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Encoding of point of view during action observation in the local field potentials of macaque area F5

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Abstract

The discovery of mirror neurons compellingly shows that the monkey premotor area F5 is active not only during the execution but also during the observation of goal-directed motor acts. Previous studies have addressed the functioning of the mirror-neuron system at the single-unit level. Here, we tackled this research question at the network level by analysing local field potentials in area F5 while the monkey was presented with goal-directed actions executed by a human or monkey actor and observed either from a first-person or third-person perspective. Our analysis showed that rhythmic responses are not only present in area F5 during action observation, but are also modulated by the point of view. Observing an action from a subjective point of view produced significantly higher power in the low-frequency band (2–10 Hz) than observing the same action from a frontal view. Interestingly, an increase in power in the 2–10 Hz band was also produced by the execution of goal-directed motor acts. Independently of the point of view, action observation also produced a significant decrease in power in the 15–40 Hz band and an increase in the 60–100 Hz band. These results suggest that, depending on the point of view, action observation might activate different processes in area F5. Furthermore, they may provide information about the functional architecture of action perception in primates.

Introduction

Primates are endowed with very sophisticated social abilities that rely on a detailed level of analysis of the actions and movements of their con-specifics. Although the specific cognitive mechanisms underlying action understanding are still largely unknown, the discovery of mirror neurons has strongly suggested a role of the motor cortex in this process (Rizzolatti *et al.*, 2001). Mirror neurons constitute a class of neurons in the monkey premotor (area F5), motor and parietal areas that respond during both the observation and the execution of goal-directed motor acts (Gallese *et al.*, 1996; Fogassi *et al.*, 2005; Dushanova & Donoghue, 2010). The mirror responses of area F5 have been so far investigated predominantly at the single-neuron level. Here, we complemented this approach by studying the mirror responses of area F5 at the network level by analysing the local field potentials (LFPs) recorded during action observation and execution. LFPs are signals confined to the lower temporal frequencies (usually below 150 Hz) recorded invasively with microelectrodes. They are considered to be mainly determined by the integrative synaptic processes in a small sphere centered around the tip of the electrode (Mitzdorf, 1987; Logothetis, 2003), and are thought to provide information relevant to understanding the functioning of an area at the network level (Mazzoni *et al.*, 2012). The analysis of LFPs allowed us to address two relevant research questions concerning area F5.

First, LFPs can reveal important details of action encoding in area F5. In particular, we previously reported that, at the single-unit level, mirror neurons seem to encode actions in a view-dependent manner (Caggiano *et al.*, 2011). Furthermore, we found that a higher, albeit not significantly different, number of mirror neurons seemed to be selective for the first-person perspective. Here, we investigated this issue at the level of LFPs, which represent the pooled activity of thousands of neurons. They can thus reveal effects that might not be evident at the single-unit level.

Second, LFPs can provide information on the functioning of area F5 at the network level. In particular, it has also been proposed that there is an inverse relationship between the frequency of cortical rhythms and the spatial scale of the underlying neuronal processes, with lower frequencies indicating broad, potentially inter-areal, integrative processes, and higher frequencies indicating more localised processes (Von Stein and Sarnthein, 2000). Such information can be relevant in view of the recent reports of mirror neurons in other brain regions that are anatomically connected to area F5 (Fogassi *et al.*, 2005; Dushanova & Donoghue, 2010; Philipp *et al.*, 2013;

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Vigneswaran *et al.*, 2013; Pani *et al.*, 2014), and may provide important hints about the functional connectivity of this network or areas.

Materials and methods

Subjects, surgery, and recording methods

Subjects, surgery and recording methods have been described elsewhere (Caggiano *et al.*, 2009, 2011, 2012). In summary, two male rhesus monkeys (*Macaca mulatta*) of weight 8 kg and 9 kg, respectively, were used in the experiments. During the experiments, the monkeys sat comfortably in a primate chair. The movements of the left arm were restrained by a gentle gauze bandage, and the right arm was free to move. The movements of the monkey's head were restrained painlessly by means of a head-holder attached to the skull, and eye position was monitored continuously with chronically implanted search coils. All animal preparations and procedures fully complied with the NIH Guide for Care and Use of Laboratory Animals, and were approved by the local ethics committee.

Extracellular action potentials and LFPs were recorded with glass-coated micro-electrodes (impedance, 0.5–1 MΩ) via a multi-electrode system equipped with up to eight probes (Alpha Omega Engineering). The electrodes were inserted through the intact dura. The movement of each electrode was independently controlled by means of a dedicated hardware/software package (electrode positioning system; Alpha Omega Engineering). LFP activity was digitised at 500 Hz and bandpass-filtered (0.1–200 Hz) with a Butterworth filter with two poles. For our experiments, we used up to eight independent electrodes that were arranged in a rectangular-like shape with a minimum distance of 1 mm between neighboring electrodes. Area F5 was identified on the basis of known response properties of motor and premotor areas (Gentilucci *et al.*, 1988; Maranesi *et al.*, 2012).

Motor task

In order to test the motor responses of the recorded neurons, we trained the two monkeys to grasp and lift three small metallic objects placed at defined locations within their workspace (Caggiano *et al.*, 2009, 2011, 2012). The three objects were placed in front of the monkey on a plexiglass tablet tilted towards the monkey at ~45° with respect to the horizontal plane and on a line perpendicular to the sagittal plane at a distance of ~25 cm from the monkey's body. Each object afforded one of three possible grips – power grip (a large cylinder with diameter 4 cm and height 2.5 cm), precision grip (a small, thin rectangular plate with dimensions 0.5 × 0.8 × 0.5 cm), and finger prehension (a wide and thin circular plate with diameter 3.5 cm and height 1.2 cm). The objects were anchored by means of a nylon wire passing through a hole in the tablet to a piece of metal weighing ~250 g that provided a small amount of mechanical resistance. An LED was placed on the tablet above each of the three objects, giving a total of three LEDs. A button, placed centrally at the base of the plexiglass tablet, constituted the hand rest position.

Each trial of the motor condition consisted of the following sequence of events: (i) the trial was initiated by the monkey by placing his hand on the button at the base of the tablet; (ii) if the button press was maintained for a random time uniformly distributed across trials between 1 s and 2.5 s, one of the three LEDs was randomly selected and turned on; the switching on of the LED cued the monkey to grasp the corresponding object; (iii) the monkey had 2 s to detach his hand from the hand rest position, grasp the cued object, and hold it for a minimum time of 300 ms;if the monkey did not grasp the object within 2 s, the trial was aborted; (iv) the monkey lifted the object from the tablet; (v) if the monkey kept the object lifted for at least 300 ms, the trial was considered to be successful, and the monkey was rewarded with a drop of water/juice; otherwise, the trial was aborted. The motor task was executed in complete darkness. Both the spatial position of the LED (i.e. further away from the monkey's body with respect to the goal objects) and its very low luminosity ensured that the monkey could not receive any visual feedback during execution of the motor task. Furthermore, both monkeys were highly overtrained, and very rarely used visual feedback to perform the motor task, as shown by their eye movements, even when it was executed under normal illumination conditions.

