

End or Means—The “What” and “How” of Observed Intentional Actions

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Abstract

■ Action understanding and learning are suggested to be mediated, at least in part, by the human mirror neuron system (hMNS). Static images as well as videos of actions with the outcome occluded have been shown to activate the hMNS. However, whether the hMNS preferentially responds to *end* or *means* of an action remains to be investigated. We, therefore, presented subjects with videos of intentional actions that were shown from two perspectives (factor 1, perspective: first vs. third person) while subjects directed their attention to the *means* or the *end* thereof (factor 2, task: means vs. end). End- or means-related changes in BOLD signal and corticospinal excitability (CSE) were assessed using fMRI and TMS, respectively. Judging the *means* of an action compared with its *end* differentially

activated bilateral ventral premotor (vPMC) and inferior parietal cortex (IPL), that is, the core regions of the hMNS. The reverse contrast revealed left precuneus and bilateral superior frontal, angular, and middle temporal gyrus activity. In accordance, the two tasks, although identically in stimulus properties, modulated CSE differentially. Although recent studies suggest that the hMNS may prefer the presence of a goal or context, our data show that within the *same* context, it responds preferentially when attention is directed to the action *means*. Consequently, in addition to inferring action goals, a key function of the hMNS may be to anticipate the trajectories and dynamics of observed actions, which is a prerequisite for any timely interaction. ■

INTRODUCTION

As human beings, we interact with other people. For example, we observe and imitate their actions to learn from their successes or failures. We also judge and predict others' behavior to prepare our reactions well in advance. The human mirror neuron system (hMNS), defined as those brain regions engaged in action performance as well as action observation, has been suggested to subservise those features by transforming visual information into personal knowledge (Rizzolatti, Fogassi, & Gallese, 2001; Jeannerod, 1994). Brain imaging studies demonstrate that the rostral part of the inferior parietal lobe (inferior parietal cortex; IPL), the lower part of the precentral gyrus (ventral premotor cortex; vPMC), and the posterior part of the inferior frontal gyrus constitute the core regions of the hMNS (for a review, see Rizzolatti & Craighero, 2004). Complementary experiments using TMS demonstrate that movement observation leads to increased corticospinal excitability (CSE) closely related to the representations of the muscles involved in the observed movements (Fadiga, Fogassi, Pavesi, & Rizzolatti, 1995). More recent studies characterizing the hMNS indicate that both the action *means* as well as the action outcome may suffice to activate the mirror neuron sys-

tem (MNS): Johnson-Frey (2003) showed that even if a dynamic action is lacking but denoted by static images of the action outcome, the hMNS is selectively activated. In monkeys, Umiltà et al. (2001) demonstrated that in situations in which the outcome of an action is hidden, mirror neurons may nevertheless discharge, as long as certain cues allow the monkey to delineate what the experimenter does. However, whether the hMNS preferentially responds to action end or means remains to be investigated.

Furthermore, an increasing interest in the influence of the perspective from which an action is observed and its interaction with the hMNS has emerged recently: Although observation from an allocentric, third person perspective was suggested to be more goal oriented (Bekkering, Wohlschläger, & Gattis, 2000), an egocentric, first person perspective might favor direct matching of movement parameters and thereby differentially increase mirror neuron activity (Jackson, Meltzoff, & Decety, 2006).

We accordingly investigated whether the hMNS is differentially activated when attention is directed to the *end* or *means* of an observed action, and whether the perspective from which the action is observed interacts with the focus of attention. Using fMRI, we first studied the respective differential BOLD responses in the cortical areas known to be involved in the hMNS, that is, premotor and inferior parietal cortices. To eliminate functional differences related to differences in stimulus

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features, we presented identical sets of video stimuli (showing the experimenter placing a red cube from the right to the left side and vice versa; see Figure 1). The subject's attention was directed either to the *means* or to the *end* of the action by two different tasks imposed: Subjects either judged how the movement was performed (means) or where the cube was placed (end). Perspective (first of third person) was introduced as a second factor to investigate whether it interacts with the attentional orientation induced by the two tasks. Observed movements and cube positions as well as response button assignments were counterbalanced, and the order of the sequence of the video blocks was fully randomized. In a second study, we applied TMS to address the question whether attentional modulation of the hMNS is transmitted to and beyond the cortical motor output stage, that is, the hand area of primary motor cortex (M1Hand). Because changes in CSE induced by action observation were found to be effector specific, that is, the degree of change in CSE depends on the involvement of a muscle in the observed action, previous TMS studies on action observation argued that the observed changes reflect activity of the hMNS. Thus, we hypothesized that the additional finding of differential CSE changes depending on the focus of attention would provide further support for the concept that the hMNS is responsive to attentional modulation.

EXPERIMENTAL PROCEDURES

Subjects

Twenty volunteers (10 men), aged 20 to 37 years (mean = 26 ± 4.7 years), participated in the fMRI study, and 10 volunteers (8 men), aged 23 to 34 years (mean = 29.1 ± 3.8 years), participated in the TMS study, all with informed consent. None of the volunteers participated in both studies. All subjects were right-handed according to the Edinburgh inventory (Oldfield, 1971) and had normal or corrected-to-normal vision. None of the subjects had a history of psychiatric or neurological disease. The study was approved by the local ethics committee.

Experiment 1: fMRI Study

Behavioral Paradigm

Subjects were presented with video sequences lasting 24 sec each, in which a hand placed a cube from left to right and vice versa (Figure 1). Hand movements were shown from an egocentric (i.e., first person) or an allocentric (i.e., third person) perspective. Stimuli were presented during measurements using the software of Presentation (Neurobehavioral Systems, Albany, CA). In half of the trials, subjects indicated by button presses whether the hand was turned (45°) during the movement, in the other half whether the cube was placed onto or next to the marked target location. The mark-

ings were constant during all trials. Subjects were told that placing the cube on top or next to the marking as well as turning the cube or not were all to be regarded as correct and intended actions. Subjects used the left and right index finger for their responses with button assignments randomized across subjects.

In total, 48 video sequences were shown, each of which lasted 24 sec and included 12 hand movements, separated by 16-sec baselines that showed the empty table, but no hands and no cube. Each video was used twice, that is, once for each task. Each block was balanced for cube position and hand turns and, thus, button presses for responses.

To avoid differential eye movements between conditions, we required subjects to continuously fixate on a fixation cross, which was implemented into the videos. They were instructed to respond accurately rather than as fast as possible. However, they were told not to be too slow either. Before entering the scanner, subjects performed four to eight practice blocks.

