) but not when they observed a grasping action performed by a robot model. We also performed a more conservative analysis by applying small-volume correction to limit the search volume to the left premotor cortex. The voxels show significant rCBF even after correction for multiple comparisons ($P = 0.040$ corrected; Table 1).

Our results are broadly consistent with electrophysiological recordings from monkey brains in which regions of premotor cortex were reported to contain mirror neurons selective for the observation of grasping actions performed by a human model [4–7]. The results also concur with neuroimaging data showing that during observation of hand/arm actions there is activation in the left ventral premotor cortex [9–14].

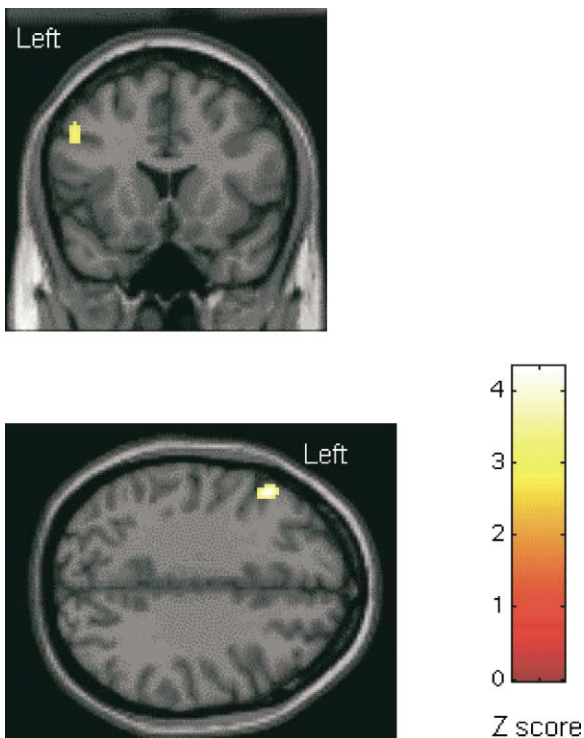The crucial aspect of this study is the revelation that

Figure 1. Left Premotor Cortex Activation

Activation of the left premotor cortex in the interaction analysis (HA − HS) − (RA − RS) superimposed on single-subject T1 MRI on SPM is displayed in sagittal (top) and transverse (bottom) views. Voxel of maximal activation $x = -48$, $y = 20$, $z = 36$, threshold $P < 0.005$.

Table 1. Results for the Hypothesis-Driven Analysis of Left Premotor Cortex for Responses to the Human versus the Robot Model

	Coordinates (x, y, z)			Z Score	P Value
HA − HS	−48	22	38	2.98	0.001[a]
RA − RS	-	-	-	-	-
(HA − HS) − (RA − RS)	−48	20	36	4.04	0.000[a]
After small-volume correction					0.040[b]

HA = human action; HS = human static; RA = robot action; RS = robot static. All the coordinates are in MNI space.
[a] Uncorrected P values.
[b] P values corrected for multiple comparison.

in humans, as in monkeys, the "mirror" property of the premotor cortex appears to be biologically tuned. In this respect we provide the first evidence that the human premotor cortex can discriminate between observations of hand grasping actions performed by a biological and a nonbiological model.

A natural question is why this biological tuning has developed and persists in the human brain. One possibility is that it reflects a "cortical matching," i.e., a match between an observed action and the internal motor commands one might use to make the action. The lack of activation in the monkey's mirror system in response to grasping actions performed with tools has been interpreted as suggesting that those actions are not part of the behavioral repertoire of the animal [4–7]. That is, observation of the action of a tool grasping an object cannot be interpreted by the premotor cortex because of the lack of cortical matching between the observed actions and internal motor commands.

But can we use the same argument to account for the absence of premotor cortex activity in the human subjects in the present study after they observed a robot performing grasping actions? If we espouse this hypothesis, we would assume that interpreting robotic movements is not part of the human behavioral repertoire and thus that cortical matching cannot occur. Just as for monkeys, the association between the nonbiological agent performing the action and the object of the action

cannot be formed. A possible explanation might be concerned with the different type of kinematic information conveyed by the robotic arm and hand. Although the robot model was programmed to show the classic opening/closing phases that characterize grasping by humans, the robotic grasping action was clearly different from that of a human. For example, the opening and closing phases were jerky and lacking in "human" smoothness and temporal coordination [17]. Thus, cortical matching may not have occurred because the robot's kinematic pattern might not be recognized as a natural grasping pattern. In other words, there was no match between the perceptual information of an observed act with the stored kinematic engram concerned with that specific executable act.