The contact between the monkey's hand and the hand rest button, and touching and lifting of the object, triggered digital events that were time-stamped and acquired along with neuronal recordings for offline data analysis.

The monkey performed the motor task in darkness with no direct visual access to his own hand. The experimental apparatus was controlled by means of a digital board, and the sequence of events was managed by means of in-house-developed LAB-VIEW software. For consistency with stimuli presented during the visual task, which consisted of power grips (see below), only motor responses during the execution of the power grip were included in the present study.

Visual task

The visual responses of mirror neurons in the naturalistic setting were tested by having the experimenter execute a power grip in front of the monkey. In each trial, the experimenter grasped either an object or piece of food placed on the tip of a stick positioned outside of the reaching distance of the monkey. The experimenter stood at a distance of ~50 cm from the monkey, and his body covered an area of approximately 50° × 50° of the monkey's visual field (Caggiano *et al.*, 2009). The experimenter started a trial when the monkey was sitting still in the primate chair and gazing at him. We found, in agreement with previous studies, that salient features that attracted the initial attention of the monkey were either the face of the experimenter or the goal object (Maranesi *et al.*, 2013). Thus, when the experimenter detected that the monkey was fixating at either of these two locations, he started the trial. The movement of the experimenter's hand usually captured the attention of the monkey, which readily shifted his focus of attention towards the action. Trials in which the monkey was not gazing towards the experimenter or moving during observation of the motor act were aborted and not considered for further analysis. The contact between the experimenter's hand and the goal object triggered a digital event that was time-stamped and acquired along with neuronal signals.

Visual responses to filmed actions [see also Caggiano *et al.* (2011) for additional details] were tested by showing previously videotaped motor acts on an LCD screen placed in front of the monkey at a distance of 40 cm. The LCD had a refresh rate of 60 Hz. The experimental paradigm consisted of the following sequence of events: (i) the trial started with the monitor showing a uniformly black background; (ii) a red spot (0.25° × 0.25°) appeared in the middle of the screen, and was displayed for a random time uniformly distributed between 1000 ms and 2500 ms; the trial was aborted if the monkey moved his gaze outside a circular region of radius 3° centered around the red dot; (iii) the red dot disappeared, and a movie lasting 4000 ms was presented; the movie had a size of ~15° of visual angle, and was centered at the position of the red spot; the trial was aborted if, during movie presentation, the monkey

moved his gaze outside of the sector of his visual field covered by the movie; and (iv) after movie presentation, a red spot (0.25° × 0.25°) was presented again for a random time uniformly distributed between 500 ms and 1500 ms; the trial was aborted if the monkey moved his gaze outside a circular region of radius 3° centered around the red dot. Successful trials were rewarded with a liquid reward. Visual stimuli were presented by means of in-house-designed real-time software (http://nrec.neurologie.uni-tuebingen.de).

Visual stimuli

Filmed actions used as visual stimuli displayed either a monkey or a human executing a goal-directed motor act, and were generated in the following manner. Actions performed by monkeys were recorded by means of a Sony DCR-HC23E video camera at 30 frames/s at a resolution of 720 × 480 pixels in a non-compressed format. The recorded video sequences were edited (ADOBE PREMIERE PRO 1.5) in order to generate video clips with a duration of 4 s (120 frames) at a resolution of 360 × 240 pixels in a non-compressed format. The performing subject in the movies was one of the two monkeys used in our experiments. The same light sources (back-projected/diffused) were used for all videos.

Monkey actions filmed from a frontal point of view (180°) were video-recorded by placing the camera on a tripod at a distance of 1.5 m from the monkey, with the camera positioned ~0.5 m above his head. The filmed actions showed a monkey in a primate chair, and consisted of the following sequence of events. At the beginning of the movie (time 0), a piece of red pepper held by pliers was presented approximately in the sagittal plane of the monkey. The piece of red pepper was then moved towards the monkey. After ~1700 ms, the food was at a reachable distance. The monkey made a movement, and his hand contacted the food at ~2500 ms. He then grasped the piece of pepper with a power grip, removed it from the pliers (at 2750 ms), and brought it to his mouth (end of the lifting phase at 3000 ms).

Monkey actions filmed from a subjective point of view (0°) were video-recorded by attaching the camera to a support placed immediately adjacent to the head of the monkey and pointing towards his working space. This arrangement produced a view of the monkey's hand very similar to that experienced by the monkey during the performance of hand-related motor acts. The filmed action consisted of the following sequence of events. At the beginning of the movie (time 0 ms), a piece of red pepper held by pliers was presented at the center of the visual scene. After ~1500 ms, a monkey hand entered the scene and performed a movement directed towards the piece of food. The hand contacted the piece of food at 1850 ms, grasped the food from the pliers at 2900 ms by means of a power grip, and removed it from the scene after 3300 ms.

The same camera arrangement was used to video-record human actions observed from a subjective point of view. That is, the camera was positioned immediately adjacent to the head of the human subject, and was tilted ~60° downwards so as to point towards his working space for hand actions. The filmed action consisted of the following sequence of events. At the beginning of the movie (time 0 ms), a piece of red pepper held with pliers was present at the center of the visual scene. After ~1700 ms, a human hand entered the scene and performed a movement directed towards the piece of food. The hand contacted the piece of food at 1900 ms, grasped the food from the pliers by means of a power grip at 2800 ms, and removed it from the scene after 3100 ms.

The three experimental conditions were presented in blocks, and the order of the conditions was as follows – motor execution (i.e. the monkey executing actions), naturalistic testing (i.e. the experimenter executing actions in front of the monkey), and movie condition (i.e. filmed actions presented as visual stimuli). It is important to stress that, within each condition, trials were randomly presented. That is, in the motor task, the type of grip (precision grip, power grip, and finger prehension) that the monkey was cued to execute was randomly selected from trial to trial. Similarly, the movies used as visual stimuli were presented in a random order.

Data analysis

Data were analysed with custom software written in MATLAB (Mathworks) and by means of EEGLAB (Delorme & Makeig, 2004) and CHRONUX (http://chronux.org/) toolboxes. Signals were originally recorded at a sampling rate of 12.5 kHz, and were subsequently subsampled at 500 Hz and bandpass-filtered (0.1–100 Hz, two-pole Butterworth filter). In all experimental conditions, the trials were aligned with the hand–object contact event, and we extracted the part of the recorded signal between 2 s before and 2 s after that event for further analysis. We then subtracted the baseline for each condition, and reduced that window to between 1.25 s before and 1.25 s after the hand–object contact event for further analysis.