Statistical Analysis of Behavioural Data

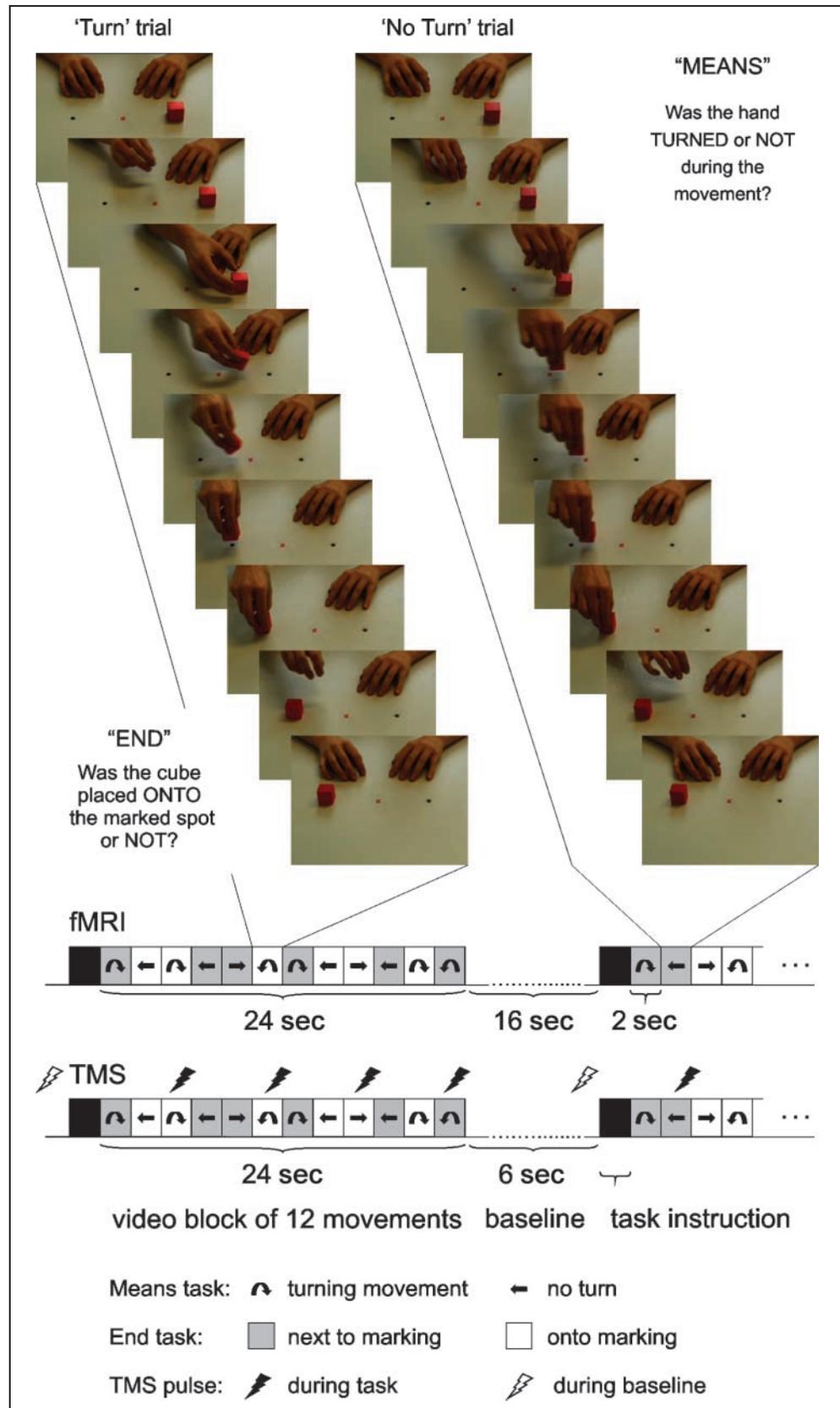
Error rates were calculated for each trial type for each subject and analyzed with ANOVA (with Greenhouse–Geisser correction) for repeated measures with the factors Task and Perspective for the fMRI. In addition to the overall analysis, errors were calculated for each block separately. Blocks, in which subjects responded incorrectly to more than three movements ($<2\%$), were modeled as a separate regressor to avoid confounding effects of error processing as well as the possibility that subjects had performed the other task by mistake. One subject responded incorrectly to more than three movements in a total of four blocks and was, thus, excluded from further analysis of the MRI data.

Functional Imaging

In the scanner, subjects lay supine with their head fixated by firm foam pads. Stimuli were projected via goggles mounted on the head coil. fMRI was carried out using EPI on a 1.5-T MRI system (SIEMENS Sonata, Erlangen, Germany) and the standard head coil for radio-frequency transmission and signal reception. Sequences with the following parameters were employed: repetition time = 2500 msec, echo time = 66 msec, field of view = $200 \times 200 \text{ mm}^2$, $\alpha = 90^\circ$, matrix size = 64×64 , voxel size = $3.125 \times 3.125 \times 4.8 \text{ mm}^3$. Using a mid-sagittal scout image, 24 axial slices (0.8-mm interslice gap) were positioned to provide whole brain coverage. fMRI time series consisted of 780 images, including six preceding dummy images allowing the MR scanner to reach steady state.

For all subjects, additional high-resolution anatomical images were acquired using the 3-D magnetization-prepared, rapid acquisition gradient-echo (MP-RAGE)

Figure 1. Behavioral paradigm. Subjects watched video sequences of 24 sec duration showing 12 hand movements that lifted a cube from the left to the right or vice versa. In half of the trials, the hand was turned during the movement by approximately 90° (left sequence; from third person perspective a clockwise turn is depicted), in the other half it was not (right sequence). In half of the trials, the cube was positioned on the marked dot on the table, in the other half at different positions next to the marked dot (left, right, behind). The cube was grasped in different ways to allow for a greater variation of movements to be judged. In the TMS study, TMS pulses were administered 500 msec before each block (baseline control) and at the second or third movement and every third movement thereafter (task conditions).



sequence with the following parameters: echo time = 4.4 msec, repetition time = 11.4 msec, flip angle = 15°, inversion time = 300 msec, matrix = 200 × 256, field of view = 230 mm, and 128 sagittal slices of 1.33 mm thickness.

Image Processing

All calculations and image manipulations were performed using MATLAB 6.5 (The Mathworks Inc., Natick, MA) and SPM2 (Statistical Parametric Mapping software, SPM; Wellcome Department of Imaging Neuroscience, London, UK; <http://www.fil.ion.ucl.ac.uk>). SPM2 was used for image realignment, slice timing, image normalization, smoothing, and creating statistical maps of significant regional BOLD response changes.

Spatially normalized functional data were smoothed with a Gaussian kernel of 8-mm full width at half maximum to meet the statistical requirements of the theory of Gaussian fields presupposed by the general linear model employed in SPM and to compensate for interindividual anatomical variability across subjects (Friston, Holmes, et al., 1995).

Individual subject analysis (fixed effects analysis: level 1). A general linear model for blocked designs (SPM2; Wellcome Department of Imaging Neuroscience; Friston, Holmes, et al., 1995) was applied voxelwise to the functional data. For each subject, four regressors for the four different experimental conditions (task ["end" or "means"] × perspective ["first person" or "third person"]) were used. In addition to the four experimental conditions, seven additional regressors modeled effects of no interest (blocks with more than three errors as well as the six head movement parameters obtained from the realignment procedure).

Data were high-pass filtered at 1/275 Hz. Video sequences were modeled as blocks lasting 24 sec. Individual motor responses (button presses) were not added as individual events but comprised within the blocks.

Parameter estimates and variance were computed for each regressor in the model using a subject-specific fixed effects model. The following contrast images of interest were calculated for each subject: effects of action observation independent of task (i.e., all tasks vs. baseline) and differential effects of task (i.e., means vs. end and vice versa) and perspective (i.e., "first person" vs. "third person" and vice versa).

Group analysis (random effects analysis: level 2). For each contrast, the contrast images of each subject from level 1 were entered into a one-sample *t* test to create an SPM_{t} statistic image. This two-stage random effects analysis enables inferences based on these contrasts to be extended to the general population from which the subjects were drawn (Friston, Holmes, & Worsley, 1999).