The lack of activation of the premotor mirror system found here for observation of actions performed by the robotic arm is consistent with the behavioral responses of both human adults and children when presented with grasping actions performed by mechanical devices. They code and/or attend to grasping actions performed by another person but not necessarily to those performed by a mechanical device [1–3]. For example, infants react differently to a claw representation of a human hand than to a human hand itself [1], and they are more likely to reproduce movements performed by a human model than by a mechanical device attempting, but failing, to pull apart a dumbbell [2, 18].

Whereas our primary interest was in activity in the left premotor cortex, we also conducted a secondary analysis of activation (corrected for comparisons) with the entire brain. This secondary analysis revealed significant activation in bilateral visual association areas when grasping versus static conditions were contrasted in both human and robot models (Figure 2 and Table 2). These areas are known to be activated during motion tracking and correspond to the putative motion area V5 identified in the human brain [19]. The interaction between type of model and type of observation was not significant (Table 2). This suggests that these activations were solely concerned with motion and were independent of whether the subjects observed "human" or "robotic" motion.

A final issue with our results relates to the lack of differential activity in areas concerned with biological motion. Oram and Perrett [20] showed that neurons buried within the superior temporal sulcus (STS) respond to walking motion. These responses occurred regard-
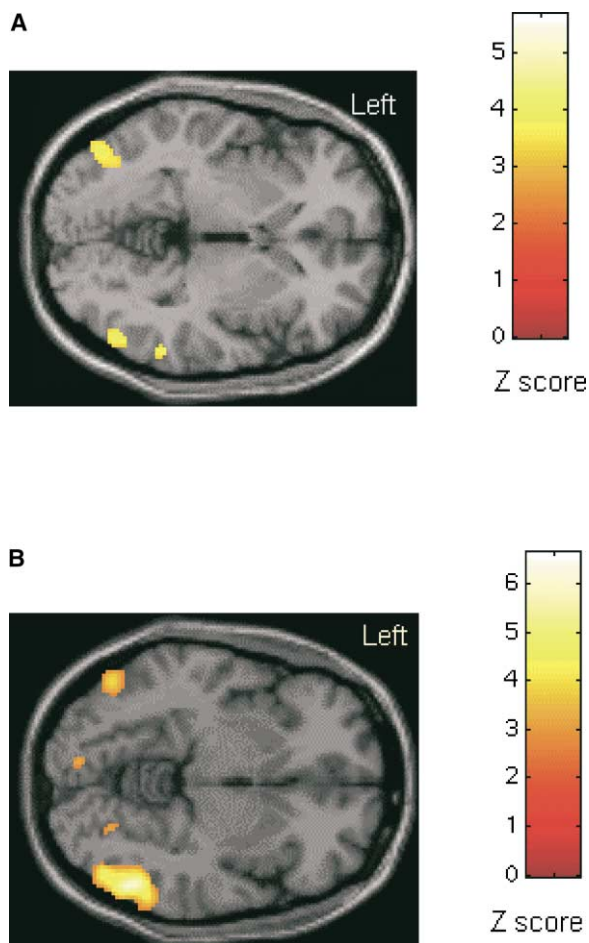
Figure 2. Activation of Visual Areas

Activation of the visual areas in the grasping versus static conditions for the human (A) and the robot model (B). Threshold P < 0.05.

less of whether the motion was presented with real images or point-light displays. However, these neurons did not respond to various types of random dot motion. In line with these results, we did not observe differential activation in the STS areas according to whether the motion was human or robotic. As with both the images

Table 2. Brain Regions that Are outside Left Premotor Cortex and Show Significant Activation for the Grasping versus Static Condition for the Human and the Robot Model

	Coordinates (x, y, z)			Z Score	P Value[a]
HA − HS					
L MOG	−46	−70	8	5.09	0.016
R MOG	50	−66	4	5.01	0.022
RA − RS					
R MOG	54	−66	0	5.78	0.001
L MOG	−54	−72	0	5.77	0.001
(HA − HS) −					
(RA − RS)	-	-	-	-	-

HA = human action; HS = human static; RA = robot action; RS = robot static. L = left. R = right. MOG = middle occipital gyrus. All the coordinates are in MNI space.
[a] P values corrected for multiple comparison.

of walking and point-light displays of walking used by Oram and Perrett [20], it seems that both the human and the robotic motion can be interpreted as meaningful. Furthermore, it has been proposed that the STS is more likely to be activated when contrasting action observation with object observation rather than with a static hand [21], and a recent meta-analysis of neuroimaging studies investigating action observation revealed that STS activation is not always present [22].