Artefacts were detected and rejected by means of three methods (Caggiano *et al.*, 2013): (i) rejection of improbable trials (an improbable trial was defined as a trace containing samples that exceeded two standard deviations from the mean probability, over all traces, of the occurrence of a given value); (ii) rejection of abnormally distributed trials (an abnormally distributed trial was defined as a trace containing samples exceeding two standard deviations from the mean kurtosis over all traces); and (iii) rejection of outliers (a trace was considered to contain outliers if it contained samples exceeding two standard deviations from the mean absolute value). Only sessions with more than eight valid trials for each experimental condition were included in our analysis. To allow a direct comparison between different conditions and sessions, data were converted, by means of a *Z*-score, to a dimensionless value.

To estimate the temporal structure in the LFP, we applied multitaper spectral analysis (Percival & Walden, 1993; Jarvis & Mitra, 2001; Pesaran *et al.*, 2002). In short, a Fourier transform was applied to the tapered time series signal. We used an optimal family of orthogonal tapers, the prolate spheroidal (Slepian) functions that are parametrised by their time length T and the frequency bandwidth W. For each choice of T and W, a maximal number of $K = 2TW - 1$ tapers could be used for spectral estimation. In this study, we used $K = 5$ tapers (i.e. $TW = 3$) and a time window of 500 ms with a step size of 50 ms. Each spectrogram was obtained by averaging over all available repetitions. In general, a recording site was sampled multiple times across sessions and recording days. In our analysis, we did not use the data from the single sessions in a given recording site, but we instead defined a virtual site obtained by computing the average of the power spectrum over all sessions and recording days at a given recording site, where 'recording site' indicates a given (x,y) position within the recording chamber. In other words, we collapsed into a given 'virtual site' all LFPs recorded at a given position within the recording chamber (e.g. −3 mm, 2 mm), irrespective of day, electrode depth, and recording session. In addition, we considered all recording sites in our analysis, irrespective of whether a mirror neuron could be isolated in that particular session/day. By sorting our recording sessions into 'virtual sites', we avoided potential biases in our analysis resulting from sites being explored more often. Henceforth, the word 'site' will be used as a synonym for 'virtual site'. The data presented in Figs 2–5

were obtained from 2232 trials (where a trial is defined as site × recording day × depth) for the motor condition, 1257 trials for condition 'human actions observed from a frontal point of view' (H180), 788 trials for condition 'monkey actions observed from a frontal point of view' (M180), 766 trials for condition 'human actions observed from a subjective point of view' (H0), and 660 trials for condition 'monkey actions observed from a subjective point of view' (M0).

To better highlight modulations produced by the different experimental conditions, we used for our analysis 'net LFPs', which were computed by removing, from the stimulus-driven LFPs, the LFPs measured at baseline condition on a trial-by-trial basis. That is, for each trial and each condition, we removed the LFPs measured during the baseline condition in that trial from the LFPs measured during the experimental condition. Baseline conditions were defined as follows for each of the experimental conditions. For the motor task, the baseline period was that from 1.5 s to 1 s before hand–object contact (Fig. 1, upper row); given the design of the motor task (see 'Motor task'), in this period the monkey was still, with his hand on a switch on the plexiglass tablet and waiting for the go signal. For the naturalistic observation condition, the baseline period was that from 2 s to 1.5 s before hand–object contact (Fig. 1, lower row). In this period of time, the experimenter was still, standing in front of the monkey and preparing to perform a goal-directed motor act in front of the monkey. For the observation of filmed actions, the baseline period was that from 1 s to 1.5 s after the beginning of the presentation of the movie. Given the unfolding in time of the filmed actions used in our experiments (see 'Visual stimuli'), in this period of time the goal object was present on the screen, but no action had yet started. To assess statistical significance, LFP samples at a given frequency were compared with their respective baseline values (sign-rank test, with Bonferroni correction).

In a first analysis, potential differences in the LFPs recorded during action observation and execution were investigated by means of a discriminability coefficient (dc) (Scherberger *et al.*, 2005), defined as:

$$\frac{1}{F_{\max}}\int_{2}^{F_{\max}} |S_{\text{motor}}(f) - S_{\text{visual}}(f)|\, df,$$

where $S_{\text{motor}}(f)$ and $S_{\text{visual}}(f)$ denote the LFP log power spectra (in dB) recorded during the motor and the visual tasks respectively, and $F_{\max}$ = 100 Hz.

Correlations between motor and visual LFPs

For each site, the correlation coefficient C_f between motor and visual LFPs at a given frequency f were computed as:

$$C_f = \frac{\text{Cov}\left(V_f(t), M_f(t)\right)}{\sqrt{\text{Cov}\left(V_f(t), V_f(t)\right)}\sqrt{\text{Cov}\left(M_f(t), M_f(t)\right)}},$$

where Cov is the covariance function, $V_f(t)$ denotes the evolution in time of the LFPs measured at frequency f in a given visual condition (e.g. observing a human action from a frontal view), and $M_f(t)$ denotes the evolution in time of the LFPs at a frequency f during action execution.

Results

In the present study, we first investigated the temporal evolution of the power of the LFPs from 228 sites of the monkey cortical area F5, either during the execution of goal-directed motor acts or during the observation of similar actions performed by the experimenter in