All activations reported survived a threshold corresponding to $p < .001$ uncorrected at voxel level and $p < .05$ corrected for multiple comparisons at the

cluster level, if not indicated otherwise. Coordinates of local maxima are given according to the Montreal Neurological Institute template.

Localization of BOLD changes. For anatomical localization of local maxima of significant BOLD signal changes, SPM_{z} statistics were superimposed on the group mean 3-D MRI image, which was calculated following stereotaxic transformation of each individual's 3-D MRI image into the same standard stereotaxic space of the Montreal Neurological Institute average brain (Friston, Ashburner, et al., 1995) employed as a template by SPM2.

Eye Movement Control

Eye position was monitored during scanning using an MR-compatible infrared eye tracker (iView, SensoMotoric Instruments GmbH, Teltow, Germany). Eye data were analyzed using ILAB software (Gitelman, 2002), and artifacts related to blinking were filtered out. A region of interest subtending 3° from the center was defined as fixation zone. The relative amount of time spent in this central region was calculated for each volunteer.

Experiment 2: TMS Study

Behavioral Paradigm

Subjects watched a modified selection of the video sequences used in the fMRI study: Only videos showing the perspective of a person opposite to the one placing the cubes were presented. Half of the videos showed a right hand moving the cubes whereas for the other half those videos were mirrored, thus showing a left hand moving the cube. They were mirrored to have identical movement features. In total, 32 videos were presented in a pseudorandomized order, interrupted by a baseline of 6 sec, which was the same as in the fMRI study, showing the empty table with no hands and no cube.

Subjects performed the same two tasks (i.e., judging whether the cube was placed onto or next to the marked target location or whether the hand was turned or not during the movement) as during the fMRI measurements. However, the left foot was used for responses (two buttons) to minimize conflicting influence of movement preparation on the excitability of the right M1Hand. Subjects again continuously fixated the fixation cross and were told to respond accurately rather than as fast as possible without being too slow either. Four to eight practice blocks were given beforehand.

TMS Stimulation and Recordings

TMS was performed using a Magstim 200 stimulator (Magstim Company, Dyfed, UK) with a monophasic current waveform and a 90-mm figure-of-eight coil. Motor-evoked potentials (MEPs) were collected simultaneously

from two muscles: the right first dorsal interosseus (FDI) and the right abductor digiti minimi (ADM). MEPs were amplified and digitized using a PowerLab 16S module (AD Instruments, Colorado Springs, CO, USA) with a band-pass of 20–1000 Hz at a sampling rate of 4 kHz and stored for off-line analysis. Stimulation was delivered to the “optimal scalp site,” defined as the position from which TMS induced stable MEPs of at least 0.5–1.5 mV mean peak-to-peak amplitude in both target muscles simultaneously (FDI and ADM). The coil was held tangentially to the subject’s head surface by a mechanical device, with the handle pointing occipitally, and held at 45° from the midsagittal axis of the subject’s head. This placement is known to optimally activate the corticospinal system transsynaptically via horizontal cortico-cortical connections (Di Lazzaro et al., 2004). Mean \pm SD TMS intensity eliciting stable MEPs as stated above was $46.0 \pm 8.7\%$ of the maximum stimulator output. Mean resting motor threshold (MT) defined as the minimal intensity of stimulation capable of inducing MEPs greater than 50 mV peak-to-peak amplitude in at least 6 out of 10 consecutive trials (Rossini et al., 1994) was determined to be at $38.9 \pm 6.45\%$ of the maximum stimulator output. With reference to these individual MT, the intensity of TMS stimulation corresponded approximately to $120 \pm 5\%$ of MT. During the session, subjects were instructed to keep both hands still and as relaxed as possible.

A single TMS pulse was delivered once 500 msec before each video block as baseline and four times during each video block, either during the second or the third movement, and then every third movement thereafter (i.e., second, fifth, eighth, eleventh or third, sixth, ninth, twelfth movement). During those specified movements, half of the pulses were administered 100 msec before the hand presented in the videos crossed the midline, half of them 100 msec before the hand placed the cube on the table. The two time points were chosen first to avoid TMS pulse expectation and second to assure that we would catch the corresponding time window when selective attention is present in case attention was phasic and short lasting (i.e., in case subjects selectively paid attention only during the turning movement when performing the means task or only during the placing of the cube in the end task). Aperture between thumb and index was constant at the two time points chosen as the hand was in the process of holding and transferring the cube. Furthermore, it was assured that the interval between two TMS pulses was at least 5 sec (range = 5.3–8.9 sec; mean \pm SD = 6.6 ± 1 sec) to prevent the previous pulse from influencing the following.

For each subject and each condition (Task \times Time point \times Hand), 16 MEPs were recorded in each muscle, FDI and ADM (128 in total), in addition to the 32 baseline MEPs. Peak-to-peak amplitude was calculated. First, pooled data of all conditions were compared with baseline. To test for the effects between observation and task conditions, we then normalized data to the individual

baseline (which was set to 100%) and submitted to an ANOVA with the factors *muscle* (FDI or ADM), *task* (end or means), *identity of the moving hand observed* (left or right), and *time of stimulation* relative to the movement (just before crossing the midline or before positioning the cube). The Greenhouse–Geisser correction was used when necessary to correct for nonsphericity. Duncan’s test was used as *post hoc* test for single contrasts.

RESULTS

Behavioral Data

Depending on the task, subjects judged whether the hand was turned during the observed movement or whether a marked location at the surface of the desk was reached or not. Error rates did not differ significantly between means and end judgments (fMRI: $4.2 \pm 0.6\%$ vs. $3.0 \pm 0.4\%$, $p = .08$; TMS: $4.0 \pm 1\%$ vs. $4.5 \pm 2\%$ correct, $p = .7$), indicating that there was no relevant difference in task difficulty.

