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How your hand drives my eyes

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When viewing object-related hand actions people make proactive eye movements of the same kind as those made when performing such actions. Why is this so? It has been suggested that proactive gaze when viewing a given hand action depends on the recruitment of motor areas such as the ventral premotor (PMv) cortex that would be involved in the execution of that action. However, direct evidence for a distinctive role of the PMv cortex in driving gaze behavior is still lacking. We recorded eye moments while viewing hand actions before and immediately after delivering repetitive transcranial magnetic stimulation (rTMS) over the left PMv and the posterior part of the left superior temporal sulcus, which is known to be involved in high-order visual action processing. Our results showed that rTMS-induced effects were selective with respect to the viewed actions following the virtual lesion of the left PMv only. This, for the first time, provides direct evidence that the PMv cortex might selectively contribute to driving the viewer's gaze to the action's target. When people view another's action, their eyes may be driven by motor processes similar to those they would need to perform the action themselves.

Keywords: proactive eye movement; ventral premotor cortex; superior temporal sulcus; rTMS; action observation; grasping

INTRODUCTION

Target-specific proactive gaze shifts are crucial for planning and executing object-related hand actions (Land *et al.*, 1999; Johansson *et al.*, 2001; Bowman *et al.*, 2009; Brouwer *et al.*, 2009). Strikingly, people viewing rather than performing object-related hand actions also make proactive eye movements. Their gaze typically reaches the target well before the actor's hand (Rotman *et al.*, 2006; Webb *et al.*, 2010), especially when people can take advantage of action-related cues (Flanagan and Johansson, 2003; Rotman *et al.*, 2006; Webb *et al.*, 2010; Ambrosini *et al.*, 2011)

These findings have been accounted for by suggesting that the same motor representation might drive people's target-specific proactive gaze shifts while executing and viewing a given object-related hand action (Flanagan and Johansson, 2003; Falck-Ytter *et al.*, 2006). This would be consistent with neurophysiological and brain imaging evidence showing that viewing another's hand action recruits not only high-order visual areas such as the posterior part of the superior temporal sulcus (pSTS) (Puce and Perrett, 2003) but also the same motor cortical regions—the ventral premotor (PMv) cortex and the inferior parietal lobule including the cortex located inside the intraparietal sulcus—as if the viewer were performing that action herself (Rizzolatti *et al.*, 2001; Rizzolatti and Sinigaglia, 2008a,b, 2010; Sinigaglia, 2010). This would also explain why the temporal relation between the viewer's gaze and the actor's hand might be similar to that between the actor's own gaze and hand (Flanagan and Johansson, 2003; Falck-Ytter *et al.*, 2006).

Although it has been suggested that the recruitment of cortical motor areas is critical in implementing target-specific gaze shifts (see also Cannon and Woodward, 2008), direct evidence for this hypothesis is still lacking (Falck-Ytter, 2012). In particular, to date there is no evidence for a distinctive role of PMv cortex in proactively driving the viewer's gaze to the actor's target.

The aim of our study is to tackle this issue. To this end, we used low-frequency (1 Hz) repetitive transcranial magnetic stimulation (rTMS) to investigate whether PMv cortex might contribute to target-specific proactive gaze shifts and to what extent this contribution might differ from that of the pSTS cortex, which is typically involved in visual processing of object-related hand actions (Allison *et al.*, 2000; Puce and Perrett, 2003; Avenanti *et al.*, 2012). Indeed, with this rTMS protocol it is possible to induce transient 'virtual lesions' in neurologically intact participants by suppressing excitability to motor and non-motor cortical areas (Chen, 1997; Hilgetag *et al.*, 2001; Avenanti *et al.*, 2007; Ziemann, 2010; Sandrini *et al.*, 2011).

We recorded eye movements in separate blocks before and immediately after delivering rTMS to the PMv or the pSTS cortex in the left hemisphere while participants observed an actor reaching for and grasping with his hand one of the two objects of different sizes. In a control condition, the actor merely reached for and touched one of the two objects without grasping it. In all trials, participants were not given any prior information about which object would be the target of the observed action. If the motor processing of observed hand actions was not critically involved in driving target-related gaze shifts, we should expect that the proactivity of gaze behavior would not be impaired by the virtual lesion of the PMv cortex. In contrast, if the motor processing of observed hand actions played a distinctive role in implementing target-related gaze shifts, we should expect the lesion of the PMv cortex to selectively impact on the proactivity of the gaze.