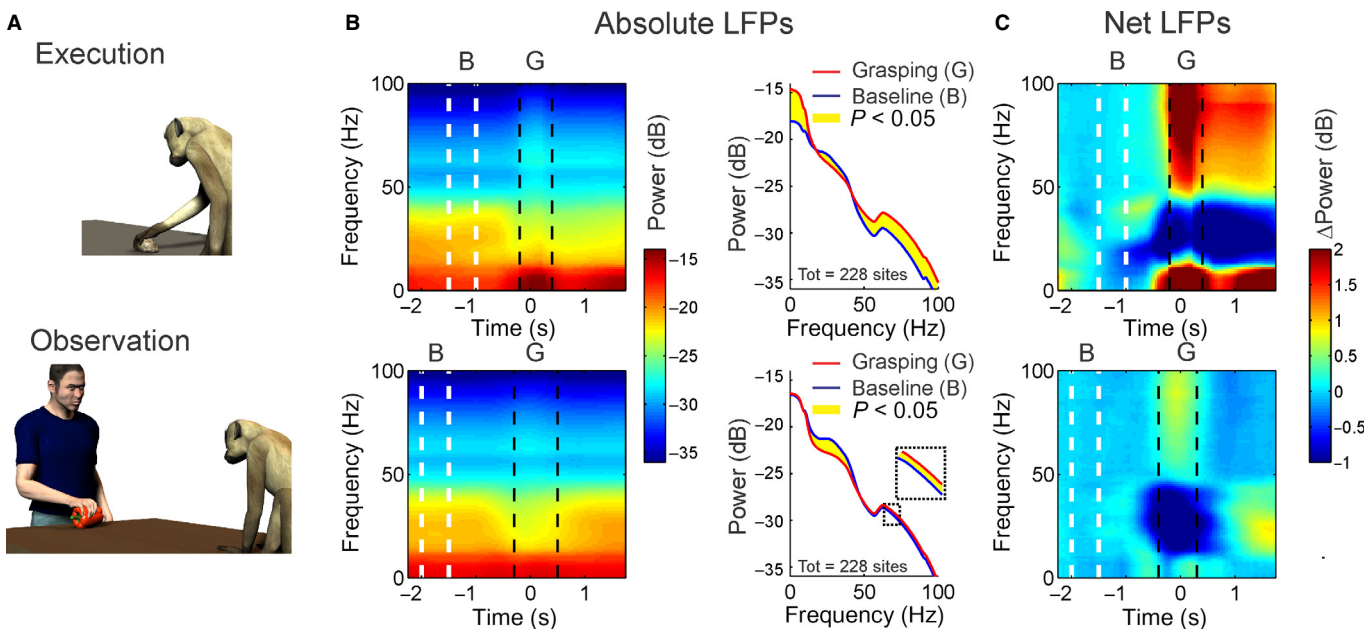

FIG. 1. LFPs produced by the execution (upper row) and observation (bottom row) of goal-directed motor acts. (A) Schematic illustration of the experimental conditions. (B) Average raw values across all sites of the LFPs. In this and in all subsequent figures, t = 0 is the time of contact between the hand and the goal object. The two figures in the left column compare the raw LFPs at time t = 0 with their baseline values as a function of frequency. The curves show clear modulation of the raw LFPs. (C) To render this modulation more evident, we subtracted from the LFPs their baseline values at each frequency. In B and C, the vertical white dashed lines signify the interval considered for computing the baseline activity, and the vertical black dashed lines signify the interval where the grasping of the object took place.

front of the monkey (Fig. 1A). The power spectra of the recorded LFPs were computed by means of multitaper time–frequency analysis (see Materials and methods). Single-neuron responses were simultaneously recorded from the same electrodes, and analysis of these demonstrated the existence of a class of mirror neurons whose responses are modulated by the point of view from which a goal-directed motor act is observed (Caggiano *et al.*, 2011).

The left column of Fig. 1B shows the average across all sites of the power spectrum of the LFPs during action execution and observation. The observation condition is represented, as in previous studies of mirror neurons (Gallese *et al.*, 1996; Fogassi *et al.*, 2005), by the experimenter executing actions in front of the monkey. Time $t = 0$ indicates the time of contact between the monkey's (execution condition, top row) or actor's (observation condition, bottom row) hand and the goal object. The white dashed lines indicate intervals when the monkey (upper panel) or human (lower panel) hands were at rest, and that were thus considered to compute baseline activity. In both the execution and observation conditions, the LFPs showed a clear modulation in power starting shortly before the moment of hand–object contact and lasting until the end of the motor act. To more closely study the characteristics of this modulation, we computed the difference in log units between the LFPs measured during baseline periods and the LFPs measured during the execution and observation conditions (net LFPs, henceforth LFPs for the sake of simplicity). The results of this analysis are shown in Fig. 1C. Action production and observation produced characteristic modulations of the LFPs in three frequency bands – a low-frequency band (2–10 Hz), a medium-frequency band (15–40 Hz), and a high-frequency band (60–100 Hz). More specifically, action execution produced an increase in power in the low-frequency range, a decrease in power in the middle-frequency range, and an increase in power in the high-frequency range (Fig. 1C, upper panel). Action observation produced a similar pattern of modulation of LFPs, with the notable exception of the absence of an increase in power in the low-frequency band (Fig. 1C, lower panel). These results complement single-unit responses measured in the same area (Gallese *et al.*, 1996; Umiltà *et al.*, 2001; Caggiano *et al.*, 2009, 2011; Kraskov *et al.*, 2009) and previous LFP studies, and demonstrate that the monkey premotor cortex shows rhythmic oscillations not only during action execution but also during action observation.

Next, we sought to characterise the functional significance of the modulations of the LFPs measured during action observation. The specific question that we addressed was whether the LFPs encoded specific characteristics of observed actions, focusing in particular on the point of view. Experimental results suggest that, at the single-neuron level, area F5 contains a view-based encoding of actions (Caggiano *et al.*, 2011). Here, we investigated whether and in which frequency bands the point of view is encoded in F5 LFPs. Our experimental design consisted of the four conditions that are graphically shown in the upper parts of the four panels in Fig. 2. That is, we presented the monkey with actions observed either from a first-person (i.e. the action as seen from the agent; Fig. 2A and C, conditions M0 and H0) or frontal (Fig. 2B and D, conditions M180 and H180) point of view, and executed either by a monkey (Fig. 2A and B, conditions M0 and M180) or by a human (Fig. 2B and D, conditions H0 and H180). By means of this extended paradigm, we collected data from a subset of 80 sites out of the original set of 228 sites. We then performed a time–frequency analysis of the LFPs recorded in each of the four observation conditions and in the execution condition. The four panels of Fig. 2 show points in the time–frequency domain where

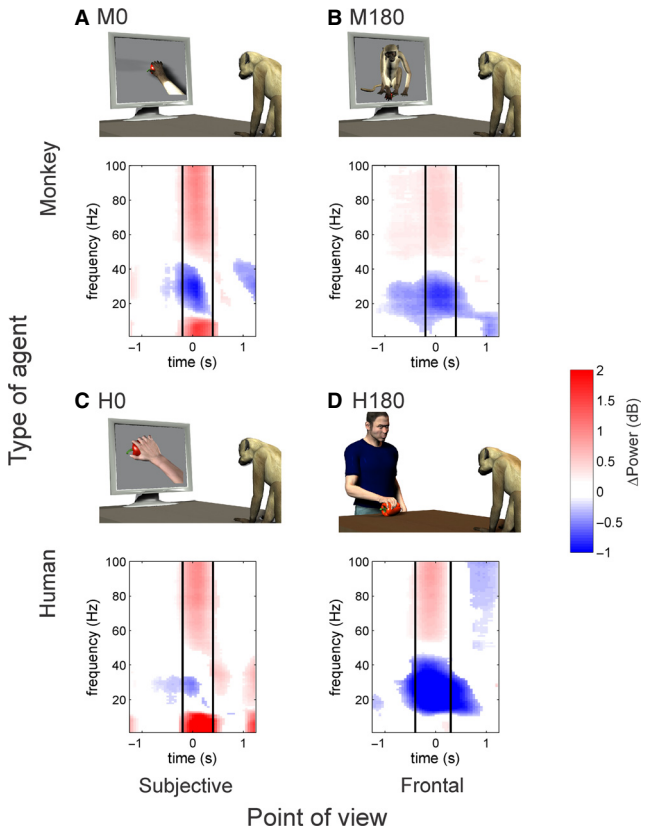

FIG. 2. LFPs measured during action observation. In each panel, the colored areas represent points in the frequency–time domain where modulations in LFP power during action observation were statistically different from their baseline values. At each colored point, the power of the LFPs is signified by the specific color (see bar on the right). White areas represent points at which LFPs were not statistically different from their baseline values. The four panels represent the four experimental conditions. (A and B) LFPs measured during observation of a goal-directed action executed by a monkey and observed from a subjective perspective (A, condition M0) or a frontal perspective (B, condition M180). (C and D) LFPs measured during observation of a goal-directed action executed by a human and observed from a subjective perspective (C, condition H0) or a frontal perspective (D, condition H180). Time $t = 0$ represents the instant of contact between the hand and the goal object. Solid black lines signify the interval where the action took place.