fMRI Data

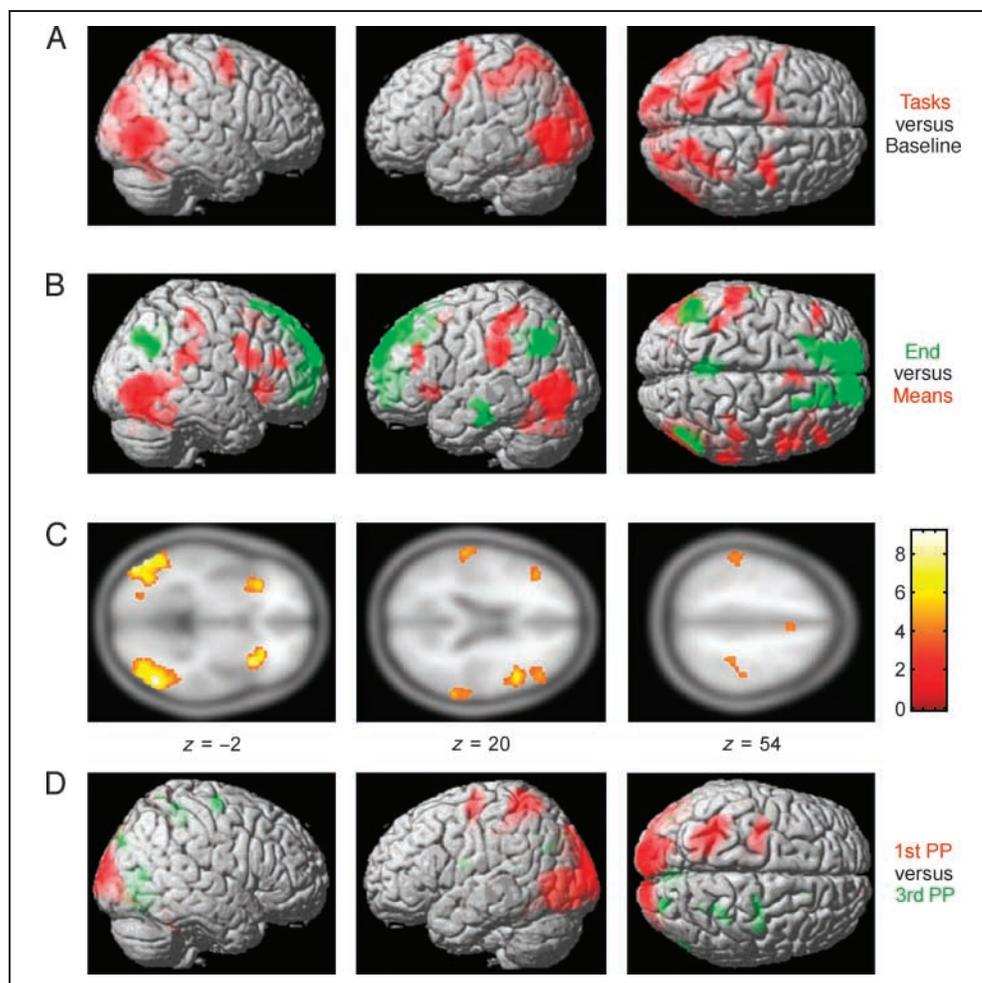
Baseline Contrast: All Conditions versus Baseline

In all conditions, subjects watched videos of a hand moving a cube from one position to another with or without a turning movement in between, whereas during the intermittent baseline, only static images of the empty table surface were shown (Figure 1). Comparing each condition to this baseline should reveal cortical areas known to form the hMNS, that is, premotor and inferior parietal cortices (Jacoboni, 2005; Grezes, Armony, Rowe, & Passingham, 2003; Koski et al., 2002; Buccino et al., 2001; Perani et al., 2001). As expected, fMRI results showed fairly symmetrical bilateral activations of the intraparietal sulcus (IPS) and premotor cortex (PMC) in addition to widespread activations of the occipital cortex during action observation compared with baseline independent of where attention was directed (end, means) (Figure 2A).

Main Effect of Task: End versus Means

Action observation is often considered to be goal directed (Fogassi et al., 2005; Buccino et al., 2001; Rizzolatti & Luppino, 2001; Umiltà et al., 2001; Gallese, Fadiga, Fogassi, & Rizzolatti, 1996). The hMNS has been shown to be active during action observation. However, whether the hMNS is goal directed and serves perception, analysis, and prediction of action goals remains unclear. If this were the case, its activity should be enhanced when the end or goal of an observed action needs to be judged and is, thus, attended to. This should be revealed by the contrast (end–means). Previous accounts further indicate that the medial prefrontal region plays a critical role in reading the intentions of others (Blakemore & Decety, 2001; Shallice, 2001; Bekkering et al., 2000; Frith & Frith, 1999) and in extracting action goals

Figure 2. fMRI Results. (A) Baseline contrast: In the comparison of all conditions independent of task and viewpoint to baseline, which showed no hands but an empty table, differential BOLD signal changes were found bilaterally in a widespread network including the IPS, PMC, and occipital cortex. (B) Main effect of task; red: means > end; green: end > means. (C) Sections (z indicated below) showing individual areas of significant differential BOLD-signal changes for means > end. (D) Main effect of perspective; red: first person (egocentric) perspective > third person (allocentric) perspective; green: third person perspective > first person perspective.



(Chaminade, Meltzoff, & Decety, 2002). Thus, this region was hypothesized to be active in this contrast.

fMRI data showed that the end task differentially activated the superior frontal and angular gyrus bilaterally, as well as the left precuneus and the middle temporal gyrus. The respective locations are represented in Figure 2B in green, whereas locations and Z values of the individual cluster peaks are listed in Table 1.

In accordance with previous data stated above, activity within the superior frontal region was indeed enhanced under this condition. However, quite surprisingly, none of those areas generally associated with the hMNS were differentially involved, when attention was directed to the end task.

Main Effect of Task: Means versus End

Judging the means of an observed action required the observer to attend particularly to the hand movement itself rather than catching its end. It should, thus, reflect cortical areas more closely related to visual analysis of the observed motion. Area V5, involved in visual motion processing, is known to be enhanced when paying attention to moving stimuli (Grossman & Blake, 2002;

Friston & Büchel, 2000; Büchel et al., 1998). It was, thus, expected to be differentially engaged during the means task when attention was directed to the moving hand—along with other cortical areas that process observed human motion in particular, such as hMNS, if it represents human action means rather than the end thereof.

This contrast showed significant differential BOLD signal changes in bilateral vPMC (BA 6, BA 44) and SMA, IPS and IPL (supramarginal gyrus), and—as expected—inferior temporo-occipital junction including V5. These results are shown in Figure 2B (in red) and in the anatomical sections in Figure 2C. Locations and Z values of the individual cluster peaks are given in Table 1. Thus, with vPMC and IPL being differentially activated in this contrast, areas associated with the hMNS differentially responded to action *means*.

Main Effect of Perspective: First versus Third Person Perspective and Vice Versa

Independent of the task, videos were presented in two different perspectives, an egocentric, first person, and an allocentric third person, perspective. In comparison to baseline, each perspective elicited a fairly bilateral

Table 1. Main Effect of Task

Cluster	Left							Right						
	x	y	z	Z Score	k_E	p_{corr} (Cluster Level)	p_{corr} (FDR, Voxel Level)	x	y	z	Z Score	k_E	p_{corr} (Cluster Level)	p_{corr} (FDR, Voxel Level)
<i>Means > End</i>														
ITG/IOG (V4/V5)	-52	-72	-4	5.26	2882	<.001	<.001	52	-66	-2	5.53	2746	<.001	<.001
Insula	-32	26	-2	4.44	248	.004	.001	36	20	-2	5.41	1221	<.001	<.001
MFG (area 45)	-48	32	32	4.1	224	.006	.002	48	34	20				
Area 44								50	14	22	4.85			.001
STG/SMG	-66	-30	28	4.84	1030	<.001	.001	64	-40	24	4.36	271	.002	.001
IPL	-36	-46	54	4.12			.002	34	-36	48	3.72			.006
Area 2	-54	-32	54					48	-32	54	4.1	257	.003	.002
SMA								2	12	52	3.85	201	.011	.004
<i>End > Means</i>														
SFG	-20	32	38	3265	5.17	<.001	.014	24	22	64	246	3.95	.004	.015
	-16	40	38		4.54		.014	24	40	52		3.83		.015
	-20	42	46		4.51		.014	14	38	56		3.73		.016
IPFm (AngG)	-48	-60	38	628	4.55	<.001	.014	48	-74	38	375	4.59	<.001	.014
	-42	-54	28		3.91		.015	60	-60	34		3.97		.015
	-56	-66	28		3.75		.016							
Precuneus (MCC)	-6	-54	40	469	4.32	<.001	.014							
	-8	-40	38		3.48		.021							
Wernicke/ TE30	-60	-20	-14	206	3.57	.010	.019							
	-60	-16	-24		3.52		.020							
	-62	-12	-12		3.47		.022							