METHODS

Participants

Twelve right-handed subjects [eight females; mean age (s.d.) = 25.4 (2.8) years] with normal or corrected-to-normal vision participated in the study. All participants provided written informed consent and were naive as to the purpose of the experiment. None of the participants had neurological, psychiatric or other medical problems or had any contraindication to TMS (Wassermann, 1998). The procedures were approved by the Ethical Committee of G. d'Annunzio University, Chieti and were in accordance with the ethical standards of the 1964 Declaration of Helsinki. None of the participants experienced discomfort or adverse effects during TMS.

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Apparatus and stimuli

The participants' eye movements were recorded by an infrared video-based eye-tracking device (RK-826PCI pupil/corneal tracking system ISCAN, Burlington, MA, USA; sample rate: 120 Hz; nominal accuracy: 0.3°) while they observed the stimulus videos. Subjects were seated at a distance of 57 cm from a 17-in LCD computer monitor (1024 × 768 pixels; refresh rate: 60 Hz), and their heads were stabilized by means of a chin and head rest.

The experimental stimuli (AVI format videos, 30 frames per second) were the same as in our previous work (Ambrosini *et al.*, 2011). They provided a side-on view of an actor performing an unpredictable reach movement toward either a small or a large tomato (the targets), which were arranged in four different layouts to counterbalance the hand trajectories. Only the actor's right arm was visible in the videos, and all the arm movements started with the actor's hand resting on the table immediately in front of his torso in a closed fist posture. In half of the videos, the actor performed a reaching movement with the closed fist to simply touch the target (no shape condition); in the other half, the actor performed a reach-to-grasp movement, during which the pre-shaping of the hand (either a precision grip or a whole hand prehension, depending on the target) was clearly visible already from the hand lift-off from the table (pre-shape condition, see Figure 1).

Each experimental movie lasted 2500 ms: the first 1000 ms (fixation phase) showed a white fixation cross superimposed on the actor's hand resting on the table in the starting position, the following 1000 ms (movement phase) depicted the entire arm movement and the last 500 ms (end phase) consisted of the last frame of the stimulus video which was shown as still. The videos were presented in the center of the screen, resolution of 640 × 480 pixels, surrounded by a black background. To sum up, there were a total of 16 different stimulus videos (four target layouts × two movement types × two targets).

Procedure

In three experimental sessions, separated by a minimum of 10 days, we tested whether the participants' proactive gaze behavior during action observation was affected by the suppression of neural activity by means of rTMS. To this end, the same action observation task was delivered in two experimental blocks, from now on called 'post-rTMS' and 'baseline', performed either within the inhibitory window created by 15 min of 1 Hz rTMS or outside the influence of rTMS. The rTMS was delivered over the left PMv cortex or left pSTS cortex to test their causal role in driving participants' goal-specific proactive gaze shifts. Moreover, in a third experimental session, rTMS was delivered over left frontal eye fields (FEFs), which served as active control site.

In each experiment, in the post-rTMS block, participants performed the action observation task immediately after 1 Hz rTMS over one of the stimulation sites. Thus, in this block, participants' eye movements were recorded completely within the inhibitory temporal window created by 15 min of rTMS, which lasted for at least 7.5 min (Robertson *et al.*, 2003; Serino *et al.*, 2011; Avenanti *et al.*, 2012). In the baseline block, the action observation task was performed either immediately before or at least 2 h after the rTMS (to exclude any residual or interfering effects).

Each experimental block consisted of 64 trials (16 repetitions for each of the four experimental conditions) and lasted ∼6 min. The order of trials within each block was randomized, and the order of blocks was counterbalanced across subjects and experiments. Each trial began with the presentation of a white cross at the center of the screen, which participants were required to fixate. After a variable inter-trial interval (3500, 4000 or 4500 ms), the stimulus video was presented, and the participants were asked to move their gaze on the fixation cross over the actor's hand until its disappearance, and then to simply watch the video.

rTMS protocol

In the preliminary part of the experiment, single pulse TMS was used to set the intensity of low-frequency rTMS. To this end, motor-evoked potentials (MEPs) resulting from left motor cortex stimulation were recorded in the right first dorsal interosseus (FDI) by means of a CED Micro 1401 (Cambridge Electronic Design, Cambridge, UK). Pairs of Ag–AgCl surface electrodes were placed in a belly-tendon montage on the muscle, with further ground electrodes on the wrist.