LFPs in each of the four observation conditions were significantly different from their baseline values. Similarly to the results shown in Fig. 1, we found that the modulations in the power of LFPs started shortly before the moment of hand–object contact (time $t = 0$) and lasted until the end of the motor act. A notable difference between conditions, which is also evident at the level of visual inspection of the data, is that only observation of an action from a subjective point of view produced a significant increase in power in the low-frequency range (2–10 Hz), irrespective of the agent (human or monkey) executing the action. Notably, this increase was also present during action execution (Fig. 1C, top row), but was absent during observation of the same action from a frontal perspective (Fig. 2B and D and Fig. 1C, bottom row). Modulations in the medium range (15–40 Hz) followed an almost complementary pattern. That is, they were stronger and more widespread in the time–frequency domain during observation of actions from a frontal point of view, and virtually absent (in condition H0) or strongly reduced and less widespread (in condition M0) during observation of an action from a subjective point of view. A

significant increase in power in the high-frequency range (60–100 Hz) was present in all four observation conditions. An intermediate pattern of results was found when actions were shown from a side view (Fig. S1). Notably, this pattern did not significantly change even when the body was masked such that only the acting hand was visible ($P > 0.05$, Kruskal–Wallis, calculated independently for the ranges 2–10 Hz, 15–40 Hz, and 60–100 Hz).

To gain insights into the functional significance of the view dependency of LFPs during action observation, we directly compared them with LFPs in the execution condition. To this end, for each observation condition and for each site, we computed the dc (dc index) (Scherberger *et al.*, 2005). This coefficient is computed by integrating in the considered frequency interval (2–100 Hz) the absolute difference in the power of the LFPs measured in the execution condition and in the considered observation condition. Higher (lower) values of the dc index indicate a larger (smaller) deviation of the LFPs in the observation condition with respect to those measured during action execution. Figure 3 shows the distributions of the dc index in the four observation conditions. The medians of the dc index measured during observation from the subjective perspective of human and monkey actions (conditions H0 and M0, respectively, in Fig. 3) were 1.115 in condition H0 and 1.053 in condition M0, and not significantly different from each other ($P > 0.05$, Friedman test, with Bonferroni correction). Similarly, the medians of the dc index measured during observation from the frontal perspective of human and monkey actions (M180 and H180, respectively, in Fig. 3B) were not significantly different from each other (1.323 in condition H180 and 1.316 in condition M180, $P > 0.05$, Friedman test, with Bonferroni correction). Notably, however, they were both significantly higher than in the H0 and M0 observation conditions ($P < 0.05$, Friedman test, with Bonferroni correction). This pattern of results reveals an important characteristic of the visual encoding of actions in area F5. That is, LFPs recorded during observation of actions from a subjective point of view show a higher degree of similarity with motor LFPs. Indeed, actions observed from a frontal point of view produced visual LFPs that were significantly more dissimilar (i.e. showed a significantly higher median dc index) from motor LFPs. Notably, this result was independent of the type of agent (human or monkey) that executed the observed action.

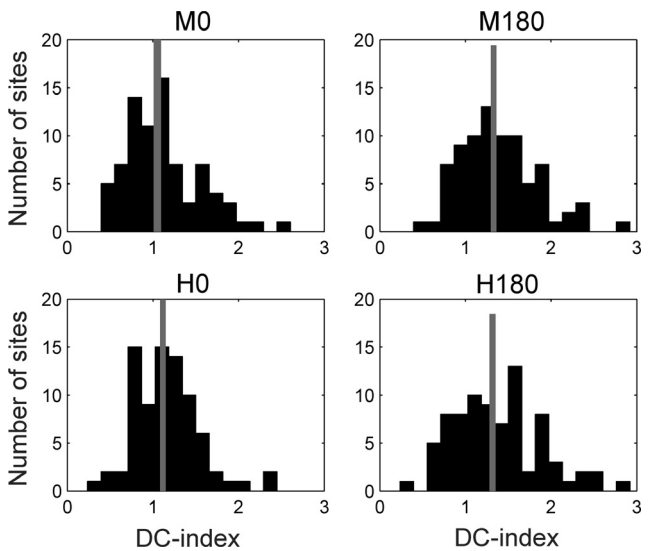

FIG. 3. The dc index. The four panels in this figure show the distributions across sites of the dc index. The dc index measures the difference between the LFPs recorded from the same site in two experimental conditions. It ranges between 0 and ∞, with 0 meaning perfect identity between the LFPs measured in the two conditions, and positive values representing progressively greater differences. The four panels show the distribution of the dc index obtained when each of the four observation conditions was compared with the execution condition. The vertical gray lines signify the median of the distribution.

In a further analysis, we investigated the relationship between motor and visual LFPs in the temporal domain. To this end, for each site and for each frequency, we computed the correlation coefficient between the LFPs measured during action observation and those measured during action execution (see Materials and methods). The correlation coefficient of two time-varying signals is a number between −1 and 1 that represents a measure of their similarity. A value of 1 indicates a perfect match in time between the two signals; a value of −1 indicates perfect anti-correlation. The four panels in Fig. 4 show, for each frequency, the distribution of the correlation between LFPs measured in each of the four observation conditions and those measured in the execution condition. The solid white line represents the median of the distribution, and the two broken lines represent the 25th and 75th percentiles. Figure 5 shows, for each of the three considered frequency bands (low frequency, 2–10 Hz; medium frequency, 15–40 Hz; and high frequency, 60–100 Hz), the results of the direct comparison of the medians of these distributions. In the low-frequency range, the LFPs produced during the observation of actions from a subjective point of view had a strong correlation with the LFPs measured during motor execution, irrespective of the agent (human or monkey) performing it (Fig. 4A and C). Notably, in both the M0 and H0 observation conditions, the correlation coefficients were, on average, close to their theoretically maximum value of 1 and significantly different from 0 (Fig. 5A). The LFPs produced during observation of the same action from a frontal point of view were, instead, only weakly correlated with the motor LFPs (Fig. 4B and D) and were significantly different from 0 only in the H180 condition (Fig. 5A). Together with the results presented in Figs 2 and 3, these results further stress the potentially special status of observing actions from a subjective point of view. Indeed, in the 2–10 Hz band, this observation condition produces visual LFPs that almost exactly match, in both the frequency and temporal domains, the motor LFPs, although, in this condition, the monkey is neither producing nor preparing any movement. In the medium-frequency range (15–40 Hz), the correlation coefficients between the visual and motor LFPs were, on average, low. In this case, only the correlation coefficients in the M0 and H180 conditions were significantly different from 0 (Fig. 5B). This result indicates that, in the 15–40-Hz band, the temporal evolution of the LFPs during action observation only weakly reproduced that produced during action execution. The correlation coefficients measured in the high-frequency range (60–100 Hz) tended to be positive, and were significantly different from 0 in all four observation conditions. Similarly to the low-frequency band, correlations showed strong view dependency, as both conditions H0 and M0 were significantly different from conditions H180 and M180, respectively (Fig. 5C). Taken together, these results further suggest a difference in the processing of visual information in the ventral premotor cortex (PMv) during observation of actions from a subjective point of view with respect to the observation of the same actions from a frontal point of view. More specifically, the subjective point of view produced LFPs that, in both magnitude and temporal evolution, more closely matched those produced during action execution, independently of the agent performing the observed action.