Brain regions showing relative BOLD signal increases associated with means versus end task and end versus means task, respectively. Coordinates in standard stereotaxic space (MNI) refer to the maximally activated focus within an area of activation as indicated by the highest Z score. x, distance (mm) to right (+) or left (-) of the midsagittal plane; y, distance anterior (+) or posterior (-) to vertical plane through the anterior commissure; z, distance above (+) or below (-) the intercommissural (AC-PC) plane. $p < .001$ uncorrected at the voxel level and $p < .05$ corrected at the cluster level for multiple comparisons across the whole brain.

pattern including bilateral visual, premotor, and superior parietal and cerebellar regions. However, direct comparison of the two perspectives revealed quite a striking lateralization (Figure 2D): Areas showing stronger activation during the third person perspective compared with first person perspective were lateralized to the right hemisphere and included right visual areas (mainly lingual gyrus), right extrastriate body area (EBA), right superior parietal lobule (BA 1, 2, 3a/b), and right precentral gyrus (BA 4, 6). Inversely, areas showing stronger activation during the first person perspective compared with third person perspective were lateralized to the left

hemisphere, including left precentral gyrus (BA 4, 6), left superior parietal lobule (BA 1, 2, 3a/b), and left EBA apart from engagement of bilateral (although left dominant) visual areas (BA 17/18). Locations and Z values of the individual cluster peaks are given in Table 2.

Interaction between Task and Perspective

The two perspectives were chosen to investigate whether, apart from the explicit focus of attention imposed by the task, perspective taking might implicitly favor either aspect (end or means) of the observed action. Jackson

et al. (2006) suggested an egocentric, first person, perspective to allow for a more direct matching of movement parameters and thereby increased mirror neuron activity in comparison to third person perspective. Following Bekkering et al. (2000), observation from an allocentric, third person perspective might be more goal oriented to simplify and overcome complex spatial transformations. If this were the case, an interaction between task and perspective might be observed. Interactions were investigated using the contrasts [(end 1stPP–end 3rdPP)–(means 1stPP–means 3rdPP)] as well as [(means 1stPP–means 3rdPP)–(end 1stPP–end 3rdPP)]. However, no cortical region could be detected, in which an interaction between task and perspective reached significance (even when lowered to a $p < .001$ uncorrected).

Jackson et al. (2006) had found a significant differential activation in the left sensorimotor cortex when contrasting observation from the first person perspective with observation from the third person perspective. Based on their results, we used the left precentral gyrus with the indicated coordinates $x = -36, y = -22, z = 70$ for VOI analysis, which did not yield any significant activation. Neither did for the inverse contrast VOI analysis centered on the right lingual gyrus at $x = 4, y = -78, z = -2$ as indicated by Jackson et al. show a significant differential BOLD effect.

TMS Data

Having identified both vPMC and IPL as structures differentially engaged in judging the means (compared with judging the end) of an action, TMS was used as

an alternative measure to study the effect of attention on the hMNS and, in particular, whether attentional modulation also affects the corticospinal tract as the final motor output stage. Although the TMS-induced facilitation should be considered a corticospinal effect because MEPs are observed when stimulating M1Hand, converging evidence suggests that the facilitating effect occurs at a cortical rather than at the spinal level (Baldissera, Cavallari, Craighero, & Fadiga, 2001; Strafella & Paus, 2000). MEP facilitation induced by action observation most likely originates from excitatory cortico-cortical connections from premotor mirror neurons to primary motor neurons of M1Hand (Fadiga, Craighero, & Olivier, 2005). Increases in MEP amplitude are, thus, likely to reflect increases of premotor activity.

Due to the blocked fMRI design, differences in M1Hand, which may be quite restricted in time as they follow the observed movement pattern, may have been missed and/or overridden by response-related BOLD signal changes. In addition, the fMRI study could not differentiate whether the differential modulation imposed by the focus of attention is specific for the muscles involved in the observed task or not. Previous TMS studies suggest that the muscles active during action observation are the same as those actually used in the respective action (Strafella & Paus, 2000; Fadiga et al., 1995) and faithfully follow the course of the action (Montagna, Cerri, Borroni, & Baldissera, 2005; Gangitano, Mottaghy, & Pascual-Leone, 2001). This finding of muscle specificity, that is, that observation of a certain motor act preferentially activates those cortical motor regions in the observer's M1 that correspond to the muscles used by

Table 2. Main Effect of Perspective

Cluster	Side	Egocentric > Allocentric						Allocentric > Egocentric						
		x	y	z	Z Score	k_E	p FDR-corrected (Voxel Level)	Side	x	y	z	Z Score	k_E	p FDR-corrected (Voxel Level)
Area 17/area 18	R	8	-102	6	7.05	7142	<.001	R	6	-74	0	6.08	1882	<.001
	L	-16	-98	14	6.31		<.001	R	18	-74	-10	5.87		<.001
	L	-6	-102	16	6.28		<.001	M	0	-52	4	3.56		.021
SPL: area 2/area 1/area 3a/b	L	-26	-54	66	5.26	1862	<.001	R	28	-44	58	4.68	286	<.001
	L	-28	-46	58	5.08		<.001	R	36	-36	54	4.05		.004
	L	-36	-48	68	4.98		<.001	R	24	-84	32	4.67	160	.001
Precentral gyrus: area 6/area 4a/p	L	-32	-12	62	4.99	829	<.001	R	22	-88	42	4.08		.004
	L	-24	-12	52	4.27		<.001	R	18	-16	60	4.51	238	.001
	L	-30	-12	46	4.26		<.001	R	40	-8	60	3.46		.028
MTG: EBA	L	-44	-80	6	4.91	236	<.001	R	58	-68	10	3.88	77	.008
	L	-48	-74	-8	4.57		<.001	R	62	-62	6	3.42		.032
	L	-54	-74	2	4.55		<.001							

MNI coordinates of brain regions showing relative BOLD signal increases associated with *first* versus *third person* perspective and *third* versus *first person* perspective, respectively.

the actor, was taken to argue that the observed changes in CSE actually reflect hMNS activity arriving in M1. Because reaching, grasping, and lifting as well as a precision grip involve predominantly the FDI, but not the ADM of the small hand muscles (Lemon, Johansson, & Westling, 1995), we chose FDI to test for differential effects during action observation whereas ADM served for control.

Apart from the effect of attention, the fMRI study explored the effect of perspective on hMNS activity. Perspective did not show any interaction with the focus of attention but a lateralization for the egocentric perspective to the left hemisphere and allocentric perspective to the right hemisphere. Instead of reinvestigating the ef-

fect of perspective, we restricted the TMS experiment to the allocentric perspective and set out to study whether the left motor cortex differentiates between observation of left- and right-hand movements. In the egocentric perspective, Aziz-Zadeh, Maeda, Zaidel, Mazziotta, and Iacoboni (2002) already demonstrated stronger contralateral CSE changes during unimanual hand observation.