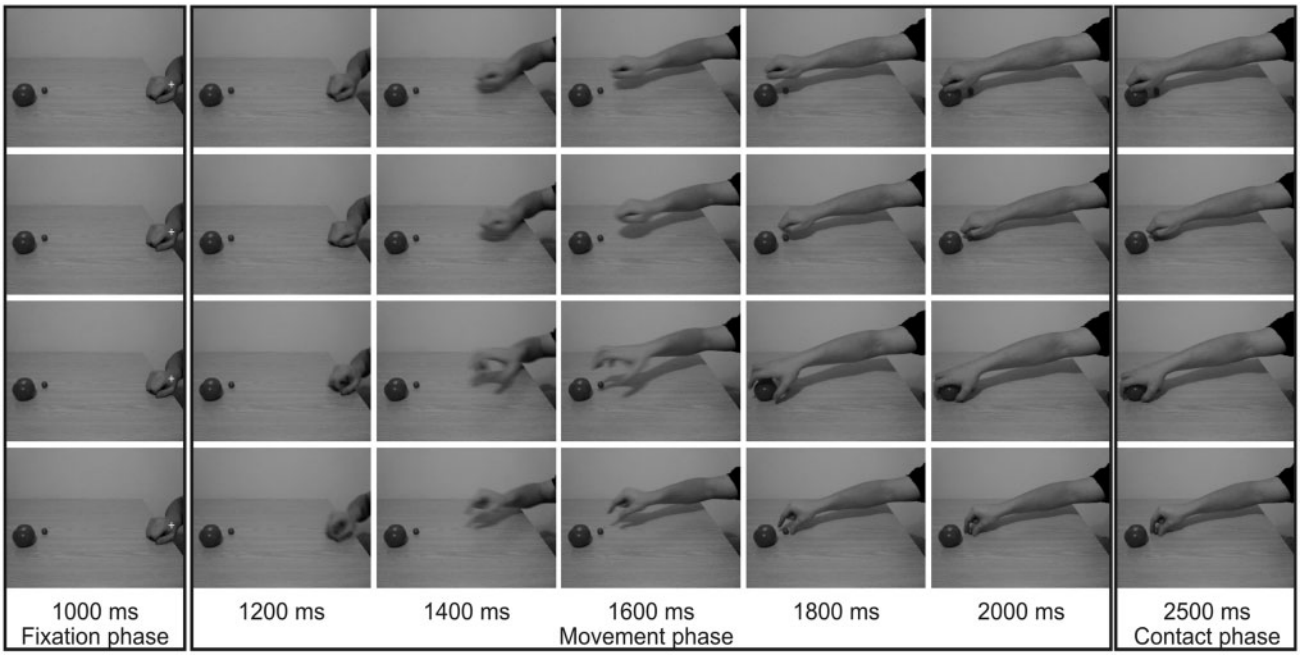

Fig. 1 Exemplar of movement kinematic in each experimental condition. From top to bottom: no shape—large target, no shape—small target, pre-shape—large target and pre-shape—small target.

Electromyography signals were amplified (1000×), digitized (sampling rate: 8 kHz) and filtered with an analogical online band-pass (20–250 Hz) and a notch (50 Hz) filter. A figure of eight coil connected to a Magstim Rapid2 stimulator (Magstim, Whitland, UK) was placed over the left primary motor cortex with the handle pointing backwards at 45° from the midline. In this way, the current induced in the neural tissue was directed approximately perpendicular to the line of the central sulcus, optimal for transsynaptic activation of the corticospinal pathways (Brasil-Neto *et al.*, 1992). Using a slightly suprathreshold stimulus intensity, the coil was moved over the left hemisphere to determine the optimal position from which maximal amplitude MEPs were elicited in the FDI muscle.

The post-rTMS block of each session was preceded by 15 min of continuous low-frequency 1 Hz rTMS (900 stimuli in total) over one stimulation site, namely left PMv, left pSTS or left FEF. Stimulation intensity was set at 90% of the individual resting motor threshold [mean intensity (s.d.): 52.3% (6.7%) of the stimulator output], defined as the lowest level of stimulation able to induce MEPs of at least 50 μV in the right FDI with 50% probability (Rossini *et al.*, 1994). During rTMS, subjects were asked to rest quietly with their eyes closed as muscle contraction may reduce the effect of rTMS (Touge *et al.*, 2001).

The simulation sites were identified on each participant's scalp on the basis of anatomical landmarks by using high-resolution T1-weighted magnetic resonance images (3-T Achieva MRI scanner Philips Medical Systems, Best, The Netherlands) and the SofTaxic Navigator system (Softaxic, E.M.S., Bologna, Italy).