Discussion

The discovery of mirror neurons in area F5 raises the question as to what is the functional and behavioral significance of the activation of motor areas during action observation. At the single-neuron level, previous neurophysiological studies identified different subclasses of mirror neurons that are selective for different features of an observed action (Gallese *et al.*, 1996; Kohler *et al.*, 2002; Ferrari *et al.*, 2003; Fogassi *et al.*, 2005; Caggiano *et al.*, 2009, 2011; Rochat *et al.*, 2010). Here, we extended the investigation of the visual encoding of actions in area F5 from the single-neuron level to the local network level by analysing the LFPs recorded in area F5. Our study revealed two important pieces of information regarding the functioning of area F5. First, rhythmic oscillations are present in the monkey premotor cortex not only during action execution but also during action observation. Second, during action observation, F5 LFPs are differentially modulated by the point of view from which an action is observed. In particular, observation of actions from a subjective point of view produced visual LFPs that were more similar to motor LFPs in a 2–10-Hz band than were visual LFPs produced during observation of the same action from a frontal point of view. These results have important implications for theories of action perception.

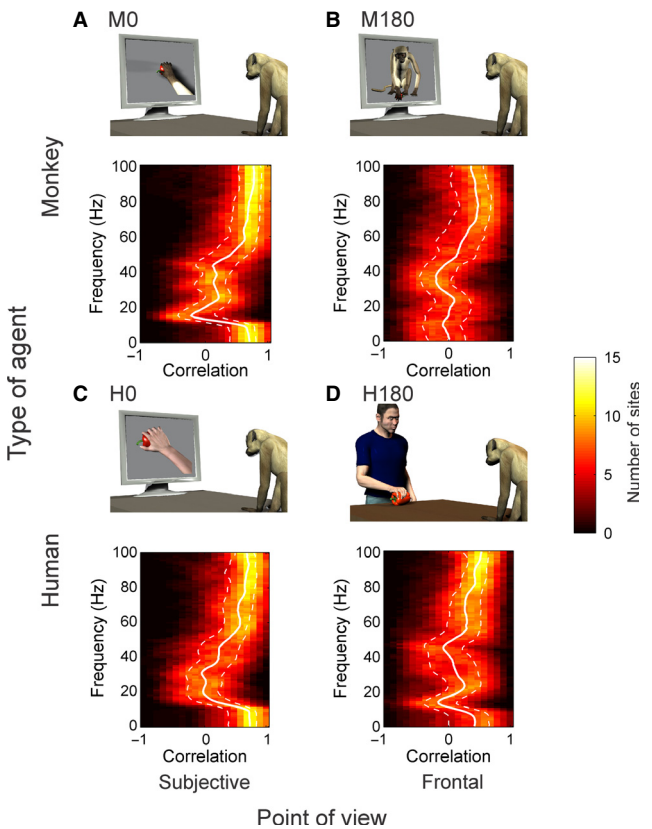

FIG. 4. Correlations between the LFPs measured in the execution condition and the four observation conditions. The layout of the figure is the same as in Fig. 2. For each panel, the 'slice' at each frequency *f* represents the distribution of the correlation coefficients between the temporal evolution of LFPs measured at that frequency in the execution condition and the considered observation condition. The correlation coefficient is a measure of the similarity between two time-varying signals; it ranges between −1 and 1, with 1 indicating a perfect match between the two signals, and −1 indicating perfect anti-correlation. At each frequency *f*, the closer the distribution peaks are to 1 (−1), the more, at that frequency, the LFPs in the execution condition and those in the considered observation condition evolved in time in a positively (negatively) correlated manner. In each panel, the white solid line represents the median, while the two dotted lines represent the 25th and 75th percentiles, respectively.

Potential caveats

A first potential caveat is that the differences in LFPs observed in the four observation conditions might be only related to differences in visual features. For example, visual features related to the body are present in the frontal but not in the subjective condition, and this difference could potentially explain our results. We can confidently exclude this interpretation of our results. Indeed, as reported in Results, we performed a control experiment in which the body is masked such that only the acting hand remains visible [see also Supporting Information in Caggiano *et al.* (2011)]. We found no significant difference ($P > 0.05$, Kruskal–Wallis, calculated independently for the ranges 2–10 Hz, 15–40 Hz, and 60–100 Hz) in the LFPs measured during observation of a goal-directed motor act seen from the side view when the body was present in the image or masked out such that only the acting hand was visible. This result strongly supports our conclusions that it is the point of view that modulates F5 physiological signals at the levels of both single neurons and LFPs, and not visual features of the scene unrelated to the action, such as the presence or absence of the body.

A second potential caveat is that our results could be, at least partially, attributable to the different stimuli used to investigate neuronal responses during the observation of actions from a frontal perspective of the human and the monkey actor. In particular, in the case of the human actor, an experimenter executed the actions in front of the monkey, whereas a filmed stimulus was used to show the action performed by the monkey actor. This different stimulus format was necessary to correctly show all the visual details of the human action, which might be otherwise be too small to be perceived in a filmed stimulus. Despite the potentially very different visual features present in the two stimulus sets, we observed very similar patterns of response to both real and filmed actions at both the single-neuron level (Caggiano *et al.*, 2011) and the LFP level (present study). These results further suggest that the features that modulate the neuronal responses and physiological signals in area F5 are those specifically related to correctly interpreting the observed action (e.g. the point of view or the actor) and not those that are unrelated to this process (e.g. the presence or not of the body of the actor, or whether the action was filmed or actually executed in front of the monkey).