Motor-evoked Potentials

Overall, movement observation (independent of any of the factors *muscle*, *task*, *time*, or *side*) significantly increased CSE compared with the baseline, which was measured before the video onset ($p = .034$; Figure 3).

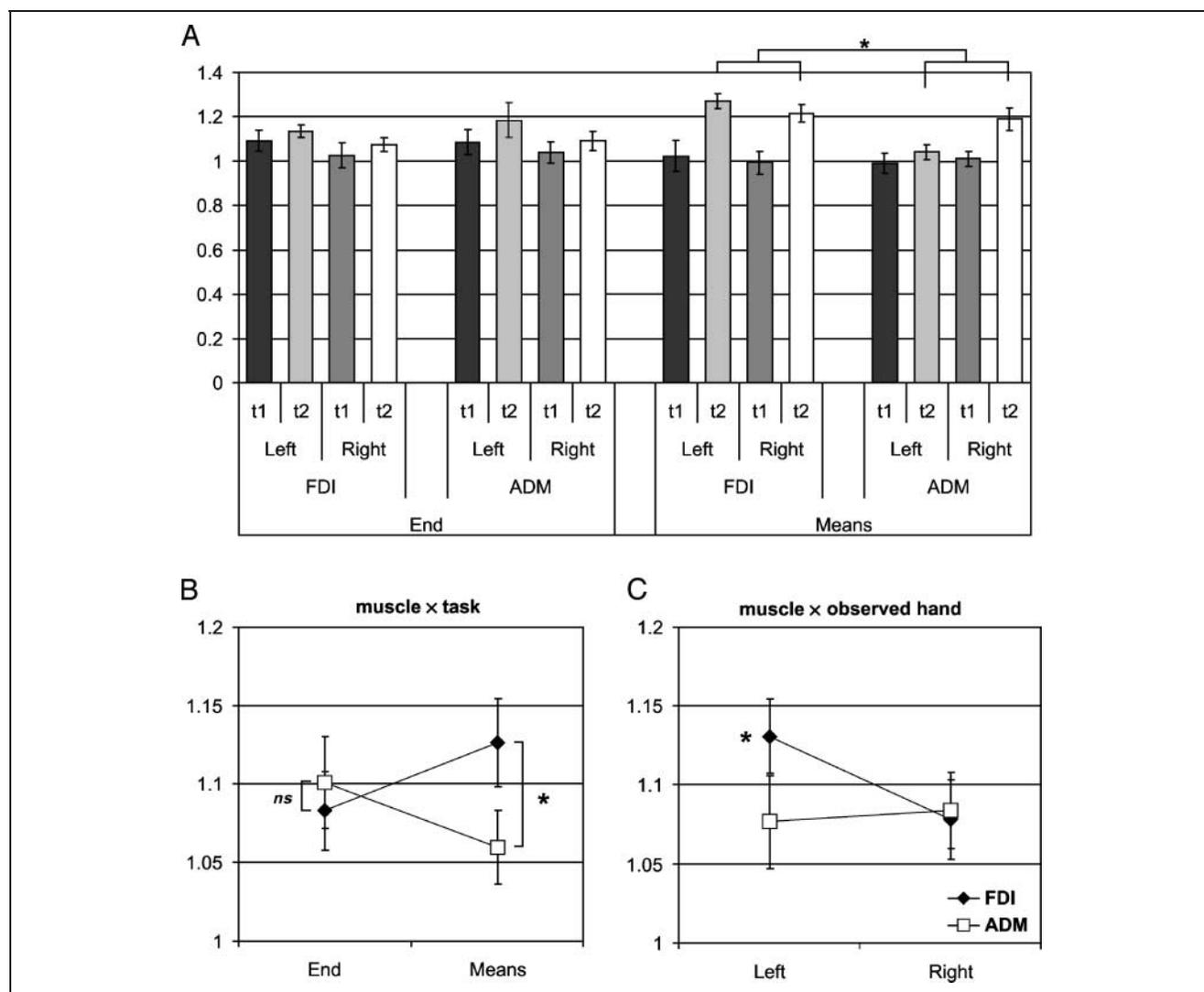


Figure 3. TMS data. (A) Mean values of recorded MEPs \pm SE normalized to the individual baseline for all subjects during the end or the means task. MEPs were recorded from the FDI (involved muscle) and the ADM (control) at two time points during observation of the transition movement: before crossing the midline (t1) or before positioning the cube (t2). Movements were performed with the actor's left or right hand. (B) Interaction between muscle and task. Post hoc tests showed a significant difference between ADM and FDI during the means task ($p = .019$). Asterisk indicates significant difference, *ns* = not significant. (C) Interaction between muscle and identity of the observed hand. Post hoc analysis showed that MEPs of FDI recorded while observing left-hand movements differed significantly from any of the other three conditions ($p \leq .020$) as indicated by the asterisk.

To analyze effects of individual factors during action observation, we performed an ANOVA based on the TMS data normalized to the individual baseline. This ANOVA included the factors *muscle*, *task*, *time*, and *side* and showed a significant main effect of time with increased MEPs at the second time point [$F(1, 9) = 7.188$, $p = .025$]. Two significant two-way interactions were found between muscle and task [$F(1, 9) = 7.505$, $p = .023$] as well as between muscle and side [$F(1, 9) = 6.418$, $p = .032$]. Finally, there was a significant three-way interaction between muscle, task, and side [$F(1, 9) = 6.283$, $p = .033$]. None of the other main effects or interactions reached significance. Crucially, there was no interaction between time and task or muscle or side, indicating that the effect of time was independent of any of the other factors.

The post hoc test on mean contrasts of the interaction between muscle and task indicated that for the means task only, MEPs recorded from the FDI were increased compared with MEPs of ADM ($p = .019$). Post hoc test on mean contrasts of the interaction between muscle and side implied that this interaction was mainly driven by FDI when left-hand movements were observed: MEPs were significantly stronger for FDI and observed left-hand movements than during any of the other conditions ($p = .014$ for comparison with FDI right-hand movements as well as ADM left-hand movements; $p = .020$ for comparison with ADM right-hand movements).

DISCUSSION

Attentional Modulation of Cortical Areas Involved in Action Observation

As the main finding, attending to the means of the observed movement rather than attending to the end differentially engaged cortical areas known to be part of the hMNS: bilateral vPMC (BA 6, BA 44) and IPL (supramarginal gyrus), along with SMA and inferior temporo-occipital junction including V5. Importantly, the core regions of the hMNS, that is, the vPMC and the IPL, were differentially activated when subjects attended to the movement *per se* rather than its end. This finding suggests that the hMNS relates more to the movement generating the action than to its outcome.

In contrast, when subjects attended the End of the action, differential BOLD responses were found in the superior frontal and angular gyrus, the left precuneus, and middle temporal gyrus bilaterally. The medial prefrontal region has been shown to play a critical role in reading the intentions of others (Blakemore & Decety, 2001; Shallice, 2001; Bekkering et al., 2000; Frith & Frith, 1999) and in extracting action goals (Chaminade et al., 2002), whereas both the angular gyrus and the precuneus were involved in long-term action planning (Ruby, Sirigu, & Decety, 2002) as well as object (angular gyrus;

Moore & Price, 1999) or action observation (precuneus; Perani et al., 2001; Grezes & Costes, 1998), respectively. Thus, our results are well in line with previous data—however, quite surprisingly, none of the “classical” hMNS areas were differentially involved when attention was directed to the action end.