We targeted the left PMv cortex as the portion of precentral gyrus below the intersection of the inferior frontal sulcus with the precentral sulcus (Mayka *et al.*, 2006; Tomassini *et al.*, 2007) (mean Talairach coordinates: $x = -48.9 \pm 3$, $y = 0.9 \pm 3.7$, $z = 22.2 \pm 2.6$; see Figure 2). The left pSTS was targeted in the posterior branch of the superior temporal sulcus, in accordance with previous studies (Van Overwalle, 2009) (mean Talairach coordinates: $x = -54.2 \pm 2.9$, $y = -46.1 \pm 4$, $z = 6.8 \pm 3.2$; see Figure 2). Finally, the left FEF was targeted immediately ventrally to the junction of the precentral sulcus and the superior frontal sulcus (Müri and Büttner-Ennever, 2006) (mean Talairach coordinates: $x = -30.5 \pm 3.2$, $y = -5 \pm 4.4$, $z = 46.5 \pm 2.5$; see Figure 2).

We choose to stimulate only sites in the left hemisphere because of its selective role in processing goal-directed features of object-related action. Several studies have shown a stronger (or even exclusive) activation of the left frontal (e.g. Hamzei *et al.*, 2003; Gazzola *et al.*, 2007), or temporal (e.g. Caspers *et al.*, 2010; Ortigue *et al.*, 2010) nodes of the action observation network during the observation of goal-directed hand actions. Moreover, to avoid unwanted effects of hemispheric differences, we stimulated the left FEF. The choice of left FEF was also intended to control for the possible spreading of the rTMS-induced current.

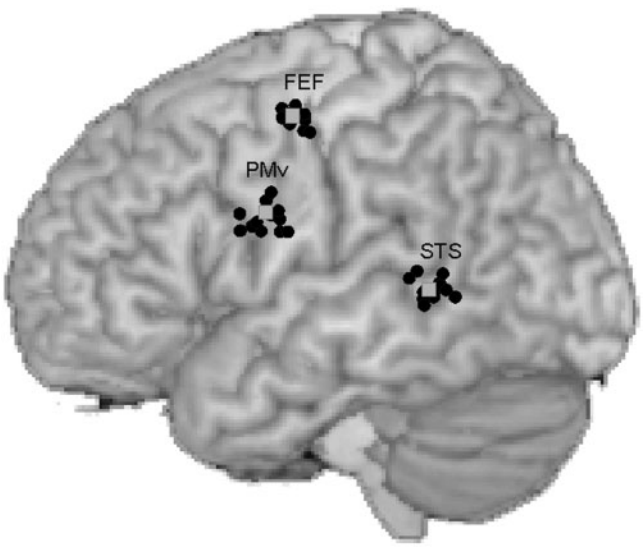

Fig. 2 TMS sites rendered over a standard brain. Black circles represent the three cortical sites in each subject. Gray squares represent the mean Talairach coordinates from the group.

Data analysis

At the beginning of each registration block, the gaze position was calibrated using a standard nine-point calibration procedure (Ambrosini *et al.*, 2011). Individual gaze traces were then analyzed by means of an I-VT (Velocity-Threshold Identification) algorithm (modified from Salvucci and Goldberg, 2000), which automatically detects saccades by means of both a velocity and a temporal threshold (point-to-point velocity of the gaze trace >50° per s for two consecutive samples). For each trial, we created two areas of interest (AOI) covering the hand (hand AOI) and the intended target (target AOI), respectively. Each AOI was actually 0.2° larger than the real stimulus to compensate for noise in the eye-tracking system, so the horizontal × vertical extent of the target AOI was 3.17° × 3.10° or 1.48° × 1.45° when the intended target was the large or the small tomato, respectively.

There were a total of 4608 trials recorded (64 trials × 2 blocks × 3 sessions × 12 participants). All the analyses were performed considering only trials in which participants exhibited a target-directed gaze behavior: trials in which participants did not fixate the hand AOI at the beginning of the movement phase (3.7% of the recorded trials), or in which they did not make a saccade to the target AOI at any point before the end of the movement phase (15.6% of the recorded trials) was excluded and not further analyzed. For each remaining trial, we calculated the time of the first saccade from the hand AOI (gaze onset time) and that of the first fixation on the target AOI (gaze arrival time) relative to the hand movement onset and offset, defined using a velocity threshold (10° per s, roughly corresponding to 0.5 m/s or 3 pixels/frame). It should be noted here that such a criterion is more conservative compared with hand–target contact. To calculate the hand velocity, we first determined from each frame of each video the location of the radial styloid process of the wrist; next, we interpolated at 120 Hz the trajectory of this marker and then we calculated its point-to-point velocity.