A third potential caveat is that differences in LFPs between conditions might be related to potential differences in eye movements rather than in visual stimuli. We can confidently exclude this interpretation of our results, for three reasons. First, conditions that potentially generated different patterns of oculomotor behavior (i.e. H180, which used natural stimulation, and M180, which used filmed actions) produced very similar patterns of LFPs, as shown in Figs 2 and 3. Second, gaze-related modulations of mirror-neuron responses are related to: (i) the time that the monkey spent fixating the goal object (Philipp *et al.*, 2013); or (ii) the execution of pro-active saccades (Maranesi *et al.*, 2013). Both (i) and (ii) are highly variable across trials, and are thus likely to have only a negligible effect or no effect at all on our results, which were obtained by averaging across a large number of trials. Third, LFPs represent the pooled responses of large neuronal populations, and experimental results have shown that whereas oculomotor behavior modulates the responses of single units in area F5 during action observation, it has no statistical effect on the population responses of mirror neurons (Supporting Information in Caggiano *et al.*, 2011; Philipp *et al.*, 2013).

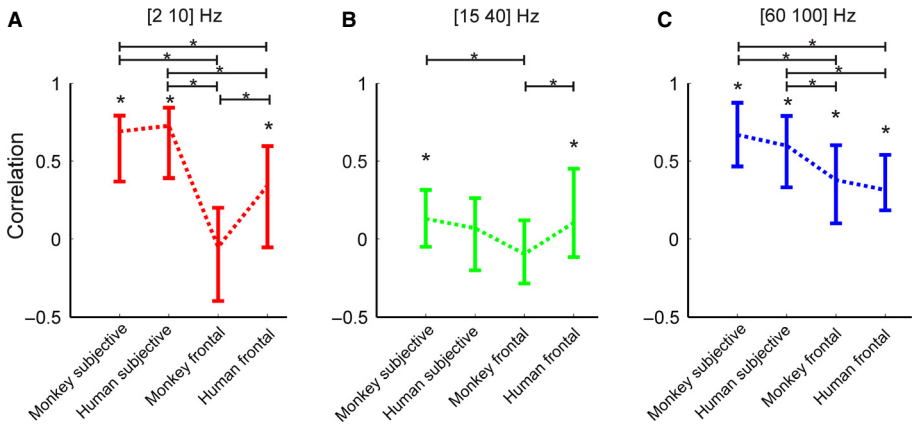

FIG. 5. Statistical analysis of the distribution of the correlation coefficients. The four values plotted in each panel signify the median correlation coefficient of the LFPs produced in the four observation conditions with the LFPs produced in the execution condition. Each panel signifies a different frequency band [low frequency, 2–10 Hz (A); medium frequency, 15–40 Hz (B); and high frequency, 60–100 Hz (C)]. Vertical bars represent the 25th and 75th percentiles. Asterisks indicate medians that are significantly different from 0 (sign-rank, $P < 0.05$, Bonferroni-corrected). Horizontal bars indicate differences between conditions (Friedman test, $P < 0.05$, followed by Bonferroni correction).

A fourth potential caveat is that differences in correlation between LFPs in the execution and the four observation conditions (Fig. 4) could be attributable to differences in the timings between filmed actions, rather than the point of view as such. We can confidently exclude this interpretation, because, in all three conditions, i.e. M0, M90, and M180 (Fig. 4 and Fig. S1), we used monkey actions as visual stimuli. The action stimuli differed in the point of view from which they were observed, but all had approximately the same timing. Thus, if timing was the main determinant of patterns of correlation between motor and visual LFPs, we would have expected approximately similar patterns of correlation. The results reported in Fig. 4 (Fig. S1) show that this was not the case.

Encoding of point of view in F5 LFPs

The observation of rhythmic oscillations during action execution in monkey area F5 is in line with previous results showing an increase in power in the low-frequency band (Bansal *et al.*, 2011) and a decrease in the medium-frequency band (Spinks *et al.*, 2008) of the LFPs measured in the monkey PMv during the performance of goal-directed motor acts.

The important finding of our study is that cortical rhythmic activity during action observation in area F5 is strongly modulated by the point of view from which an action was observed. In particular, as shown in Figs 2 and 4, observing actions from a frontal perspective produced LFPs that were, in the 2–10 Hz band, significantly different from those measured during action execution and during observation of the same action from a subjective point of view. This result was very robust. Indeed, the modulations produced by a given point of view were largely independent of the type of agent (human or monkey) that executed the action, although the displays in the two cases of human and monkey actions possessed very different visual features.

Our finding of a difference in the neuronal encoding of actions observed from the subjective and frontal views parallels similar findings in humans. In particular, Oosterhof *et al.* (2012) found, by means of multivoxel pattern analysis of functional magnetic resonance imaging data, the existence in the human PMv of cross-modal visuo-motor representations for actions observed from the first-person perspective but not from the third-person perspective (Oosterhof *et al.*, 2012). Furthermore, actions observed from a subjective point of view generated stronger facilitation of motor-evoked potentials in a transcranial magnetic stimulation experiment (Maeda *et al.*, 2002) and stronger activation of the sensorimotor cortex (Jackson *et al.*, 2006). Interestingly, stronger facilitation of motor-evoked potentials was also found when the actions were described by sentences in the first person than when the same actions were described in the third person (Papeo *et al.*, 2011). Behaviorally, the subjective perspective generated faster imitative responses (Jackson *et al.*, 2006), higher accuracy in judging the size of a to-be-grasped object from hand pre-shaping (Campanella *et al.*, 2011), and faster judgements of congruency of hand–object interactions (Bruzzo *et al.*, 2008). In agreement with the studies cited above, the results reported here seem to suggest a dichotomous encoding of the point of view, with the subjective perspective having a 'special role' with respect to all other points of view. However, our experiments, as well as studies from other laboratories cited above, compared the subjective perspective only with the frontal view. It is thus an open question whether the subjective perspective produces the same behavioral and neuronal differences as other points of view. In Fig. S1, we show LFPs produced by observation of actions from the side view (condition M90). Comparison of Fig. 2 and Fig. S1 reveals a smooth transition in the LFPs produced by the three points of view rather than an abrupt change between the subjective and the other two points of view. This finding suggests that future research needs to compare more experimental conditions to achieve a thorough understanding of how the primate brain encodes the point of view of an observed action.

Potential implications for the functional architecture of area F5

We previously reported that mirror neurons in area F5 seem to encode actions in a view-based manner, with no significant difference in the number of mirror neurons selective for different points of view (Caggiano *et al.*, 2011). Under the (potentially simplistic) assumption that LFPs reflect a mere summation of neuronal responses in an area, it would have been conceivable to expect no significant differences in the LFPs produced during observation of actions from different points of view. The results presented here show that this was not the case. Different points of view produced patterns of LFPs with different spectral distributions and levels of overall power, both in the low-frequency band (2–10 Hz) and in the

high-frequency (60–100 Hz) band. A possible interpretation of the view dependence of the F5 visual LFPs is that, during action execution, the monkey was observing his own hand. Thus, it is possible that what we interpreted as 'motor' LFPs were instead 'visual' LFPs. This could potentially explain the similarity between motor LFPs and visual LFPs produced during action observation from a subjective point of view. We can rule out this interpretation because, in our experimental paradigm, the monkey performed the motor task in complete darkness, and thus at no point during action execution had visual access to his own limb (see also Materials and methods).