In conclusion, our findings provide the first evidence of the neural substrate in humans distinguishing between human (biological) and robot (nonbiological) actions. This suggests that the mirror system performs a sophisticated analysis based on an evolutionary preference for biological actions. Although first observed in monkeys, it appears that this biologically tuned mirror system persists to this day, despite the acquisition by humans of knowledge and understanding of actions performed with artificial tools.

Experimental Procedures

Subjects and Task
Seven healthy right-handed males aged 30–59 years (mean 44.6 years) took part in the study. The handedness was determined with the Edinburgh Handedness Inventory [23]. All participants were naïve with regard to the purpose of the experiment. They all gave their written consent to the experimental procedure. The study was approved by the Hammersmith Hospitals Trust Ethical Committee.

Throughout the experiment, subjects were instructed to carefully observe the human (experimenter) or the robot model. The models either performed object-related grasping actions for the action conditions or remained static. The human model performed the grasping actions, and the robot action was initiated by the experimenter pressing a button every 5 s. Consistent timing was ensured by means of a computerized timer that indicated to the human model when to start the grasping action and to the experimenter when to activate the robot. Subjects were able to view the face and the upper body part of the experimenter both in the human and robot conditions. This was done to maintain constant experimental conditions apart from the type of model performing the grasping action. The to-be-grasped object was present in all conditions. Throughout the experimental sessions, the experimenter checked that the subjects looked at the model.

There were four different conditions: human-action (HA), human-static (HS), robot-action (RA), and robot-static (RS). Each condition was observed three times (total of 12 scans per subject), and the conditions were presented in random order.

Models
The robot model was custom-designed and built by in-house technicians. It had the appearance of an average human forearm with a gloved hand and was mounted on a metal frame. A single motor was used to move the arm from a vertical to a horizontal position. The four fingers and thumb had a common movement so as to mimic the closing of a human hand. The construction was electromechanical and controlled by an 87c751 micro-controller. The hand was constructed of nylon cords for the tendons, silicon rubber for the joints, and wooden dowels for the bones. Movement was provided by a DC electric motor that tensed the tendons to close the hand. Springs were used to store energy and thus reduce the required power and size of the DC motors. Limit sensors on the arm and hand were used by the micro-controller to control movement. The arm length was approximately 0.5 m. The maximum pickup weight was approximately 0.1 kg. The folding of the hand was comparable to a human grasping action. The robot was programmed to simultaneously move its arm and open its fingers when the experimenter pressed a button. After reaching the maximum aperture, the fingers started to close on the to-be-grasped object. The experi-

menter acted as the human model. The posture at the beginning of the action was similar for both human and robot models.

Image Acquisition and Analysis
The scans were acquired on a CTI-Siemens ECAT EXACT HR++/ 966 PET scanner in 3D mode. 6 mCi of $H_2^{15}O$ was injected intravenously for each emission scan, and the interval between successive injections was 6 min. The condition was commenced 15 s before the start of the emission scan. Each emission scan lasted 90 s and was timed to coincide with the rising phase of the head curve.

The data were analyzed with statistical parametric mapping software (SPM 99, Wellcome Department of Cognitive Neurology, London [24, 25]). All the subjects' images were realigned and then normalized to a standard cerebral blood flow (CBF) template in Montreal Neurological Institute (MNI) space available on SPM 99. An isotropic Gaussian smoothing kernel of 10 mm full-width half-maximum was applied to improve the signal-to-noise ratio. Results were analyzed with a fixed effects model. Differences in rCBF between conditions were compared on a voxel-by-voxel basis with paired t tests. A hypothesis-driven analysis for the left premotor cortex was performed (Table 1). Here the anatomical boundary of premotor cortex is defined based on criteria used in previous studies [26]. The P value thresholds were set at 0.005 uncorrected for all analyses. A spatial extent threshold of 22 voxels is also applied based on SPM 99's estimation of expected number of voxels per cluster (22.305). We performed small-volume correction for the comparison [(HA − HS) − (RA − RS)] by applying left premotor cortex as the volume of interest (search volume = 70,512 mm³).

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