We assessed rTMS effects on onset and arrival times, and on the percentage of target-directed trials, by means of repeated-measures ANOVAs with stimulated site (PMv, pSTS or FEF), block (baseline *vs* post-rTMS), shape (no shape *vs* pre-shape) and target size (small *vs* large target) as within-subject factors. Thus, there were 24 experimental conditions, corresponding to the four types of observed reaching movements, namely no shape—small target, no shape—large target, pre-shape—small target and pre-shape—large target, each repeated for the two blocks, and for the three stimulated site. When necessary, we performed *post hoc* analysis with Tukey's test.

RESULTS

Percentage of target-directed trials

The ANOVA conducted on the percentage of trials in which participants exhibited a target-directed gaze behavior revealed the significant main effect of shape factor [$F_{(1,11)} = 9.29$, $P = 0.011$], participants fixated the target AOI more often on pre-shape (82.8%) than no shape trials (78.7%). Moreover, there was a significant main effect of target size [$F_{(1,11)} = 76.72$, $P < 0.001$], revealing that participants gazed more frequently at the large target than at the small target (89.5 and

72%, respectively). Finally, the shape by target interaction was also significant [$F_{(1,11)} = 5.07$, $P = 0.046$], and *post hoc* analysis revealed that participants fixated the target AOI more often in pre-shape than no shape condition, but only when the actor's movement was directed toward the small target (75.6 and 68.4%, respectively). No other main effect or interaction turned out to be significant.

Onset time

The ANOVA conducted with the full factorial design revealed a significant main effect of the block factor [$F_{(1,11)} = 4.91$, $P = 0.049$], with an overall rTMS-induced increase of the gaze onset times (211 ms) compared with the baseline block (199 ms). The main factor shape was also significant [$F_{(1,11)} = 23.8$, $P < 0.001$], with slower gaze onset times on no shape trials (223 ms) than pre-shape trials (187 ms). Moreover, the target size factor resulted significant [$F_{(1,11)} = 6.91$, $P = 0.023$], as the onset times were slower on large (215 ms) than small trials (192 ms). Finally, the stimulated site by block by shape interaction was significant [$F_{(2,22)} = 3.88$, $P = 0.036$]. To investigate this interaction, we carried out three separate ANOVAs for each stimulated site separately, with block, shape and target size as factors.

The ANOVA conducted on the onset times in the left PMv session revealed a significant main effect of the shape factor [$F_{(1,11)} = 7.02$, $P = 0.022$], with earlier onset times on pre-shape (187 ms) compared with no shape (223 ms) trials. The block by shape interaction was also significant [$F_{(1,11)} = 5.64$, $P = 0.037$, see Figure 3]. *Post hoc* analysis (Tukey's test) revealed that the motor cues provided by the pre-shaping of the actor's hand led to earlier onset times in the baseline block only (pre-shape = 168 ms *vs* no shape = 231 ms; $P < 0.01$). In fact, the virtual lesion of the PMv cortex annulled the difference between pre-shape and no shape trials (respectively, 206 and 216 ms; $P > 0.9$).

As regards the rTMS over left pSTS, onset times analysis revealed that participants' gaze behavior was influenced only by the motor components of the observed action [shape: $F_{(1,11)} = 15.8$, $P = 0.002$], with earlier onset times in pre-shape (186 ms) compared with no shape (219 ms) trials. No other main effect or interaction resulted significant.

Finally, the ANOVA conducted on gaze onset time in the FEF session revealed a significant main effect of block [$F_{(1,11)} = 12.25$, $P = 0.005$]: as expected, in the post-rTMS block, the virtual lesion of FEF induced an increase of the gaze onset times (222 ms) compared with the baseline block (184 ms). The main factor shape was also significant [$F_{(1,11)} = 7.97$, $P = 0.017$], with earlier onset times on pre-shape (187 ms) compared with no shape (220 ms) trials. The non-significant ($F < 1$) block by shape interaction suggests that rTMS affected the participants' gaze behavior regardless of whether the kind of action they were observing was actually grasping or merely touching.