What is the functional significance of the view dependency of F5 LFPs? Increases in power in different frequency bands of the LFPs have been associated with patterns of neuronal activation/synchronisation at different spatial scales, where the spatial scale is determined by the number of synaptic connections involved. More specifically, fast oscillations are usually confined to either local circuits or monosynaptically connected regions, whereas slow oscillations are produced in neuronal networks spanning several synaptic connections. Since they were first reported in area F5 (di Pellegrino *et al.*, 1992; Gallese *et al.*, 1996), mirror neurons (i.e. neurons responding during both action observation and execution) have been reported in the inferior parietal lobule (area PFG) (Fogassi *et al.*, 2005), primary motor cortex (area M1) (Dushanova & Donoghue, 2010; Philipp *et al.*, 2013; Vigneswaran *et al.*, 2013), and anterior intra-parietal area (Pani *et al.*, 2014). Whereas the anatomical connections between these areas are relatively well known (Rizzolatti & Luppino, 2001; Davare *et al.*, 2011; Rizzolatti *et al.*, 2014), their functional connectivity is presently unknown. The results reported here might provide some hints concerning area F5. In particular, the increase in the high-frequency range that was common to all points of view might represent the neuronal signature of the local activation of area F5 or its synchronisation with monosynaptically connected areas, either upstream or downstream in the action–observation network, during action observation. An increase in power in the low-frequency range was produced only by the subjective point of view. This might indicate that this experimental condition, in addition to small-scale correlations, also produces correlated activity that probably involves several stages of the action–observation network. Multi-area recordings are necessary to investigate the existence and functional significance of such large-scale correlations.

Potential implications for electroencephalography and magnetoencephalography studies in humans

A consistent finding reported in the literature has been desynchronisation of the mu rhythm when human subjects observe goal-directed, intransitive or communicative gestures (Cochin *et al.*, 1999; Muthukumaraswamy *et al.*, 2004; Streltsova *et al.*, 2010). The mu rhythm is an electroencephalogram oscillation measured over the primary motor cortex (usually at position C3 in the standard 10–20 system) with dominant frequencies in the 8–13 Hz band. Early reports showed desynchronisation of the mu rhythm during motor preparation (Chatrian *et al.*, 1959; Pfurtscheller & Aranibar, 1979), motor execution (Pfurtscheller & Neuper, 1994; Pfurtscheller *et al.*, 1997, 2000; Babiloni *et al.*, 1999), and motor imagery (Pfurtscheller & Neuper, 1997; Schnitzler *et al.*, 1997; McFarland *et al.*, 2000). Successive investigations showed the same desynchronisation effect during action observation (Cochin *et al.*, 1999; Pineda *et al.*, 2000; Babiloni *et al.*, 2002; Muthukumaraswamy & Johnson, 2004; Muthukumaraswamy *et al.*, 2004). This functional similarity to the response properties of mirror neurons led scholars to hypothesise that mu desynchronisation was indeed indicative of the functioning of a mirror-neuron system in humans (Muthukumaraswamy *et al.*, 2004; for a review see Pineda, 2005).

In the present study, we found desynchronisation of F5 LFPs during action observation and execution in the 15–40 Hz range (see also Kilner *et al.*, 2014 for similar findings). Interestingly, in the macaque monkey, desynchronisation in the same 15–40 Hz range was observed when field potentials were recorded at the level of the scalp by means of electroencephalography. That is, in the monkey, desynchronisation during action observation is found in the same frequency range when LFPs are recorded in the premotor cortex intracortically (Kilner *et al.*, 2014 and present paper) and when an electroencephalogram is recorded over the motor cortex at the level of the scalp (Coudé *et al.*, 2014). This congruency suggests that, in the monkey, physiological signals recorded in the sensorimotor cortex in the 15–40 Hz frequency range might indeed be correlated with action observation.

Several factors make the interpretation of the mu rhythm in humans with regard to our results more complex. First, the frequency range in which desynchronisation is observed is consistently lower in humans than in monkeys (8–13 Hz in humans vs. 15–40 Hz in monkeys). Second, in humans, the identification of mirror-neuron areas is very problematic. In fact, the only direct evidence that we have to date was collected from an area, comprising the the medial frontal and temporal cortices, that is not considered to be part of the classic mirror-neuron system (Mukamel *et al.*, 2010). Third, even assuming a simplistic homology between area F5 in monkeys and the inferior frontal gyrus in humans, the issue of desynchronisation in rhythmic activity in this latter area has never been addressed.

Taken together, the similarities and differences between the mu rhythms in humans and the 15–40 Hz band that we have reported here in monkeys suggest different scenarios. First, they are truly both indicative of the functioning of a mirror-neuron system, and their different frequency ranges are only attributable to intrinsic differences in brain structure between humans and macaque monkeys. Second, the mu rhythm in humans is not indicative of the functioning of a mirror-neuron system, as its characteristics are significantly different from those of its putative 'homolog' in monkeys reported here. Third, both the mu rhythm and the 15–40 Hz range in monkeys are not causally related to action perception. They are epiphenomena produced by other cognitive processes. Further experiments are needed to clarify this point.

A final point worth discussing is that, in our experiments, the performing subject for the visual stimuli was one of the two monkeys used for the recordings. For that monkey, we could thus collect data during observation of own actions, although they were presented off-line. To investigate potential effects produced by the observation of own actions, we separately analysed the LFPs for the two monkeys. We found no significant difference in the overall pattern of results between the two monkeys for the subjective point of view. The only difference that we observed was a slight difference in the separation between the medium-frequency and high-frequency ranges, which was at a higher frequency in monkey 2 (Fig. S2). However, this difference was specific to that monkey and not related to the observation of own actions. Indeed, the same effect was produced by the observation of human actions from a subjective perspective (H0), a visual stimulus that is not related to the actions of either monkey.

Conclusions

In conclusion, the experimental results reported here clearly show that LFPs recorded from area F5 in the macaque brain are modu-

lated during action observation. These modulations reliably encode the point of view of an observed action, with the subjective point of view producing LFPs that are significantly more similar to motor LFPs than those produced by the frontal view. This result highlights the need for further studies to better understand the functional significance of the visual responses of macaque area F5.

Supporting Information

Additional supporting information can be found in the online version of this article:

Fig. S1. LFPs produced by action observation from a side view.

Fig. S2. LFPs analysed separately in the two monkeys.

Fig. S3. LFPs produced by a control stimulus showing no action.

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Abbreviations

dc, discriminability coefficient; LFP, local field potential.

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