Apart from the focus of attention, the conditions end or means may have differed with respect to timing and duration of attention: In principle, subjects could have paid attention throughout the block—or for a short moment only during the most task relevant time period of each movement, that is, the turn in the middle of the transfer from one side to the other or the placing of the cube after this transfer. However, as individual movements were quite fast and presented at a regular frequency of 0.5 Hz, event-related BOLD responses, even if transient, overlap and form sustained activity and should, thus, be adequately modeled by the chosen block design. Therefore, differences in the duration of attention paid cannot fully account for the present fMRI results.

Attentional Modulation of CSE Changes during Action Observation

We observed a significant increase in CSE during movement observation compared with baseline, irrespective of the factors involved. ANOVA analysis and post hoc tests on conditions normalized to the baseline, furthermore, revealed a significant interaction between muscle and task and a differential enhancement of CSE in FDI compared with ADM during the means task only. This enhanced differentiation between FDI, the muscle primarily involved in the observed action, and ADM, serving as a control, suggests that attention directed to the action means allows for a more specific emulation of the observed movement than attending to the action end.

Several previous TMS studies emphasized effector specificity of the hMNS by demonstrating that the same muscles facilitated during the observation of a given action were active during its execution (for a review, see Fadiga et al., 2005). This effector specificity has been taken as an indication that these changes reflect hMNS activity. Our findings support this rationale suggesting that the enhancement of hMNS activity revealed by fMRI involves a more effector specific modulation of CSE as demonstrated in the TMS study.

CSE was evaluated at the two time windows where attention, if transient, was most likely present: just before the turning or the positioning of the cube. It should be noted that a more detailed time analysis was not feasible with set up used. There was a significant effect of timing with an increase in MEP amplitude at the second time point (i.e., just before positioning the cube). The fact that this effect was independent of any of the other factors, task, muscle, or identity of moving hand, excludes that it was related to any of these. Differences in other aspects of attention or in stimulus features may

have played a role, but the current set up does not allow disentangling these further.

End or Means—Reconciling Attentional Modulation and Current Theories on the hMNS

Our findings of increased hMNS activity and effector specificity when attending to the means of an observed action need to be reconciled with previous accounts emphasizing the goal-directedness of mirror neurons (Fogassi et al., 2005; Buccino et al., 2001; Rizzolatti & Luppino, 2001; Umiltà et al., 2001; Gallese et al., 1996). In humans, the presence of a goal—in the form of explicit markings of a reaching task (Koski et al., 2002) or implied by a certain context (Iacoboni et al., 2005)—has been shown to enhance activity in the frontal operculum and dorsal PMC during imitation (Koski et al., 2002) or observation (Iacoboni et al., 2005) compared with situations in which there is no obvious goal. These findings have been taken to suggest that mirror neurons are tuned to the goal of an action rather than the movement per se. However, it remains to be elucidated whether the identified structures represent the goal (present only in one condition) or whether the presence of a goal automatically induces further cognitive processes in which the hMNS plays a role. In our set up, the “goal” refers in a rather restricted sense to the end, the final position of the cube. Keeping the context, the end, the stimuli, and the responses identical across conditions, we showed that directing attention to the action *means* (relative to directing attention to the action *end*) differentially involves the hMNS. This suggests that within the same context, the hMNS rather processes aspects of the action *means*, that is, the movement itself.

Taken to support the notion of goal-directedness, some mirror neurons were shown to display some degree of effector independence, that is, to respond to reaching regardless of the effector used, whether reaching is made with a tool, the hand, or the mouth (Ferrari, Rozzi, & Fogassi, 2005). However, Buccino et al. (2001) showed in their fMRI study that observation of both transitive and intransitive actions, compared with observation of a static image of the same action, led to the activation of different regions in the PMC and the Broca’s area, depending on the effector involved in the observed action. Those regions overlapped with the somatotopically organized motor representation of the different effectors. Similarly, as already stated above, several TMS studies emphasized effector specificity of the hMNS by demonstrating that the same muscles facilitated during the observation of a given action were active during its execution (Fadiga et al., 2005). These divergent findings may, at least in part, relate to technical or methodological differences: In contrast to single-cell recordings in monkey studies, fMRI or TMS studies do not allow to draw conclusions about individual neurons within cortical

areas. There may be different groups of neurons within the MNS, some effector dependent, some independent, which might have been differentially activated also in our setup. Overall, however, if those two classes exist, our results rather suggest that effector-specific—and, thus, rather *means*-related—neurons predominate within the hMNS.

Which functional scope may underlie the processes causing a differential activation of the hMNS associated with action *means* relative to action *end*? A recent imaging study examined the cortical structures involved in the imitation of the *means* or the *end* of an action: Chaminade et al. (2002) showed that reconstructing the *means* of an action (during imitation of the goal) differentially involves the left PMC (−20, 16, 54) and the right dorsolateral PMC (22, 6, 60), whereas extrapolating the goal of a pantomimed action (when imitating the *means*) differentially activates the medial pFC (2, 56, 36). Although their findings agree with our data regarding frontal cortex, the lack of activation of parietal areas in the study by Chaminade et al. may either be due to differences between neuronal processes underlying action imitation versus simple observation (in our study) or to a threshold effect, which they chose at $p < .0005$.

Their findings further suggest that neuronal activity in the respective condition rather relates to the active processes reconstructing the missing feature when imitating the other. Accordingly, we would like to suggest that the hMNS is involved in an active process rather than the passive reception of the movements observed. A key purpose of the hMNS may be to emulate and to predict observed movement parameters: Behavioural (Flanagan, Vetter, Johansson, & Wolpert, 2003) and TMS studies (Urgesi, Moro, Candidi, & Aglioti, 2006) provide evidence that during observation we actually *predict* rather than simply *follow* the actions of others. Furthermore, motor cortex activity has been shown to precede the onset of an observed action (Kilner, Vargas, Duval, Blakemore, & Sirigu, 2004; Haueisen & Knosche, 2001). As timing in general is crucial for almost any kind of interaction and delays due to sensory processing, planning, and preparation of actions are inevitable, predictions are indispensable for any kind of interaction with our conspecifics. In competitive situations, it may also be advantageous not only to predict the action goal, for example, that someone wants to grab my apple, but also to anticipate the action *means*, that is, to predict the movement path of an arm reaching for an apple, because this not only allows one to take the apple first (if fast enough) but also to stop the other’s hand from reaching for it. In general, our capacity to make appropriate predictions is limited to movements whose trajectories follow simple geometric principles or are stereotypic (Kerzel, 2002; Finke & Freyd, 1985). However, human body movements and actions are (although biomechanically restricted) neither simple and geometric nor stereotypic. We, thus, need a mechanism that enables

us to emulate the biomechanics of the human body, including muscle response properties and movement range of various joints (Blakemore & Decety, 2001; Arbib, Billard, Iacoboni, & Oztup, 2000; Imamizu et al., 2000; Wolpert & Kawato, 1998). Instead of creating new emulators, it seems sensible to access knowledge that is readily present. This could be provided by the (pre)-motor system: Mapping expected movements onto our own motor system probably allows the most accurate prediction possible of the temporal and spatial aspects of another human's action. The better an observed movement is known to oneself, the more precise our prediction will be, as in the case of well-trained experts (Calvo, Glaser, Grezes, Passingham, & Haggard, 2003) or if we see videos of our own movements (Knoblich, Seigerschmidt, Flach, & Prinz, 2002). However, to predict likely motor acts, vPMC may rely on the presence of goals suggestive of any motor act to come. This may explain why in the context of goals vPMC involvement is enhanced (Iacoboni et al., 2005; Koski et al., 2002).