Arrival time

The full-factorial design ANOVA conducted on the gaze arrival times showed a significant block effect [$F_{(1,11)} = 21.15$, $P < 0.001$], with higher arrival times (i.e. less proactive gaze) in the rTMS block (−88 ms) compared with the baseline block (−125 ms). There was also a significant shape effect [$F_{(1,11)} = 19.82$, $P < 0.001$], as participants gazed the target AOI earlier on pre-shape (−128 ms) than on no shape (−84 ms) trials. Moreover, the main effect of the target size factor resulted significant [$F_{(1,11)} = 121.66$, $P < 0.001$], with earlier arrival times on large (−179 ms) than small (−34 ms) trials. This finding is consistent with our findings in a previous behavioral study (Ambrosini *et al.*, 2011). In addition, the stimulated site by block by shape interaction was significant [$F_{(2,22)} = 7.51$, $P = 0.003$]. To further analyze this interaction, three follow-up block by shape by target size ANOVAs were carried out separately for the three stimulated sites.

Arrival times analysis for the left PMv session revealed a significant main effect of all the main factors [block: $F_{(1,11)} = 6.34$, $P = 0.029$; shape: $F_{(1,11)} = 9.47$, $P = 0.011$; target: $F_{(1,11)} = 117.95$, $P < 0.001$] showing earlier arrival times on baseline (−125 ms), pre-shape (−129 ms) and large (−179 ms) trials compared with post-rTMS (−88 ms), no shape (−84 ms) and small (−34 ms) trials, respectively. Crucially, the block by shape interaction was also significant [$F_{(1,11)} = 8.75$, $P = 0.013$, see Figure 3]. *Post hoc* analysis revealed earlier arrival times on pre-shape compared with no shape trials (−169 and −80 ms, respectively; $P = 0.007$) in the baseline block only. In fact, in the post-rTMS block, the virtual lesion of the PMv cortex elicited a significant increase of arrival times on pre-shape trials (−88 ms; $P = 0.013$), making it virtually equal to those on no shape trials (−88 ms; $P = 1$). To sum up, the temporal advantage in participants' gaze behavior due to the availability of motor cues provided by the

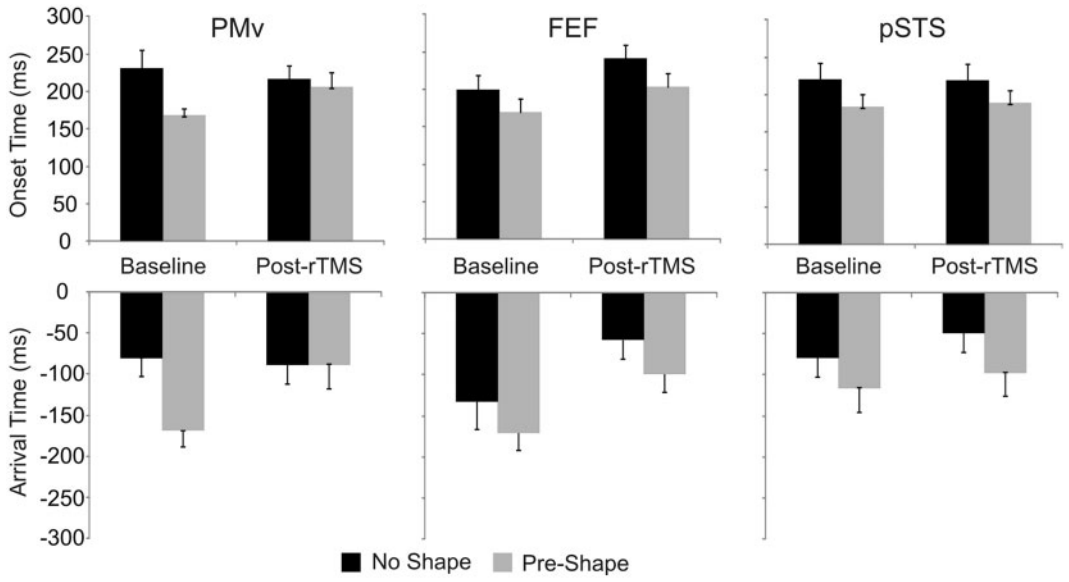

Fig. 3 Onset (upper plots) and arrival time (lower plots) of gaze behavior in the experimental conditions. The factor target (large *vs* small) was collapsed.

actor's hand pre-shape, which is typically found in the baseline condition, was disrupted by rTMS-induced suppression of PMv cortex.

As regards the left pSTS session, the arrival times analysis revealed, once again, the significant main effect of the shape factor [$F_{(1,11)} = 14.23$, $P = 0.003$], as participants fixated the target AOI earlier on pre-shape (−107 ms) than no shape (−64 ms) trials. The main factor target size was also significant [$F_{(1,11)} = 86.05$, $P < 0.001$], with higher arrival times on small (−28 ms) compared with large (−143 ms) trials. The main factor session did not reach the significance level [$F_{(1,11)} = 3.24$, $P = 0.099$], as well as all the interactions (Figure 3).

For the left FEF session, the ANOVA conducted on gaze arrival times revealed the significant main effect of both block [$F_{(1,11)} = 15.72$, $P = 0.002$] and shape [$F_{(1,11)} = 6.69$, $P = 0.025$] factors. Participants gazed at the target AOI earlier on baseline (−152 ms) than post-rTMS (−78 ms) trials; moreover, they fixated the target AOI earlier on pre-shape (−135 ms) than no shape (−95 ms) trials. The main factor target size was also significant [$F_{(1,11)} = 63.54$, $P < 0.001$], with higher arrival times on small (−53 ms) compared with large (−177 ms) trials. As for the onset times analysis, the block by shape interaction did not approach the statistical significance ($F < 1$), as well as any other interaction (Figure 3).

DISCUSSION

In this study, we recorded eye movements while participants viewed an actor interacting with two objects which required two different kinds of grip to be picked up (precision grip or whole hand prehension); in one condition, the actor reached for and grasped one of the two objects, in the other, he merely reached for and touched one of the two objects without pre-shaping his hand according to the target features. Eye movements were recorded in three separate sessions before and immediately after delivering rTMS to either the left PMv or the left pSTS cortices. In a third experimental session, the left FEF was disrupted by means of the same rTMS protocol. There were two main findings.

First, the virtual lesion of the left PMv cortex impacted on the proactivity of the participants' gaze, with slower arrival times in the rTMS block compared with the baseline condition. Second, the rTMS-induced effects were selective with respect to the different kinds of viewed hand action following the temporary inactivation of the left PMv cortex only. The effect of the virtual lesion of the left PMv cortex was so marked that participants' gaze behavior while viewing a grasping hand came to resemble that recorded while viewing a merely touching hand (which involves no pre-shaping phase). No selective rTMS-induced effects were found following the inactivation of both pSTS and FEF.

Previous behavioral investigations demonstrated that gaze proactivity may be facilitated by motor processing of the observed action (Flanagan and Johansson, 2003; Falck-Ytter *et al.*, 2006). In particular, it has been shown that people viewing object-related hand actions may take advantage of specific motor cues (such as a hand pre-shaping a given grip) in selecting action targets, even when the targets are not previously known (Ambrosini *et al.*, 2011, 2012; Costantini *et al.*, 2012). This study highlights the neuronal underpinnings of this gaze behavior, showing that target-specific proactive gaze shifts may rely on the recruitment of motor cortical resources such as the PMv cortex.

Of course, this does not exclude the possibility that non-motor processing of others' actions also facilitates gaze proactivity. Indeed, it has been shown that when observing unpredictable actions such as block stacking actions, people tend to adopt a default strategy, gazing at this or that target object just because of its spatial location (Rotman *et al.*, 2006). Similarly, it has been proposed that proactive eye movements occur as a function of the combination of the intention of an agent to achieve a goal and the desirability of a goal state with motor system recruitment reflecting action understanding rather than providing the origins of it (Eshuis *et al.*, 2009).

Nevertheless, our findings provide direct evidence for a distinctive role of the PMv cortex in proactively driving the viewer's gaze to the target of the actor's action. Indeed, they indicate that when specific motor cues (such as a grasping hand with a given grip) are available and might help in selecting the target of another's action, people capitalize on their own motor representation of that action in proactively gazing at the object to be manipulated by the other's hand.