Previous TMS data support this reasoning by showing that the most likely movement (in that case, a direct grasp) is automatically anticipated and that this prediction is abandoned, as soon as it fails (when an artificial delay in aperture or a sudden closure of the fingers is introduced)—although the anticipated final goal is reached (Gangitano, Mottaghy, & Pascual-Leone, 2004). Thus, although Iacoboni et al. (2005) as well as Umiltà et al. (2001) suggested that the MNS automatically infers a forthcoming *goal*, our data offer a new perspective suggesting that the MNS deduces a forthcoming *motor act*.

Apart from differential task-dependent enhancement of CSE, our TMS data also revealed a significant effect of time, with an increase in MEP amplitude just before positioning the cube compared with just before crossing the midline. The effect of time was independent of any of the other factors, task, muscle, or identity of moving hand. At first sight, enhancement at the later time point seems to contradict the concept of prediction. However, the temporal relationship between hMNS activity and its effects on CSE changes is not known. Although Gangitano et al. (2001) showed that the degree in CSE change faithfully correlates with the movement, the exact temporal coherence with cortical activity has not been studied. If there is a time lag between the cortical activity in the hMNS and the CSE, prediction would even be a prerequisite to allow for timely changes in CSE. In addition, a more detailed analysis of the time course of MEP changes, which was not feasible within our design, is necessary before drawing further conclusions.

Our view that vPMC and IPL predict action features does not exclude that the MNS subserves other previously suggested functions, such as facilitating imitation (Oztup, Kawato, & Arbib, 2006; Iacoboni, 2005; Wohlschläger & Bekkering, 2002) and observational learning (Mattar & Gribble, 2005; Stefan et al., 2005; Edwards, Humphreys, & Castiello, 2003; Heyes & Foster,

2002), allowing interpersonal bonding by imitating others (Lakin & Chartrand, 2003; Chartrand & Bargh, 1999) or forming the grounds for the evolutionary development of language (Arbib, 2005; Corballis, 2004). However, as far as an understanding of other people's actions is concerned, our data suggest that vPMC and IPL most probably play a more motor-related role of reading forthcoming actions *means* rather than their *end*.

Effect of First versus Third Person Perspective Taking on Action Observation

As a secondary finding, the comparison of the two perspectives revealed quite a striking lateralization with a right hemispheric bias for the allocentric and left hemispheric dominance for the egocentric perspective. More specifically, contrasting third versus first person perspective showed activation of right visual areas (mainly lingual gyrus), right EBA, right superior parietal lobule (BA 1, 2, 3a/b), and right precentral gyrus (BA 4, 6), whereas in the inverse contrast, left precentral gyrus (BA 4, 6), left superior parietal lobule (BA 1, 2, 3a/b), and left EBA and bilateral visual areas (BA 17/18) were activated. Similarly, Jackson et al. (2006) found increased activity of the contralateral left precentral gyrus and bilateral cuneus during observation of intransitive actions from a first person compared with third person perspective, whereas observation and imitation from a third person perspective resulted in subthreshold activation of the right lingual gyrus.

One might argue that the laterality effect observed when comparing each perspective to the other resulted from lateralized stimuli: All videos presented in the fMRI study showed right-hand movements only; thus, the moving stimuli were presented predominantly (although not exclusively as the hand crossed the midline in each movement) in the right visual hemifield in the condition of egocentric perspective and in the left visual hemifield in the allocentric perspective. Then, despite a bilateral representation of the movement as a whole (as revealed by the individual contrasts against baseline), a significantly greater portion seems to be mapped onto the hemisphere contralateral to the predominant visual field stimulation (as revealed by the differential contrasts). Presenting static images of left- and right-hand actions in the first person perspective in the left and right visual field, respectively, Aziz-Zadeh, Koski, Zaidel, Mazziotta, and Iacoboni (2006) had shown similar activation of the contralateral primary motor, posterior parietal, and extrastriate visual fields. Their main finding of ipsilateral pars opercularis activation was—according to a more detailed analysis—significant only for imitation, which might explain the lack of this result in our experiment asking subjects to observe but not imitate the movement.

Finally, an interaction between perspective and hand identity might have caused the laterality effect: Right-hand

movements observed in the first person perspective showed a bias to the contralateral left hemisphere, whereas right-hand movements observed in the third person perspective lateralized to the ipsilateral right hemisphere. Complementary, our TMS data indicate that in the third person perspective, observation of left-hand movements compared with right-hand movements significantly increased CSE of FDI representation in the ipsilateral left motor cortex. Previously, Aziz-Zadeh et al. (2002) presented stronger contralateral CSE changes, when unimanual hand actions were observed in the egocentric perspective. Taken together, these findings suggest that whereas in the first person perspective actions are directly matched onto our sensory-motor system (i.e., observed right-hand actions are preferably mapped onto the contralateral left motor cortex), movements seen in the third person perspective are represented in a mirrored fashion (i.e., observed left-hand actions are preferably mapped onto the ipsilateral left motor cortex, which generally controls our own right-hand movements, and vice versa). This finding might help to explain why preschool as well as school-aged children spontaneously prefer mirror-image imitation as more “natural” than anatomical imitation (Bekkering et al., 2000; Gleissner, Meltzoff, & Bekkering, 2000; Schofield, 1976; Wapner & Cirillo, 1968). However, further investigations including left-hand movements are necessary to disentangle contribution of visual field stimulation, perspective, and hand identity to this laterality effect.

The perspectives were chosen as a second factor to investigate whether perspective influences perception of one aspect or the other of an observed action: Previously, Bekkering et al. (2000) suggested that observation from an allocentric, third person perspective might be more goal oriented, whereas Jackson et al. (2006) proposed that an egocentric, first person perspective might favor direct matching of movement parameters and increase mirror neuron activity. However, no significant interaction between task and perspective could be shown to support those previous accounts.

In summary, presenting subjects with identical stimulus material (i.e., action videos) under two different tasks, we showed that brain areas that previously have been associated with the hMNS are sensitive to attentional modulation: vPMC and IPL were differentially activated by attending to the *means* of an observed movement rather than its *end*, as revealed by fMRI. Importantly, any differences between the activation patterns of the two tasks cannot be attributed to differences in visual features of the stimuli or the responses made as these were identical across the two tasks. Effects of perspective suggest a direct matching onto the (contralateral) sensory-motor system in the first person perspective, whereas actions observed from a third person perspective seem to be matched in a mirror-like fashion (i.e., to the sensory-motor cortex ipsilateral to the moving hand). The finding of effector-specific modulation of M1Hand during the

means task most probably reflect excitatory influence from vPMC exerted upon M1Hand.

Contrary to previous views emphasizing the goal-directedness of the hMNS, our results show that within the same context, the hMNS is differentially activated when attending to the action *means*. This suggests that the context may be used to predict likely movement parameters, which is a prerequisite for any timely interaction with our conspecifics, and that the hMNS serves as an emulator for this prediction.

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