This is consistent with evidence showing that the PMv cortex is critically involved not only in planning and executing object-related hand actions (Rizzolatti *et al.*, 1988; Jeannerod *et al.*, 1995) but also in processing both others' object-related actions and action-related features of objects. Indeed, a large number of studies have demonstrated that viewing another's object-related action recruits the left PMv cortex as if the viewer were performing that action herself (Grafton *et al.*, 1996; Rizzolatti *et al.*, 1996; Buccino *et al.*, 2001; Calvo-Merino *et al.*, 2005; Gazzola *et al.*, 2007), and that this recruitment is selective for the outcome to which the action is directed rather than for its kinematic and dynamic features (Lewis *et al.*, 2005; Gazzola *et al.*, 2006; Lewis *et al.*, 2006; Galati *et al.*, 2008; Alaerts *et al.*, 2009; Ortigue *et al.*, 2010). Interestingly, the left PMv cortex has also been shown to be crucially involved in processing visual features of objects in terms of the actions they might afford (Grafton *et al.*, 1997; Chao and Martin, 2000; Grezes *et al.*, 2003; Buccino *et al.*, 2009).

This might explain why the virtual lesion of the left PMv cortex impaired the proactivity of participants' eye movements. We propose that the inactivation of the PMv cortex selectively prevented participants from exploiting motor information concerning the pre-shaping hand and concerning the related target object. It was as if they were viewing an un-shaped hand merely touching the target.

Comparison with the rTMS-induced effects following the temporary inactivation of pSTS is instructive. Though the virtual lesion of pSTS seemed also to affect the gaze behavior of the participants ($P = 0.099$), this impact was not selectively related to the different kinds of viewed action. The pSTS is a high-order visual region that has been shown to be involved in the processing of another's actions (Allison *et al.*, 2000; Puce and Perrett, 2003; Avenanti *et al.*, 2012). However, the pSTS action selectivity is far from that exhibited by the PMv cortex (Jellema *et al.*, 2004; Rizzolatti and Sinigaglia, 2010), as it is more bodily effector specific than goal specific (Cattaneo *et al.*, 2010).

This explanation is also in line with previous studies showing that virtual lesions of the PMv cortex selectively impair finger positioning on the objects during grasp (Davare *et al.*, 2006). Notably, selective impairments were also found in the visual discrimination of static (Urgesi *et al.*, 2007) and dynamic displays (Pobric and Hamilton, 2006) of bodily actions as well as in the visual discrimination of biomechanical plausible bodily postures (Candidi *et al.*, 2008).

Furthermore, our findings showing a distinctive role of PMv cortex in proactively driving gaze behavior are consistent with a series of studies demonstrating that PMv is critically involved in outcome prediction (for a review, see Schubotz, 2007). For instance, a functional magnetic resonance imaging study (Schubotz and von Cramon, 2004) and lesion (Schubotz *et al.*, 2004) data showed that predictions of outcomes even more abstract than bodily movements recruit the premotor cortex, where this recruitment does not amount to simply to a task-irrelevant outflow into the motor system.

Finally, a natural question arises as to how motor information concerning another's actions and on their targets processed by the PMv cortex might be exploited by the frontal oculomotor cortical areas. Certainly, the interplay of eye and hand movements relies on brain mechanisms and circuits that are far from being understood

(Bekkering and Sailer, 2002; Carey *et al.*, 2002). Nevertheless, there is evidence that fronto-parietal circuits may play a key role in eye–hand coordination (Boussaoud and Bremmer, 1999; Battaglia-Mayer *et al.*, 2006). Indeed, the PMv cortex and the anterior intraparietal area, with their comparable functional properties, are robustly connected to one another (Luppino *et al.*, 1999; Rizzolatti and Luppino, 2001; Borra *et al.*, 2008; Gerbella *et al.*, 2011) and involved in the visuo-motor transformations needed for executing (Rizzolatti *et al.*, 1988; Jeannerod *et al.*, 1995) as well as for observing object-related actions such as grasping actions (Rizzolatti and Sinigaglia, 2010). Interestingly, the anterior intraparietal area is also connected with the FEF both directly and indirectly throughout the lateral intraparietal area (Schall *et al.*, 1995; Borra *et al.*, 2008; Nelissen *et al.*, 2011); it is thus a candidate for what conveys hand- and object-related information from the PMv cortex to frontal oculomotor cortical areas. Of course, this does not rule out the possible contribution of other cortical or subcortical pathways such as, for instance, those mediated by adjacent sectors of area 46 that are mutually connected to each other and differentially connected with the PMv and the FEF (Barbas and Mesulam, 1985; Gerbella *et al.*, 2010) and those projecting to the superior colliculus (Stanton *et al.*, 1988; Borra *et al.*, 2010).

In conclusion, we provide support for a new twist to an old idea. As Mead argued, seeing 'involves a continued control of such an organ as that of vision by such an organ as that of the hand' (Mead, 1907), the twist is that seeing can be controlled not only by one's own but also by others' hand.

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